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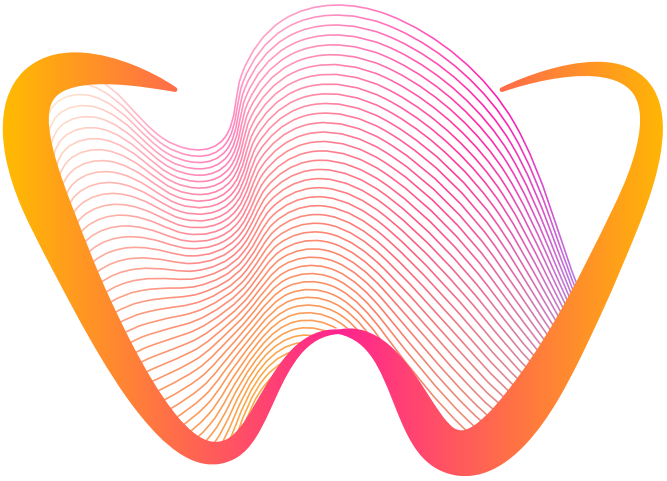

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16–19 MAIO 2024

CENTRO DE CONVENÇÕES FREI CANECA

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Sociedade Brasileira de Endocrinologia e Metabologia

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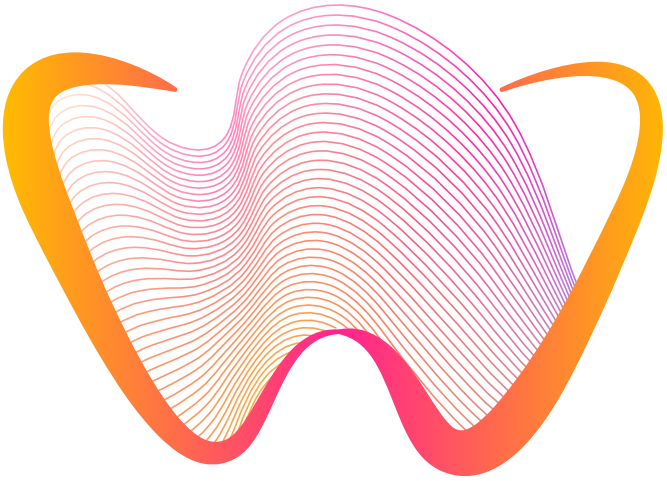

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SUMÁRIO

AUTOIMUNIDADE

BIOLOGIA CELULAR DA TIREOIDE

CIRURGIA DA TIREOIDE

DISFUNÇÕES TIREOIDIANAS

EPIDEMIOLOGIA

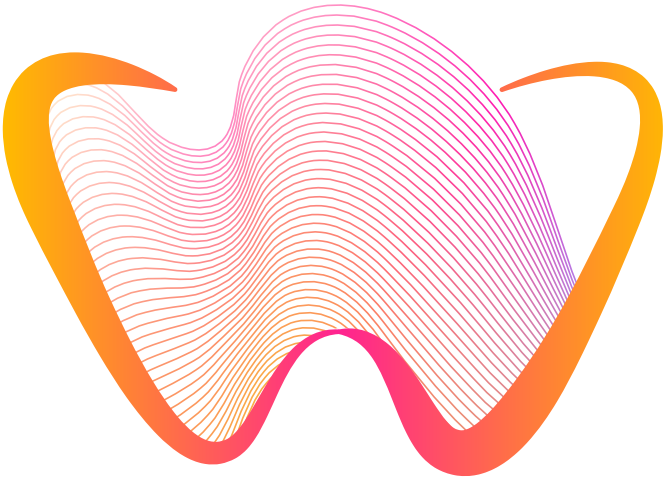
IODO

METABOLISMO E AÇÃO DOS HORMÔNIOS TIREOIDIANOS

MÉTODOS DE DIAGNÓSTICO

NÓDULOS E CÂNCER DE TIREOIDE

REGULAÇÃO DA FUNÇÃO TIREOIDIANA



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130603 – ASSOCIATION BETWEEN ANTI-MULLERIAN HORMONE AND ANTRAL FOLLICLE COUNT WITH ANTITHYROID ANTIBODIES DETECTABILITY AND POSITIVITY IN SUBFERTILE WOMEN

MAIN AUTHOR: ANA BEATRIZ WINTER TAVARES

Yuri Ian de Oliveira[1], Paulo Gallo de Sá[2], Arnaldo Cézar Couto[3], Lenora Maria Camarate Silveira Martins Leão[1], Ana Beatriz Winter Tavares[1]

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Introduction: Ovarian reserve can be compromised by autoimmune diseases. Chronic reduction in thyroid hormone levels could result in premature ovarian failure, which is assessed by dosage of anti-Müllerian hormone (AMH). The detection of anti-thyroid peroxidase antibody (TPOAb), even lower than the positivity cuttof, is associated with increased mortality. There are no studies about thyroid antibodies detectability in subfertile women. **Objectives:** To evaluate the association between ovarian reserve through AMH levels and antral follicule count (AFC) and anti-thyroid antibodies (TPOAb and anti-thyroglobulin antibody – TgAb) detectability and positivity in subfertile women seeking for assisted reproductive treatment. **Methods:** Observational study in women submitted to ovarian stimulation and oocyte retrieval. Anti-thyroid antibodies levels were assessed through electrochemiluminescence assay. AMH cutoff values ≤ 1,1 ng/mL and/or AFC 34 IU/mL); b) TgAb: undetectable (115 IU/mL). **Results:** 248 subfertile women were included in the study, with median age of 38 years (IQR 35-44). The median TSH was 1.65 µIU/mL (IQR 1,22-2,4), median AMH 1,47 ng/mL (IQR 0,71-3,05), and median AFC was 11 follicles (7-17). TPOAb was positive in 14,1%, and TgAb in 11,6% of the patients. The majority had low negative levels of TPOAb and TgAb (43,1% and 66,9%, respectively). There was no statistical association between AMH levels nor AFC in the different categories of anti-thyroid antibodies, independently of normal or altered values that define low ovarian reserve. There was no statistical association between different categories of TPOAb nor TgAb and ovarian reserve. Endometriosis and age were the parameters evaluated with statistical association with AMH and AFC (p = 0,001), as expected, with exception for AFC and endometriosis. **Conclusion:** the presence of detectable or positive anti-thyroid antibodies did not demonstrate association with AMH nor AFC in subfertile women. These results suggest that thyroid autoimmunity do not have influence on ovarian reserve.

130594 – NEUTROPHIL-LYMPHOCYTE AND PLATELET-LYMPHOCYTE RATIOS IN GRAVES OPHTHALMOPATHY AND ITS ASSOCIATION WITH DISEASE SEVERITY AND ACTIVITY: A CROSS-SECTIONAL ANALYSIS IN A SPECIALIZED OUTPATIENT CLINIC

MAIN AUTHOR: ANA MARIA GARCIA DARZE

Ana Maria Garcia Darze[1], Patrícia de Fátima Teixeira[1], Natália Treistman[1], Natalia Schara[1]

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Introduction: Graves' ophthalmopathy (GO) is an autoimmune condition and the main extrathyroidal manifestation of Graves' disease (GD). It occurs in the context of current or previous elevation of TSH receptor antibodies and ocular infiltration of activated T cells. Neutrophil-lymphocyte (NLR) and platelet-lymphocyte (PLR) ratios have been studied as new inflammatory markers of severity and prognosis in critical, autoimmune and inflammatory conditions, little explored in thyroid pathologies. **Objective:** To evaluate a possible association between NLR, PLR and the severity and activity of GO. This is one of the first clinical studies on the relationship between OG and PLR. **Methods:** We performed a cross-sectional study with GO patients from a specialized outpatient clinic at a tertiary hospital. GO activity was based on the Clinical Activity Score (CAS) and severity based on the EUGOGO criteria. The white blood cell count was obtained from medical records at the time of ophthalmologic evaluation. NLR was calculated by dividing neutrophils by lymphocytes, PLR by dividing platelets by lymphocytes. CAS > 3 defined as active, NRL > 2 as abnormal. Statistical analysis was performed using IBM SPSS Statistics 26. **Results:** We evaluated 86 patients (62 women); with a mean age of 50 years (min 16; max 87). Active CAS was present in 36% of the sample and 19.8% had moderate to severe GO (MSGO). Intravenous corticosteroid therapy (ICV) was common (36% on time and 30.2% previously to study assessment). Among those with active CAS, 38.5% were on their second ICV. PLR was not associated with CAS, but higher in MSGO (Me 144.6; Md 148.4) compared to those without (Me 117.5; Md 109.9; p = 0.04). NLR did not differ between active or inactive CAS (p 0.57). Abnormal NLR was detected in 35.7% of those with active CAS (and in ICV), *vs.* 0% in those with inactive CAS (p 0.218). NLR was higher among MSGO (Me 2.75; Md 2.7) than among those without (Me 1.86; Md 1.83), with a trend towards association (p 0.07). 61.5% of MSGO had abnormal NLR, *vs.* 41% of those without OGMS (p 0.199). **Conclusions:** PLR was associated with greater disease severity, while NLR showed a trend towards association. NLR and PLR were not associated with GO activity. Results suggest that PLR may serve as a clinical prognostic parameter for GO. A larger sample is needed to complement the study.

129210 – LABORATORY CLINICIAN PROFILE OF PATIENTS WITH THYROID EYE DISEASE FOLLOWED AT A REFERRAL CENTER IN MARANHÃO

MAIN AUTHOR: CARLA SOUZA PEREIRA SOBRAL

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Introduction: Graves' Orbitopathy (GO) is the most common extrathyroidal manifestation of Graves' Disease (GD). It is an autoimmune inflammatory disease that affects the eye orbit. The stimulating anti-TSH receptor antibody (TRAB) acts on TSH receptor in the thyroid, leading to hyperthyroidism, while in the fibroblasts of the orbit, it acts on these same receptors and causes inflammation of the orbital tissues. **Objectives:** To assess the epidemiological profile of patients with OG and the clinical characteristics and risk factors; to relate risk factors and clinical presentation of OG (activity and severity); to relate the response to pulsotherapy to risk factors for OG. **Methods:** An observational, longitudinal, retrospective study carried out by reviewing the medical records of 22 patients with OG followed up at the Endocrinology Clinic of the University Hospital of the Federal University of Maranhão between January 2021 and December 2023. **Results:** The majority of patients with active OG were female, with previous hyperthyroidism and a mean age at diagnosis of 47.4 years. There was no association between OG and smoking or previous radioiodine therapy. The median age of individuals with the moderate-severe form was 46 years, younger individuals compared to those without severity criteria. There was a better response at the 9th week of pulse therapy and a significant positive correlation between the TRAB value at diagnosis (high) and the CAS value at the 9th week of treatment. **Conclusion:** Knowing the clinical characteristics, risk factors and pathophysiology of DOT will allow us to choose a personalised and effective treatment and to predict the better response time.

129208 – ORBITAL LYMPHOMA AS A DIFFERENTIAL DIAGNOSIS OF GRAVES ORBITOPATHY

MAIN AUTHOR: CARLA SOUZA PEREIRA SOBRAL

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Introduction: Thyroid eye disease (TED), also called Graves orbitopathy (GO), is the most common cause of orbital tissue inflammation. Although, other causes of orbital inflammation should be suspected. We aimed to report a case of orbital lymphoma (OL) in a patient with previous history of hyperthyroidism. **Case report:** A 67-year-old woman started 3 years ago a painful proptosis with visual impairment in both eyes. She also complained about fever and weight loss. On physical examination, she had bilateral proptosis with swollen and erythematous eyelids, conjunctival congestion with chemosis and painful and restricted eye movement. Also, she had neck lymph node enlargement. She had a past history of hyperthyroidism at 32 years old but now thyroid function was normal. GO was suspected and she receive IV glucocorticoids for 3 days. A little clinical response was noted. Orbital MRI showed a diffuse enlargement of orbital muscles which is a feature suggestive of OL. Then, she was submitted to a lymph node biopsy that confirmed lymphoma. Finally, she started chemotherapy followed by an improvement on eyes. **Conclusion:** Bilateral cases of proptosis can pose a diagnostic dilemma specially in patients with previous history of thyroid disfunction. Age at diagnosis and MRI help to differentiate GO and OL, since OL is primarily a disease of the elderly and MRI shows a diffuse muscle involvement.

130516 – HASHIMOTO THYROIDITIS CONTRIBUTION TO DEVELOPMENT OF LARGE GOITER

MAIN AUTHOR: CAROLINE PAMPONET DA FONSECA OLIVEIRA

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Introduction: Chronic autoimmune thyroiditis (CAT) with goiter and hypothyroidism is known as Hashimoto thyroiditis (HT), characterized by positive autoantibodies, such as antithyroperoxidase (ATPO) and/or antithyroglobulin (ATg). Thyroid is diffusely enlarged, heterogeneous and hypoechoic parenchyma, with pseudonodular areas on ultrasound (US). Distribution of thyroid volume (TV) in patients diagnosed with CAT is unimodal, and it is therefore rare to find patients with large goiters (>50 mL). Total thyroidectomy (TT) in patients with HT is even rarer, being indicated if there is deviation or compression of the trachea and esophagus, presence of a substernal component, of an indeterminate or suspicious nodule and local pain. **Objective:** To evaluate clinical and laboratory characteristics of patients undergoing TT for large goiter associated with HT in a single university center. **Patients and methods:** From 2008 to 2019, we retrospectively evaluated patients who underwent TT for benign thyroid disease. Goiter size was determined by routine US. Presence of tracheal deviation/compression and substernal component were seen by chest X-ray or tomography. Thyroid function and autoimmunity were determined using commercial kits. ATPO, ATg and anti-TSH receptor (TRAb) were considered positive if >9 IU/mL, >4 IU/mL and >1.75 IU/L, respectively. Histological findings were collected from medical records. We selected patients with VT >50 mL and positive ATPO and/or ATg, excluding cases of Graves' disease (positive TRAb), previous surgery or malignancy on fine needle aspiration. **Results:** From a total of 407 patients undergoing TT, we selected 29 individuals, with mean age 52.8 ± 11.8 (23.6-73.5 years), 97% female, with mean TV 146.4 ± 127.7 (median 108.7, 55-724 mL). Tracheal deviation/compression was identified in 80% and substernal component in 45%. Benign needle aspiration suggestive of CAT was seen in only 2 cases (9%). Typical histology of CAT was reported in 69%, associated with adenomatous goiter in 93%. Three papillary microcarcinomas were identified. There was no correlation between age and TV, as well as TV and autoantibody positivity or serum concentrations and TSH concentrations. **Discussion and conclusions:** HT is a rare cause of large goiter and no correlation between concentrations of thyroid autoantibodies and its development were found. Probably other trophic factors participate in the development of such large thyroids and not just the autoimmune inflammatory process.

130555 – NUTRACEUTICALS PRESCRIBED TO PATIENTS WITH GRAVES' DISEASE IN REMISSION DID NOT PREVENT RELAPSE IN A SAMPLE FROM A UNIVERSITY HOSPITAL

MAIN AUTHOR: IASMIN SCHUMANN SEABRA MARTINS

Iasmin Schumann Seabra Martins[1], Luiza Macedo Travalloni[1], Ivia Fonseca de Oliveira[2], Bianca Freitas dos Santos[1], Ana Beatriz Winter Tavares[2], Tânia Maria Ortiga-Carvalho[1], Patrícia de Fátima dos Santos Teixeira[1]

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Introduction: Nutraceuticals are foods or parts of foods that can act on diseases, including nutrients and supplements. The most found in medical prescriptions for patients with Graves' disease (GD) are selenium and vitamin D. **Objectives:** The aim of this study is to assess whether the use of these nutraceuticals would be associated with a lower risk of relapse after clinical remission in patients with GD. **Methods:** Retrospective cohort with cross-sectional analysis of patients with GD referred to the outpatient clinic of a university hospital who had progressed to clinical remission with the use of antithyroid drugs (ATD). Medical records were analyzed to observe possible clinical recurrence at follow-up. Remission was defined by negative TRAb, normal TSH and Free T4 levels and discontinuation of ATD. Relapse was defined by TRAb positivity or return of hyperthyroidism. At the time of the cross-sectional analysis, all patients underwent a questionnaire, a physical examination and blood test for 25OH vitamin D (VitD). **Results:** 59 patients with GD in remission were included. Of these, 10 relapsed during follow-up. The median time in ATD among patients who maintained remission was 36 months (CI 31.4-56.2), similar to the group that relapsed (34 months [CI 20.2-65.7]; p = 0.700). The time between remission and relapse was 20 months (CI 7.6-68.7) and reassessment in those who remained in remission was 36 months (CI 32.8-60.5). Age and gender distribution were the same between the groups (57 years and 90% women). Graves' ophthalmopathy (GO) was more frequent in the group that relapsed (90%) than in those who maintained remission (42.9%). Among the patients who relapsed, there was a higher frequency of selenium use prescribed after remission (44.4% *vs.* 11.4%; p = 0.02). Among the patients taking selenium, the majority (63%) had already received corticosteroid pulse therapy for GO. The frequency of vitamin D use did not differ between the groups, but patients who relapsed had higher VitD levels (34.8 [CI 30.6-41.3] *vs.* 27.8 [CI 23.6-32.8]; p = 0.03). **Conclusion:** The nutraceuticals selenium and vitamin D prescribed to patients with GD were not associated with a lower risk of relapse, and higher serum levels of vitamin D were even found in patients with this outcome. The study of possible effects associated with excessive replacement of these elements deserves consideration, as does the study of vitamin D receptor polymorphisms. (Faperj E-26/211.288/2021).

130551 – VITAMIN D LEVELS IN GRAVES' DISEASE REMISSION AND ITS INTERFACE WITH THE PRESENCE OF ORBITOPATHY

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Introduction: The relationship between vitamin D and the prognosis of Graves' disease (GD) is questioned. **Objectives:** To compare the levels of 25OHVitamin D (VitD) in patients who went into GD remission *versus* those who required definitive treatment and; subsequently, compare VitD levels between those who relapsed and those who did not. Additionally, to assess whether VitD levels differ in the presence of Graves' orbitopathy (GO) or are associated with clinical activity. Finally, to describe the interface between GO and evolution to remission and/or relapse of GD. **Methods:** Retrospective cohort including patients with GD referred to the outpatient clinic of an universitary hospital and who had been using antithyroid drugs (ATD) for at least 18 months. The defined outcomes were the need for definitive treatment (surgery or radioiodine therapy), evolution to clinical remission and subsequent clinical relapse during follow-up. The VitD levels considered were those at the time of outcome. Remission was defined by negative TRAb, with normal TSH and T4L levels and suspension of ATD. **Results:** Of the 55 patients included, 42 had clinical remission (9 relapsed) and 13 underwent definitive treatment. The average time on ATD was 42 months for those who went to definitive treatment and 53.9 months for those who remitted (p = 0.415). The frequency of vitD use was higher among definitive treatment than among clinical remission (75% *vs.* 35.9%; p = 0.05), but VitD levels were similar in both groups (32.9 ± 9.6 *vs.* 32.9 ± 21.8). Recurrence was not associated with frequency of use or VitD levels. GO was more common in those referred for definitive treatment than in those who remitted, as well as more frequent in those who relapsed (88.9% *vs.* 50%; p = 0.039). Patients with or without GO used vitamin D at similar frequencies, but VitD levels were higher in those with GO (36.2 ± 23.6 *vs.* 26.4 ± 11.1; p = 0.08) especially in those with clinical activity (45.9 ± 10.6 *vs.* 28.1 ± 34.9; p = 0.01). **Conclusions:** VitD levels at the time of clinical remission did not differ from those found in patients referred for definitive treatment, but there was a higher frequency of VitD use in the latter. GO was associated with higher levels of VitD, as well as with lower chances of remission and higher chances of relapse, regardless its severity. The results are preliminary and an increase in the sample size as well as the study of vitD receptor polymorphisms are necessary. (FAPERJ E-26/211.288/2021)

130499 – UNILATERAL GYNECOMASTIA AS AN INITIAL PRESENTATION OF GRAVES' DISEASE: CASE REPORT

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Introduction: Graves' disease (GD) is a result of autoimmune antibody stimulation of TSH receptor resulting in increased production and release of thyroid hormone and is the most common cause of hyperthyroidism. Symptoms of bilateral gynecomastia in association with GD can be found as frequently as 40%. However, the presentation of unilateral gynecomastia in association with hyperthyroidism remains rare. **Case report:** A 24-year-old man presented with non-painful enlargement of the left breast along with symptoms of palpitation, excessive sweating, and weight loss of 3 kg over the duration of 2 months. He revealed no alcohol or drug abuse history. He was not taking any medication. His height was 174 cm and weighed 72.8 kg with calculated BMI of 24.04 kg/m^2. Laboratory investigation revealed FSH: 5.2 IU/L (NR: <10 IU/L), LH: 3.3 IU/L (NR: <9.0 IU/L), estradiol 2.3 ng/dL (NR: 1.1-4.3 ng/dL); total testosterone: 572 ng/dL (NR: 240-816 ng/dL); free testosterone: 352 pmoL/L (NR: 131-640 pmol/L). Breast ultrasound showed mild gynecomastia and testicular ultrasound did not reveal a testicular mass. Thyroid function tests (TFTs) revealed TSH < 0.001 mU/L (NR: 0.4-4.3 mU/L) and fT4 3.42 ng/dL (NR: 0.7-1.48 ng/dL). Repeat TFTs confirmed low TSH < 0.001 mU/L and elevated thyroid hormone levels [fT4: 3.54 ng/dL; tT3: 284 ng/dL (NR: 40-180 ng/dL)], His diagnosis of GD was confirmed biochemically with a highly elevated TRAb: 24 U/L (NR: <1.75 U/L). Then, 20 mCI radioiodine was given as definitive treatment for GD in this patient since he had a high expression level of TRAb and displayed symptoms of thyrotoxicosis at a young age. Following treatment, the patient remained in euthyroid state without recurrent gynecomastia. Thyroid hormone supplement was continued due to post-ablative hypothyroid, but symptoms of hyperthyroidism were completely resolved. **Conclusion:** This case highlights the rare presentation of unilateral gynecomastia in hyperthyroidism from GD and the importance of precise diagnosis for prompt treatment of this reversible condition.

130061 – AUTOIMMUNE THYROID DISORDERS INDUCED BY ALENTUZUMAB THERAPY IN A PATIENT WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS: A CASE REPORT

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Introduction: Alemtuzumab is a monoclonal antibody used as second-line therapy in high-activity relapsing-remitting multiple sclerosis (RRMS). The onset of autoimmune thyroid diseases is one of its main complications, with 42% risk in a 6-year follow-up, and it is probably associated with self-tolerance breakdown during the immune reconstitution phase. Graves' disease is the most common manifestation and has an atypical evolution when compared with its classical form. This case report aims to warn professionals about this condition and to provide early treatment. **Case report:** A 38-year-old woman seeks medical consultation with palpitation, hand tremors, nausea, and diarrhea for 2 weeks, with a weight loss of 4 kg in this period. She has had an RRMS diagnosis since childhood, being treated with natalizumab for four years, and then suspended by her neurologist because of seropositivity for JC virus. Currently is receiving therapy with alemtuzumab annually, initiated 11 months before the onset of these symptoms. An endocrinologist is also accompanying her because of a nontoxic multinodular goiter, with previous exams: TSH 0.91 um/L (VR:0.45-4.5), T4L 1.0 ng/dL (VR 0.8-1.7); non-reagent thyroid autoantibodies; FNAA: Bethesda II. Negative history for thyroid disease. Physical examination: good overall condition, afebrile, hand tremor, tachycardia (120 bpm); diffuse thyroid goiter, with palpable nodules, thyroid bruit. Orbitopathy, dermatopathy, and acropathy non-detected. Labs: TSH 0.01 um/L; T4L 7.77 ng/dL; T3T 6.82 ng/mL (VR: 0.7-2.4); TRAb 22.19 UI/L (VR: <3.1); Anti-TPO 95.7 UI/mL (VR: <5.61). Doppler US: Diffuse Thyroid goiter (Vol 34.7cc) with nodules and diffuse increased blood flow in Doppler. The clinical-laboratory evidence of hyperthyroidism associated with TRAb in high titration confirms the suspected diagnosis of alemtuzumab-induced Graves' disease. Besides, positive anti-TPO also confirms overt chronic lymphocytic thyroiditis. Therefore, it was initiated methimazole therapy (20 mg/day) and propranolol 40 mg 8 x 8 h; the patient had rapid regression of symptoms and received hospital discharge. **Conclusion:** This report reinforces the need to evaluate thyroid function before and after initiating immunobiological therapy with alemtuzumab, enabling quick diagnosis and therapy for thyroid dysfunction.

130606 – ASSOCIATION BETWEEN IODURIA AND THE PRESENCE OF THYROID AUTOIMMUNITY

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Introduction: Iodine is an essential micronutrient in the formation of thyroid hormones. It is well known that its deficiency is a risk factor for nodular goiter. Parallel to this, studies have demonstrated a possible increase in the prevalence of hypothyroidism, subclinical hypothyroidism and autoimmune thyroiditis through increased iodine intake. It is assumed that there is an increase in the immunogenicity of thyroglobulin, a reduction in peripheral tolerance due to inhibition of T regulatory cells, thyroid parenchymal damage due to oxidative increase and an increase in the activation of autoreactive T cells (produces an increase in the secretion of cytokines and can trigger signaling of apoptosis). **Objective:** To evaluate, in women, followed in the outpatient service of an university hospital, the association between urinary iodine concentration (UIC) and thyroid autoimmunity. In parallel, we analyzed the correlation between antithyroid antibody titers and UIC. **Methods:** Female patients from the endocrinology outpatient clinic of a tertiary hospital were invited to participate in the research by collecting a urinary sample to assess UIC using the ICPMS method. Antithyroid antibody titers (Antithyroid peroxidase, ATPO and Antithyroglobulin, ATG) were obtained by active search in the electronic medical record, considering the highest registered titers for analysis. The results were expressed as medians and interquartile range and compared using non-parametric tests between the different groups of iodine status established by the OMS (insufficient when 299 µg/L). **Results:** The median age of the 169 participants was 53 (20) years and UIC was 175.8 µg/L, with 19.5% having a median concentration compatible with insufficiency, 34.9% adequate and 44.4% above the adequate/excessive. The frequency of positivity for ATPO was 44.9%. This positivity occurred in 45.5% of those with insufficiency, 30.4% in those with adequate and 41.3% in those with above-adequate ioduria. The median titer was lower, without reaching statistical significance, in the group with adequate iodine status (3.5) than in the insufficient group (13.3) or above 199 µg/L (13). There was no correlation between ATPO titers and CUI. **Conclusion:** Anti-TPO titers did not differ according to iodine categories and there was no association between positivity and iodine status in the studied sample.

130538 – ASSOCIATION OF THYROID PEROXIDASE ANTIBODIES AND HIGH-SENSITIVITY C-REACTIVE PROTEIN: A CROSS-SECTIONAL ANALYSIS FROM THE ELSA-BRASIL STUDY

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Introduction: Thyroid peroxidase antibodies (TPOAb) is a relevant marker of thyroid autoimmunity. Previous studies have suggested that increased TPOAb levels are a low-grade inflammation marker; however, little information is available about its association with high-sensitivity C-reactive protein (hs-CRP). **Objective:** Our aim was to explore the association between TPOAb titers and high hs-CRP using baseline data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). **Methods:** Participants with information on hs-CRP, TPOAb and covariates; hs-CRP < 10 mg/L; and, without previous cardiovascular disease or stroke, were included (n = 12,078; mean age 51.6 ± 8.9; 54.6% women). Fasting serum of hs-CRP and TPOAb were measured. High hs-CRP was defined as values between 3-10 mg/L. TPOAb was categorized as undetectable (≤5.00 IU/mL), low detectable (5.01-14.99 IU/mL), high detectable (15.00-33.99 IU/mL), and positive TPOAb (≥34.00 IU/mL). Logistic regression models assessed high hs-CRP as the dependent variable and TPOAb titers as the independent variable (reference: undetectable category) adjusted for demographic (sex, age, and race), cardiovascular risk factors (diabetes, hypertension, dyslipidemia, smoking, eGFR < 60 mL/min/1.73 m^2 and BMI ≥ 30 kg/m^2) and thyroid hormones (TSH and FT4 levels). For sensitivity analysis, we excluded individuals with subclinical and clinical thyroid diseases and those on medications that affect thyroid function. **Results:** Prevalence of high hs-CRP was 20.7%, 23.6%, 25.9%, and 25.4% for undetectable, low detectable, high detectable and positive TPOAb categories, respectively (chi-square test, p = 0.022). In the univariate analysis, participants with high detectable (OR: 1.34; 95% CI: 1.07-1.68; p = 0.011) and positive (OR: 1.30; 95% CI: 1.03-1.65; p = 0.027) TPOAb levels were more likely to have high hs-CRP than the reference group. After multivariable adjustment, only the high detectable group showed higher odds of having high hs-CRP (OR: 1.33; 95% CI: 1.04-1.68; p = 0.020). In the sensitivity analyses, the association was attenuated by risk factors (OR: 1.28; 95%CI: 0.99-1.67; p = 0.061) and by thyroid function markers (OR: 1.30; 95% CI: 1.00-1.70; p = 0.048). **Conclusion:** There was an association between TPOAb and hs-CRP, and this association was consistent even when considering thyroid function. These findings suggest a potential relevance of TPOAb detectability as a marker of low-grade inflammation.

BIOLOGIA CELULAR DA TIREOIDE

130616 – EXPLORING THE ROLE OF RET GENE POLYMORPHISMS THROUGH *IN SILICO* ANALYSIS AND THEIR RELATIONSHIP WITH MEDULLARY THYROID CARCINOMA

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Introduction: The proto-oncogene RET plays a pivotal role in cellular processes as in proliferation, differentiation, and migration. This gene is associated with endocrine disorders, notably multiple endocrine neoplasia type 2 (MEN2A and B) and medullary thyroid carcinoma (MTC), often attributed to mutations in the RET gene. Genetic polymorphisms have been identified as potential influencers of susceptibility and manifestations of MTC. This study aims to assess molecular biomarkers of the RET gene and their correlation with the clinical presentation and behavior of MTC. **Methods:** This is an *in silico* analysis in which missense polymorphisms reported for the RET gene in Single Nucleotide Polymorphisms Database (dbSNP) were evaluated, as well as information on the protein structure was obtained from Universal Protein (UniProt). Bioinformatics tools used include: PredictSNP2.0 (CADD, FATHMM, FunSeq2, GWAVA), SIFT, PredictSNP1.0 (PredictSNP, SIFT, PolyPhen-1, PolyPhen-2, MAPP, PhD-SNP, SNAP, PANTHER, and nsSNPAnalyzer), iStable (iStable, MuPRO, I-Mutant), and DynaMut. **Results:** 172 polymorphisms were evaluated, and the impacts of their amino acid alterations on the protein structure were assessed. Data from PredictSNP2 demonstrates that rs17028, rs2075912, rs2075913, rs2435355, and rs10900297 possess characteristics capable of modifying the DNA structure. The evaluation by the PredictSNP1.0 consensus showed 24 polymorphisms considered deleterious by at least six tools. Especially, the exchanges C609R (rs77558292), C609F (rs77939446), C609Y (rs77939446), C611W (rs80069458), C618R (rs76262710), and C620W (rs79890926) promote a structural approximation associated with a decrease in molecular flexibility. The rs1799939 (G691S) is the only missense SNP with an amino acid exchange that has a MAF>0.1; however, it was considered deleterious only in the FunSeq2 tool of PredictSNP2.0. Despite being neutral in all PredictSNP1.0 tools, it was observed that this exchange promotes a decrease in protein stability, but does not promote a modification of the interaction pattern with adjacent amino acids. **Conclusion:** In this way, the data demonstrates 24 polymorphisms capable of promoting significant modifications in the structure, function, stability, flexibility, and interaction with adjacent amino acids in the protein structure. To sum up, these SNPs may be important targets for studies in the search for biomarkers for the development of CMT and prognosis based on their behavior.

130165 – ENHANCING THYROID CELL DIFFERENTIATION IN RAS-MUTATED ANAPLASTIC THYROID CANCER CELLS BY EZH2 INHIBITION

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Introduction: Anaplastic thyroid cancer (ATC) stands as the most lethal endocrine malignancy, characterized by its aggressive behavior and rapid growth. Despite its aggressive nature, ATC remains refractory to radioiodine treatment, primarily due to the loss of thyroid differentiation genes' expression, such as NIS, TPO, and TG. Common mutations in ATC involve MAPK signaling genes (BRAF V600E, NRAS, or HRAS), coupled with TERT promoter and TP53 genes mutations. Notably, RAS-mutated ATC patients have poorer survival rates and lack targeted therapy compared to BRAF-mutated patients. Our previous research indicated that inhibiting the EZH2 methyltransferase improved cell differentiation and had antitumoral effects *in vitro* and *in vivo* in BRAF-mutated ATC cells. Given EZH2's central role in the PRC2 complex, which promotes gene silencing via histone methylation, we hypothesized that inhibiting methyltransferase activity could yield antitumoral effects and enhance differentiation in RAS-mutated ATC cells. **Methods:** Hth7 (NRASQ61R) and C643 (HRASG13R) cells were treated with EPZ6438 (EZH2 methyltransferase inhibitor) for 6 days at 5 µM, alone or with U0126 (MEK1/2 inhibitor) at 10 µM. Subsequently, we assessed the expression of thyroid differentiation genes via qPCR and functional effects via clonogenic and iodine uptake assays. Furthermore, BRAF-mutated ATC cells (KTC2 and SW1736) were used to validate the effects of EZH2 inhibition in an iodine uptake assay. **Results:** EPZ6438 treatment significantly enhanced NIS, TPO, TG, GLIS3 and NKX2-1 genes' expression in Hth7 and C643 cells, indicating improved differentiation. Combined treatment further augmented the effects on TG, TSHR, NKX2-1 and FOXE1 genes. Interestingly, C643 cells exhibited increased sensitivity to U0126, with additional upregulation of PAX8 gene. Functionally, EZH2 inhibition reduced colony formation in both cell lines and increased iodine uptake by 15-fold and 1.7-fold in Hth7 and C643, respectively. Moreover, the iodine uptake also increased in BRAF-mutated KTC2 and SW1736 cells by 2.7-fold and 2.56-fold, respectively, validating that EZH2 inhibition improves differentiation in thyroid cancer cells. **Conclusions:** Our results show that inhibiting EZH2 activity in RAS-mutated ATC cells enhances thyroid function and suppress colony formation. Combined MAPK signaling pathway inhibition amplifies these effects, highlighting promising directions for future therapeutic interventions in ATC management.

130534 – PERMANENT AND TRANSIENT UPREGULATION OF MIR-200C INHIBITS EMT AND CONTROLS ANAPLASTIC THYROID CANCER CELLS AGGRESSIVENESS

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Introduction: Anaplastic thyroid cancer (ATC) is a rare and deadly form of thyroid neoplasia that urgently needs new therapeutic strategies. The microRNA miR-200c, molecule that has been linked with tumor suppressor activity, is downregulated in ATC. However, the biological effects of miR-200c deregulation in ATC remains unknown. So, it appears relevant to understand the molecular mechanisms modified by miR-200c deregulation in ATC cells in order to better understand their aggressive behavior. **Objective:** To evaluate the effects of ectopic expression of miR-200c in ATC cell aggressiveness. **Methods:** Permanent expression of miR-200c was performed in KTC2 and SW-1736 ATC cells using transfection with PMSCV-pp plasmid carrying MIR200C gene. Cells were then cultured permanently with puromycin to effectively select transfected cells. Transient expression of miR-200c was performed in SW-1736 using miR-200c-mimic (12pmol) for 48 hours. The efficacy of the transfection was analyzed by targeted RT-qPCR towards this microRNA. EMT markers expression was quantified by RT-qPCR. Cell counting was used to evaluate cell proliferation. TranswellTM assay and scratch assay was performed to evaluate migration. **Results:** Permanent or transient transfection effectively induced upregulation of miR-200c levels in KTC2 and SW-1736 ATC cells. Further, RT-qPCR results have shown that both techniques of miR-200c transfection in ATC cells reversed EMT by enhancing mRNA expressions of the epithelial marker CDH1, while diminished the mRNAs levels of the mesenchymal markers VIM and ZEB1/2. Also, both techniques of miR-200c transfection diminished mRNA expression of SMAD4, a component of TGF pathway and modulator of EMT program. Further, permanent upregulation of miR-200c in ATC cells reduced TGF pathway activation measured by gene reporter assay using plasmid pSBEx4 that had binding sites for SMAD4/luciferase. Moreover, permanent expression of miR-200c in ATC cells reduced cell colony formation, proliferation and migration *in vitro*. **Conclusion:** This study highlights the tumor suppressive effect of miR-200c by inhibiting EMT in ATC cells and controlling their aggressive behavior. Further, ectopic expression of miR-200c appears to be a useful molecular tool to reverse the undifferentiated phenotype of ATC cells and to develop novel treatment strategies.

130293 – RESISTANCE OF BCPAP CELLS TO BISPHENOL A DAMAGING EFFECTS ON VIABILITY, METABOLIC ACTIVITY AND DNA FRAGMENTATION MAY BE ASSOCIATED TO THE INCIDENCE OF CLINICALLY CONFIRMED PAPILLARY THYROID CARCINOMAS WITH BRAF MUTATIONS

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Epidemiological and experimental evidence indicates that exposure to Bisphenol A (BPA) can affect the proliferation, migration, and invasion of various cell types. However, the mechanisms involved in these effects are still poorly understood. Furthermore, these effects may differ in normal and mutated thyroid cells, which may be common because the prevalence of thyroid nodules is very high in the population. Using cytotoxicity and cell viability analyses, we previously demonstrated that BPA has a more harmful effect in control (Nthy-ori 3-1) than in papillary thyroid carcinoma (PTC)-derived cells (TPC-1 - containing the RET/PTC1 rearrangement; BCPAP - harboring the BRAF V600E mutation) and 8505C – anaplastic carcinoma. In addition, we found that BPA produced a very low DNA fragmentation rate in BCPAP cells, which tended to decrease after 48h in comparison to the positive control, suggesting that these cells have resistance and/or repair mechanisms. To better understand the effects of BPA, we used the comet assay to measure the percentage of DNA damage in diverse thyroid cell lines after 24 and 48h of exposure to different concentrations, including the Specific Limit concentration of Migration (SML) considered acceptable by our National Health Surveillance Agency (Anvisa). Genotoxicity rates were compared with negative and positive (100 µM H202) controls using CometScore software, and statistical analysis was performed using the ANOVA test. The BCPAP strain was more resistant to the genotoxic effect of BPA, even at a high concentration (100 µg/mL), whereas 8505C was very sensitive. The BPA SML dose caused DNA fragmentation in 19.21% ± 1.9 of control cells and in 23.03% ± 1.86 of 8505C cells ($p = 0{,}4631$), in contrast to only 3.17% ± 0.07 of TPC1 ($p = 0{,}0085$) and 2.76% ± 0.64 of BCPAP cells ($p = 0{,}0095$). Our data demonstrated that BPA has a non-monotonic and distinct uneven genotoxicity pattern in different thyroid cells. Even low concentrations, considered acceptable, have important effects, especially on 8505C and Nthy-ori 3-1 cells. BCPAP cells, on the other hand, exhibit greater resistance to the genotoxic effects of BPA. This, along with their vitality and metabolic tolerance, raises the possibility that these cells have survival advantages. We suggest that the unique effects of BPA, a chemical that is extensively used worldwide, on thyroid follicular cells may be linked to the high prevalence of clinically confirmed PTC with BRAF mutations.

130078 – A SYSTEMS BIOLOGY APPROACH REVEALS NEW TARGETS FOR THYROID GLAND TOXICITY IN ADULT INDIVIDUALS

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Introduction: Thyroid hormones participate in several biological processes, from metabolism to development. Many compounds, classified as endocrine disruptors, alter the synthesis, secretion, metabolism, and transport of thyroid hormones, inducing thyroid dysfunctions. **Objectives:** To identify new potential targets of endocrine disruptors in the thyroid gland. **Methods:** Previously published data on embryonic and adult thyroid gland transcriptomes was used in this study. One hundred genes whose expression was specifically upregulated or downregulated in the adult thyroid gland in comparison to the embryonic gland were subjected to systems biology analysis by functional network formation using Cytoscape 3.9.1 software and the ClueGO v2.5.9 + CluePedia v1 plugins 5.9. Therefore, using the Comparative Toxicogenomics Database tool, possible interactions of several chemicals with the proteins coded by these genes were determined. The chemical classes were verified in PubChem. **Results:** The higher expressed proteins in the thyroid gland were related to the following categories: metallothionein binding metals (56.67%), steroid hormone biosynthetic process (16.67%), and cellular response to vascular endothelial growth factor stimulus (6.67%). For the proteins whose expression was reduced in the thyroid of adult individuals, the main categories were related to alpha-defensins (45.59%), antimicrobial humoral response (10.29%), and fluoropyrimidine activity (8.82%). The compounds that were found to interact with the proteins encoded by the highly expressed genes included antineoplastic agents (fenretinide, silybin, and tretinoin), antihypertensive agents (losartan, reserpine, and enalapril), and enzyme inhibitors (propargylglycine, decitabine, and digoxin). Otherwise, the chemicals that interact with the proteins encoded by the lower expressed genes were antineoplastic agents (neocuproine, triptolide), nonsteroidal anti-inflammatory agents (acetovanillone, mesalamine, and indomethacin), and enzyme inhibitors (benazepril, cyclosporine, and nolatrexed). **Conclusion:** Several compounds that humans are commonly exposed, from antihypertensive drugs to enzyme inhibitors, have been identified as potentially harmful to the thyroid of adult individuals. Therefore, these data highlight the need for additional research on the toxicity of these substances to thyroid function and provide a roadmap for future investigations and treatment strategies intervention.

130050 – INVESTIGATION OF POTENTIAL CHEMICAL TARGETS AS ENDOCRINE DISRUPTORS OF THE EMBRYONIC THYROID

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Introduction: Some compounds of natural or synthetic origin present in personal care products, food additives, and packaging, among others, interfere with hormonal regulation and are called endocrine disruptors. The thyroid gland is an important target of these compounds. Thyroid dysfunctions may lead to altered hormonal signaling, especially in sensitive windows of development, such as during the embryonic period. **Objectives:** To analyze the public data about human embryonic thyroid transcriptome and investigate potential new targets of endocrine-disrupting chemicals in the embryonic thyroid gland. **Methods:** Firstly, we compared the transcriptome public data of adult and embryonic thyroid glands. Therefore, we have selected the 100 higher up- or down-regulated genes that were subsequently subjected to functional enrichment analysis using the ClueGo+Cluepedia plug-in of Cytoscape 3.9.1 software. Next, the possible interactions between several chemicals and the proteins encoded by those genes were investigated using data from the Comparative Toxicogenomics Database (CTD). **Results:** The three largest groups of upregulated genes were: PRMT6, which methylates arginine-4 of histone H2A (86.21%); IFNG-stimulated genes (6.9%); and the negative regulation of the inflammatory response to antigenic stimuli (6.9%). In the downregulated genes group, plasma lipoprotein particles (39.24%), endopeptidase inhibitory activity (24.05%), and artery morphogenesis (12.66%) were identified. According to the CTD analysis, some of the main categories of compounds that possibly interact with the proteins encoded by the upregulated genes were antineoplastic agents, such as tamoxifen and triptolide; antioxidants, such as resveratrol and selenic acid; and anti-inflammatory agents, such as nimesulide and methylprednisolone. Meanwhile, the main categories of compounds that possibly interact with the proteins encoded by the upregulated genes were antihypertensive agents, such as atenolol and valsartan; antioxidants, such as ascorbic acid and isoquercitrin; and natural compounds, such as ginsenoside Rf and soybean oil. **Conclusion:** New targets of commonly used chemical compounds were identified in the embryonic thyroid gland. Therefore, the data presented herein reinforces the importance of investigating the impact of chemical compounds in the development and programming of the thyroid gland.

CIRURGIA DA TIREOIDE

130615 – CASE REPORT: ROBOTIC TOTAL THYROIDECTOMY WITH MODIFIED BILATERAL NECK DISSECTION VIA RETROAURICULAR APPROACH ON A 12-YEAR OLD BOY

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Introduction: Oncologic surgery has been making remarkable progress with the development of minimally invasive surgical procedures, leading to significant improvement in satisfaction and quality of life. In selected cases, surgical technologies could eliminate the need for large visible neck incisions with an acceptable cost and low complication rates that are equal or lower than those of classical procedures. These alternative approaches initially gained space in Asia, with robotic thyroidectomy via facelift or retroauricular approach, performing promising results and encouraging the occident to improve the robotic technique in head and neck field. After more than 10 years of experience in adult patients, the children began to be studied, showing good results. **Case report:** This case is about a 12-year-old male patient. After investigating the appearance of painless cervical nodules, he was referred by the endocrinologist to suspicion of thyroid cancer with cervical metastasis. The medical history was normal without a family history of thyroid cancer. US showed a solid nodule, with irregular contours, imprecise limits and microcalcifications at the right lobe/isthmus transition, measuring 1.7 x 2.3 x 1.2 cm. Multiple, bilateral and rounded cervical lymph nodes with microcalcifications, the largest at level IV. The cytologic analysis of the nodule results as Bethesda VI and the levels IV lymph nodes compatible with metastasis of papillary thyroid carcinoma. Additional exams were performed for staging and surgical planning. The MRI showed multiple prominent cervical lymph nodes at bilateral levels II to VII. The chest tomography was normal. Parents asked about remote access to avoid the visible scar so we proposed a total thyroidectomy with modified bilateral neck dissection via retroauricular approach. The operative time was 6 hours, 4 days of hospitalization and 6 days with cervical drains. Anatomopathological analysis showed a classic, multifocal papillary carcinoma, the largest focus with 2.1cm at isthmus, without extrathyroidal extension. They found positive vascular and perineural invasions. During neck dissection, 279 lymph nodes were removed, of those 47 were compromised. The largest focus with 11mm and presence of extracapsular rupture. The patient underwent a whole-body scan and radioiodine therapy with 150 mCi with recombinant TSH, Thyrogen. At this moment, after 2 years of follow-up together with endocrinology, he maintains an excellent response.

130589 – OUTCOMES OF THE FIRST 52 CASES TREATED AT THE HOSPITAL ALBERT EINSTEIN

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Introduction: Conventional thyroidectomy via Kocher's incision has been the standard technique for more than a century now. In the last decade, remote approaches to the thyroid were described avoiding the visible and variable neck scar associated with conventional thyroidectomy. In this scenario, transoral endoscopic thyroidectomy vestibular approach (TOETVA) is the most recently and widely adopted. This approach can also be performed combined with robotic instrumentation – transoral robotic thyroidectomy (TORT). In this paper, we evaluate the feasibility and surgical outcomes of TORT in the largest robotic surgery reference center in Latin America. **Methods:** This was a retrospective review of the first 52 patients who underwent TORT in a single center. **Results:** The study included 38 (73%) females and 14 (27%) males, with a mean age of 40 years. There were 28 (54%) total thyroidectomies (of which 3 combined with central neck dissection and one with parathyroidectomy) and 24 (46%) lobectomies. All cases were performed by a single surgeon (RBL), who accumulates an experience of more than 350 transoral thyroid surgeries. We didn't have any conversions, reoperations, infections, hematomas, skin lesion or mental nerve definitive paresthesia. The transient vocal cord palsy rate was 1.9% (1 patient). Mean hospital stay was 1.2 day and we had one readmission related to symptomatic hypocalcemia. In comparison with more than 1,000 conventional thyroidectomies performed at the same center, we had no difference on cost, hospital stay or surgical time. **Discussion:** This is a study with the largest cohort of TORT patients treated in Latin America to date that, despite its retrospective nature and selection bias, reached outcomes comparable to previously reported series and conventional thyroid surgery, reinforcing safeness and feasibility for this technique when performed by high volume trained surgeons.

128558 – INSTITUTIONAL CASE VOLUME OF THYROIDECTOMIES IN BRAZIL AND THE COVID-19 IMPACT: INSIGHTS FROM A NATIONAL DATABASE

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Introduction: Providing widespread access to thyroidectomies while consolidating services in high-volume centers is a significant challenge in healthcare. It is uncertain how Brazilian institutions performing thyroidectomies responded to the COVID-19 pandemic from an institutional case volume perspective. **Objectives:** In this context, from a national perspective, we aimed to analyze the impact of the COVID-19 pandemic on the institutional case volume of thyroid surgery in Brazil. **Methods:** We analyzed retrospective thyroidectomy data from the Department of Informatics of the Unified Health System (Datasus), stratifying institutions by surgical volume into low, intermediate, and high-volume (<10, 10-100, and >100 thyroidectomies/year, respectively). We assessed the differences in absolute numbers and percentages of thyroidectomies performed in the pandemic years (2020-2022) compared to 2019. Differences in the proportion of institutions based on case volumes from 2019 to 2022 were assessed using Cochran's Q test. **Results:** In 2019, 556 Brazilian institutions performed 15,331 thyroidectomies, with 46.4%, 48.4%, and 5.2% classified as low, intermediate, and high-volume institutions, responsible for 5.5%, 61.4%, and 33.1% of thyroidectomies, respectively. The COVID-19 pandemic has led to a 41.2% decrease in thyroidectomies in 2020, with 37.0% and 12.8% reductions in 2021 and 2022, respectively. When analyzing the proportions of institutions classified by case volume that maintained their pre-pandemic year classification in the first pandemic year, intermediate and high-volume institutions experienced reductions of 34.9% ($p < 0.001$) and 58.6% ($p < 0.001$), respectively, and low-volume institutions presented a 4.3% reduction ($p = 0.081$). **Conclusions:** The COVID-19 pandemic disrupted the landscape of thyroidectomies in Brazil, particularly in intermediate and high-volume institutions, while low-volume institutions proved more resilient. Our data provide valuable insights into the dynamics of healthcare delivery during crises.

130599 – COMPLICATIONS AND ONCOLOGICAL OUTCOMES OF TRANSORAL ENDOSCOPIC THYROIDECTOMY VESTIBULAR APPROACH (TOETVA) FOR THYROID CANCER: EXPERIENCE FROM A SINGLE BRAZILIAN ONCOLOGICAL CENTER

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Introduction: Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) has emerged as a viable remote access method in comparison to the traditional surgical technique for thyroid disorders, offering the advantage of avoiding skin incisions and delivering established cosmetic benefits. **Objective:** The aim of this study is to assess both early and late postoperative complications, as well as the oncological outcomes of patients undergoing TOETVA at a prominent oncology center in Brazil. **Patients and methods:** A retrospective analysis was conducted on patients with papillary thyroid carcinoma (PTC) undergoing partial and total thyroidectomy via the transoral approach (TOETVA) between 2018 and 2022, aged over 18 years, with staging T1-T2, N0-N1a, while excluding cases with N1b stage and salvage procedures. **Results:** The study involved 157 patients, predominantly female with a mean age of 39 years. Of these, 86 (54.8%) underwent total thyroidectomy (TT), 59 (37.6%) underwent partial thyroidectomy (TP), 3 (1.9%) received isthmectomies, and 9 (5.7%) had TT with central neck dissection. Adjuvant treatment with RIT was administered to 33 (21%) patients. Complications included a 3.2% incidence of transient vocal cord paresis (5 cases) and 0.6% permanent paresis (1 case). Surgical site infection was observed in 2 cases (1.3%), while there were no instances of conversions to open surgery. Transient and permanent hypocalcemia rates were reported at 20.1% and 0%, respectively. At follow-up, the mean thyroglobulin level post-TT was 0.46 ± 1.08 (with 92.6% of patients demonstrating thyroglobulin levels <1) and anti-TG 28 ± 34. Five recurrences (3.18%) have been identified, all within regional lymph nodes. **Conclusion:** TOETVA presents itself as a safe alternative to traditional surgical techniques for patients harboring well-differentiated carcinoma who seek to avoid visible cervical scarring.

130536 – CLINICAL AND EPIDEMIOLOGICAL PROFILE OF PATIENTS UNDERGOING THYROIDECTOMY IN A PUBLIC HOSPITAL IN SOUTHERN MINAS GERAIS

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Introduction: Thyroidectomy is a common surgical intervention for various thyroid gland conditions. Understanding the clinical and epidemiological profile of patients undergoing this procedure is essential for improving healthcare quality and guiding health policies. This study aims to analyze the clinical and epidemiological profile of patients undergoing thyroidectomy at a public hospital in southern Minas Gerais. **Objectives:** To assess the clinical and epidemiological characteristics of patients undergoing thyroidectomy and to identify common indications and surgical outcomes in this population. **Methods:** This is a retrospective observational study conducted by analyzing medical records of patients who underwent thyroidectomy from January 2018 to December 2019 at a public hospital in southern Minas Gerais. Variables analyzed include age, sex, preoperative diagnosis, surgical indication, type of thyroidectomy performed, postoperative complications, and clinical outcomes. **Results:** The clinical epidemiological profile of patients undergoing thyroidectomy showed a higher prevalence in women (76.1% of cases) and a most common age range between 51 and 60 years. The main surgical indication was the presence of high suspicion for thyroid neoplasms (37.7% of cases). Total thyroidectomy was the most performed procedure (95.6% of cases), with a low incidence of postoperative complications (3.1% of cases). **Discussion:** The results obtained are aligned with the literature, which also indicates a higher prevalence of thyroidectomies in women and a frequent indication for the treatment of thyroid nodules. The low incidence of postoperative complications suggests good quality of care and highlights the importance of medical staff training. **Conclusion:** The clinical epidemiological profile of patients undergoing thyroidectomy at a public hospital in southern Minas Gerais shows characteristics similar to those described in the literature. Analysis of these data is essential to guide health policies and improve the quality of care provided to patients with thyroid diseases.

130493 – FACTORS INFLUENCING NET PROMOTER SCORE IN TRANSORAL ENDOSCOPIC THYROIDECTOMIES (TOETVA): A SURVEY INVESTIGATING RISK PERCEPTIONS AMONG NON-THYROID PATIENTS

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Introduction: Transoral Endoscopic Thyroidectomies (TOETVA) are becoming comparable to conventional surgeries in selected cases, yet the perception of risk and willingness to recommend TOETVA among the general population remain uncertain. **Objective:** To investigate factors influencing risk perception among the general population, not affected by thyroid disease, towards TOETVA endorsement. **Methods:** A structured questionnaire was developed to assess the risk perception of TOETVA and the impact of cervical scarring in a population without a history of thyroid disease using Net Promoter Score (NPS) as a likelihood to recommend it. Snowball sampling was employed to recruit participants. Respondents were categorized as promoters or not if they exhibited a willingness to accept risks associated with TOETVA > 90% in a scale 0-100%. NPS was calculated for each of the four TOETVA risk axis (same risk as conventional surgery, increased length of surgery [ILOS], mouth incision, and chin numbness). Logistic regression was conducted to predict factors associated with being a promoter of TOETVA, examining the influence of demographic variables and risk perception preferences related to TOETVA. **Results:** Out of 205 respondents, 135 were classified as promoters. Age, gender, BMI, educational attainment, occupation in healthcare, and skin color (Fitzpatrick scale) did not differ significantly among promoters. However, a family income >$2,000 USD (37,14% *vs.* 55,97%, p = 0.011) and hypertrophic scar burden in a scale from 0 to 100 (60 *vs.* 74, p = 0,015) were significantly higher among promoters. The overall NPS for TOETVA risk acceptance was 31,22%, with specific scores for ILOS at 24,39%, mouth incision at 25,85%, and chin numbness at 13,17%. Univariate logistic regression revealed that having a university degree, family income, and concern about hypertrophic scarring were associated with being a promoter. However, in a multivariate model, only family income > $2,000 USD (OR 2,26, CI 1,26-4,17) and concern about hypertrophic scarring (OR 2,26, CI 1,22-4,18) remained independent predictors. **Conclusion:** The positive NPS indicates a general acceptance of risk associated with TOETVA among the population studied, where trade-offs for increased surgical duration, mouth incision, and chin numbness were considered. Trends in TOETVA recommendation for individuals categorized as promoters were associated with socioeconomic factors and concerns regarding hypertrophic scarring.

130443 – DESCRIPTIVE ANALYSIS OF TRANSIENT AND PERMANENT HYPOPARATHYROIDISM IN A COHORT FOLLOWING THYROIDECTOMY IN A UNIVERSITY HOSPITAL

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Introduction: Hypocalcemia (hypoCa) is the most common complication of thyroidectomy, reaching up to 30%-50% in different series. The main cause is hypoparathyroidism (HypoPT), due to iatrogenic damage of the parathyroid glands. Fortunately, this is mostly a transient condition. **Objectives:** To describe the frequency and clinical predictors related to transient and permanent HypoPT after thyroidectomy at a university hospital. **Methods:** A retrospective cohort was performed, including all 975 patients who underwent thyroidectomy from 2001 to 2017 at a university hospital. Data was collected from medical records from surgery until one year later. For statistical analysis, we selected two groups for comparison: those with malignancies and those with Graves' disease (GD). Patients who presented hypoCa (corrected serum calcium < 8.5) and/or hyperphosphatemia (hyperP) (serum phosphorus > 4.5) postoperatively were considered to have post-surgical HypoPT. Permanent HypoPT was defined as: requirement of calcitriol or high doses of cholecalciferol to maintain calcemia; hyperphosphatemia or serum PTH below reference range, after 12 months of follow-up. **Results:** From the whole cohort, 60 underwent surgery for GD and 261 for cancer. The majority (77%) of cancer patients were treated with total thyroidectomy and 22% with associated neck dissection (ND). Postoperative hypoCa was detected in 36.3% of patients undergoing surgery, with no difference between GD or cancer patients (35.6% and 39.3%, respectively). However, after excluding patients with partial thyroidectomy, the frequency of postoperative HypoCa reached 45.2%. When in association with ND it increased to 63.2% (<0.01). Other factors associated with postoperative HypoPT were: postoperative use of a drain (63.6%) and having undergone surgery during the first semester of medical residency. Following those subjects with HypoPT, 8.2% developed permanent HypoPT, this outcome being less common in GD (6.3%) compared to those who underwent ND for cancer (9.3%; $p < 0.05$). Serum phosphorus was significantly higher among those that developed permanent HypoPT (6.5 ± 1.0 *vs.* 4.5 ± 0.9; $p < 0.01$). **Conclusion:** The frequency of HypoPT after TT was similar to that found in the literature, more commonly transient. Risk factors for postoperative HypoPT were: TT for cancer, mainly with ND; use of drain in the postoperative period and lower expertise of the medical group. Permanent HypoPT was associated with serum levels of phosphorus and ND.

130579 – STRUCTURAL RECURRENCE AND SURVIVAL IN DIFFERENTIATED THYROID CARCINOMA: IS MINIMAL LOCAL INVASION RELEVANT?

MAIN AUTHOR: MARCUS VINICIUS LOPES HORIUCHI

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Introduction: Minimal local invasion has been considered a minor risk factor for recurrence and death in differentiated thyroid carcinoma (DTC); however, there is no clear consensus. **Patients and methods:** 629 patients submitted to thyroidectomy for DTC were retrospectively reviewed. They were grouped into tumors without invasion (413; Group 1) and with minimal invasion (216; Group 2). Structural relapse, variables related to prognosis, and long-term survival rates were analyzed. The average follow-up time was 71.5 months (5-243 months). The minimum follow-up time was set at 30 months or death due to the tumor. **Results:** In Groups 1 and 2, 6.5% and 22.7% of the patients, respectively, presented structural relapse (P 10 ng/mL (P < 0.001). **Conclusion:** Although patients with local minimal invasion presented higher rates of structural relapse when compared to those without this condition, local minimal invasion was not identified as an independent risk factor in this cohort.

DISFUNÇÕES TIREOIDIANAS

130607 – CORRELATION BETWEEN THYROID FUNCTION AND URINARY PROTEIN-TO-CREATININE RATIO IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3 AND 4

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Introduction: The relationship between proteinuria and thyroid function remains controversial in patients with chronic kidney disease (CKD). Serum thyroid are bound to thyroxine-binding globulin (TBG) and albumin. Thus, proteinuria in the nephrotic range (>3.5 g/day) is associated with loss of TBG, levothyroxine or both, which may lead to hypothyroidism (subclinical). Thyroid function can also be influenced by kidney function, but results are still conflicting. The correlation between proteinuria and thyroid function also remains controversial in the literature. **Objectives:** To correlate thyroid function and the proteinuria-to-creatinuria ratio (Ptn/Cru) in patients with CKD stages 3 and 4. **Methods:** Observational, cross-sectional study, including 150 patients with CKD stages 3 and 4. 64 patients (42.6%) had CKD stage 3 (GFR 30-59 mL/min/1.73 m²), and 86 patients (59,3%) had CKD stage 4 (GFR 15-29 mL/min/1.73 m) – GFR was calculated through CKD-EPI formula. TSH and free T4 (FT4) were measured using chemiluminescence (reference values: TSH: 0.3 to 4.0 µIU/L; FT4: 0.7 to 1.8 ng/dL); Ptn/Cru (mg/g) was performed on an isolated urine sample. Proteinuria was defined as levels above 200 mg/g in a urine sample. **Results:** Median age was 68 years (IQR 61-76 years), median GFR 27 mL/min/ 1.73 m² (IQR 21-37.2), median TSH 2.9 µIU/L (IQR 1.89-4.04), median FT4 1.26 ng/dL (IQR 1.10-1.41), and median Ptn/Cru 315.5 mg/g (IQR 108.3-830). 91 patients (60.6%) had proteinuria. There was a statistically significant positive correlation between Ptn/Cru and TSH (r = 0.23; p = 0.003), and a statistically significant negative correlation between Ptn/Cru and FT4 (r = -0.17; p = 0.03) in the total sample, maintaining statistical significance after excluding patients (n = 7) with nephrotic proteinuria. There was a statistical difference in the median age (p = 0.004), GFR (p = 0.002), TSH (p = 0.001) and FT4 (p = 0.05) between the Ptn/Cru < and >200 mg/g groups. There was no statistically significant difference in TSH, FT4 or Ptn/Cru between CKD stages 3 and 4. **Conclusion:** The results demonstrated a positive correlation between TSH and Ptn/Cru, and a negative correlation between FT4 and Ptn/Cru, which corroborates that urinary protein loss, even at non-nephrotic levels, can alter thyroid function. Larger population studies on CKD are important to confirm the data found in our total sample.

130605 – LOW RESPONSE TO OSTEOPOROSIS TREATMENT IN A PATIENT WITH PLUMMER'S DISEASE

MAIN AUTHOR: AYLA LORANNE REBELO CANÁRIO

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Introduction: Thyroid hormones are essential for skeletal metabolism, but can be harmful to bone structure in states of gland hyperfunction, increasing the risk of osteoporosis and fractures. This is the case of Plummer's disease or toxic nodular goiter, which usually presents in a mild form, without the classic adrenergic symptoms. Scintigraphy reveals only a hypercaptivating nodule, however, often with normal thyroid function. **Case report:** We present the case of an 84-year-old woman, who was diagnosed with osteoporosis at the age of 65, through bone densitometry (Dxa) which recorded bone mineral density (BMD) of the lumbar spine (L1-L4) of 0.825, T -score of -3.0. He used alendronate for 3 years, but developed a duodenal ulcer and needed to switch to raloxifene. There was a worsening of bone mass with Dxa (2014) L1-L4 BMD 0.743 T-score -3.6 Z-score -2.6; femoral neck BMD 0.835 T-score -1.5; total femur BMD 0.865 T-score -1.1. She received two doses of zoledronic acid (2014 and 2015), but the 2016 Dxa still worsened L1-L4 BMD 0.723 T-score -3.8; femoral neck BMD 0.818 T-score -1.6. Strontium ranelate was used in 2016, risedronate in 2017 to 2020 and again from 2021 to 2023. The 2023 Dxa records in L1-L4 BMD 0.806 T-score -3.1; femoral neck BMD 0.820 T-score -1.6. A vertebra fracture (L4) was detected on a lumbar spine x-ray (2018). The patient had no symptoms of hyperthyroidism and thyroid function was always normal, however with TSH at the lower limit of normality 0.54 mIU /L (0.34-5.6) and T4L 9.7 ng /dL (7.5-21.1) from 2017 and TSH 0.48 mIU/L (0.34-5.6) and T4L 16.6 ng /dL (7.5-21.1) from 2024. In 2006 a nodule was detected thyroid gland 3.4 cm in the left lobe and four aspiration punctures were performed with a Bethesda II result. In 2024, given the patient's condition, we requested a thyroid scintigraphy, detecting a focal area in the lower third of the left lobe with suppression of the rest of the parenchyma. **Conclusion:** Excess endogenous thyroid hormone stimulates osteoclast activity and bone resorption. There are reports of decreased BMD in postmenopausal women with subclinical hyperthyroidism due to nodular goiter. This case highlights the importance of evaluating the possibility of a toxic nodule in a patient with osteoporosis with a low response to treatment, even asymptomatic and with TSH and T4L within normal limits.

130556 – CENTRAL HYPOTHYROIDISM DUE TO OXCARBAZEPINE TREATMENT

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Introduction: Antiepileptic drugs such as carbamazepine, phenytoin and oxcarbazepine cause low free T4 (FT4) concentrations and low end of normal range of T3 without increasing TSH, mimicking central hypothyroidism. The mechanism for this change in thyroid function is still unclear and it is possible that these drugs interfere with hypothalamic regulation. The clinical significance of the reduction in FT4 is also unknown as many patients are clinically euthyroid. Fatigue is the most common complaint among patients taking antiepileptic drugs and may be misdiagnosed as a symptom of hypothyroidism. **Case report:** A 76-year-old male patient presented with dizziness, dyspnea on moderate exertion and sinus bradycardia (heart rate of 51 bpm). He also reported intolerance to cold and hair loss in recent months. The patient has been diagnosed with trigeminal neuralgia since 2015 and has been taking oxcarbazepine since 2020, currently at a dose of 1,500 mg/d. He also has systemic arterial hypertension, pre-diabetes, dyslipidemia and prostate cancer and takes gabapentin 1,200 mg/d, amitriptyline 25 mg/d, enalapril 10 mg/d and atorvastatin 40 mg/d. On physical examination, he presented slowed speech, body mass index of 25.8 kg/m² and a normal palpable thyroid. Thyroid function revealed repeated low FT4 0.77 ng/dL (NR 0.93- 1.7) and an inappropriately normal TSH of 2.09 mIU/L (NR 0.35- 4.94). Total T4 and T3 were also low. Other pituitary hormones were all within normal range. There was no lesion at the hypothalamic and pituitary area at magnetic resonance and the cerebral cortex showed a pattern compatible with aging. As neurology evaluation contraindicated suspension of the medication, levothyroxine was started at a low dose (25 mcg/day) with normalization of thyroid function. **Discussion and conclusion:** Central hypothyroidism occurs in about 20% of patients taking oxcarbazepine or carbamazepine, and it is not related with dosage. Therefore, it is important to monitor thyroid function before and during its use. If central hypothyroidism is identified, it is recommended to change to another antiepileptic drug. If it is not possible and the patient has symptoms of hypothyroidism, levothyroxine therapeutic trial is suggested as an attempt to improve symptoms.

130617 – ACUTE TOXIC HEPATITIS INDUCED BY THE USE OF METHIMAZOLE: A CASE REPORT

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Introduction: Hyperthyroidism is a disease that presents with increased production of thyroid hormones and is most commonly treated with antithyroid medication. Among these, methimazole, an inhibitor of the enzyme thyroperoxidase, stands out as a drug with a good safety profile and comfortable dosage for the patient. Drug hepatitis caused by the use of this medication is an uncommon condition which can lead to serious consequences. **Case report:** Female, 51 years old, with nausea and diffuse abdominal pain, no apparent triggering factors, jaundice, choluria and fecal acholia, hospitalized for suspected severe acute hepatitis. The patient denied alcohol consumption and had negative serological tests for hepatotropic viruses and autoimmune liver diseases, and reported previous diagnosis of hyperthyroidism, taking methimazole with good clinical control. Her thyroid was globose and palpable, without apparent nodules, and mobile on swallowing. Laboratory tests showed high levels of transaminases and direct bilirubin, with the following values: aspartate aminotransferase (AST) = 317; alanine aminotransferase = 762; alkaline phosphatase (AF) = 589, gamma glutamyl transpeptidase = 203; direct bilirubin = 17; indirect bilirubin = 9. Methimazole was discontinued and corticosteroid therapy was started due to the severity of the liver markers. Therefore, there was progressive laboratory improvement and a liver biopsy was carried out, strengthening suspicions of methimazole toxicity. Corticosteroid doses were progressively reduced and the patient was discharged in 1 month, but without compensation of thyroid function. The patient was followed up for treatment with radioiodine (I131). **Conclusion:** It is vital that patients with hyperthyroidism taking methimazole are monitored regularly, especially with regard to their liver function, due to the potential for hepatotoxicity of this drug. Although this condition is rare, attention should be paid to the signs that may indicate drug hepatitis, so that the diagnosis can be made early and the drug can be discontinued.

130613 – DIAGNOSIS AND MANAGEMENT OF HASHIMOTO'S ENCEPHALOPATHY: A CASE REPORT

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Introduction: Hashimoto's encephalopathy (HE) is a rare condition that mostly affects women. The cause of HE is not yet fully understood. Its diagnosis is made on the basis of a strong clinical suspicion based on the patient's history, as well as the exclusion of infections and other metabolic, toxic or tumour-related disorders. The presence of high levels of anti-thyroid antibodies and alterations in the cerebrospinal fluid corroborate the diagnosis. The clinical presentation of this condition involves myoclonus, altered state of consciousness, rapid cognitive decline and neuropsychiatric symptoms. This condition is a potentially reversible cause of dementia, as it can be resolved with appropriate treatment. **Case report:** Female, 48-year-old, retired, referring behavioural changes, psychomotor agitation, mental confusion, difficulty concentrating and tremors in extremities for 6 months, with a progressive worsening of symptoms in the last month. Reports difficulty carrying out her daily activities, such as eating and bathing, as well as auditory hallucinations. The patient was admitted to the emergency department due to a generalized seizure on the same day. She had previously been diagnosed with hypothyroidism and was taking levothyroxine daily. She underwent an extensive investigation with tests to exclude infectious, immunological causes or metabolic disorders. No alterations were found on brain magnetic resonance imaging (MRI) and electroencephalogram. Analysis of the cerebrospinal fluid revealed hyperproteinaemia. Laboratory tests showed increased levels of anti-thyroid antibodies (anti-TPO and anti-thyroglobulin). The hypothesis of Hashimoto's encephalopathy was raised, and the patient was given methylprednisolone pulse therapy, with rapid improvement of the symptoms. Therefore, the patient was discharged and continued to be followed up as an outpatient. **Conclusion:** HE is a subacute condition which, although rare and with heterogeneous presentations, should be suspected early in the presence of characteristic symptoms, so as not to delay diagnosis and worsen the patient's prognosis. Thus, complementary tests, such as MRI and laboratory, are extremely important for excluding other possible causes of encephalopathy and to reach the right diagnosis to offer the best treatment to the patients.

130610 – DIFFICULT-TO-TREAT HYPERTHYROIDISM DIAGNOSED DURING PREGNANCY, CONVERTED TO HYPOTHYROIDISM AFTER RADIOIODINE TREATMENT: CASE REPORT

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Introduction: During pregnancy, especially in the first trimester, the maternal organism experiences an increase in the hypothalamic-pituitary-thyroid axis stimulation, resulting in lower concentrations of TSH. Thus, a common diagnosis in this period is transient thyrotoxicosis (GTT), which is limited to the first half of pregnancy and does not require anti-thyroid drugs. However, a small group of predisposed women may develop Graves' disease during pregnancy, characterized by overt hyperthyroidism with TSH < 0.1 mIU/L and elevated T4L. **Case report:** D.L.O., 32 years old, was diagnosed with hyperthyroidism in the 18th week of gestation with TSH = 0.012, T4L = 2.24 and TRAB = 4.06, asymptomatic, initiating treatment with methimazole (MMZ). Entering the 35th week, T4L levels reached normality and the medication was discontinued. However, symptoms such as sweating, palpitations, and insomnia recurred after birth, which led to the resumption of treatment. She continued to be monitored without normalization, when Propranolol and optimized doses of MMZ were added to the treatment. Nevertheless, the patient developed new symptoms, such as lower limb edema, scleral erythema and pain on ocular movement, marking an intense relapse of hyperthyroidism without response even with maximum dosage of MMZ. Due to the refractoriness of drug treatment, and with the aim of studying the possibility of treatment with radioactive iodine (I131), thyroid ultrasound and subsequently thyroid scintigraphy were requested. Therefore, treatment with I131 was performed, achieving euthyroid function. During follow-up, she complained of brittle nails and hair, and generalized fatigue, which led to the diagnosis of symptomatic hypothyroidism, confirmed by T4L = 0.64, TSH = 11.02. Treatment with Levothyroxine was initiated, reaching laboratory control and symptom improvement. **Conclusion:** Even though hyperthyroidism during pregnancy is not uncommon, the recurrence of the condition after labor, without any drug response, deserves special attention. The use of I131 can be considered as the first therapeutic choice in hyperthyroidism patients with recurrence or difficult control by drug treatment, as in the presented case. This choice, besides being well-tolerated, achieves a response rate of up to 90%, with the development of euthyroidism or hypothyroidism, which is the main side effect.

130563 – ELEPHANTIASIC PRETIBIAL MYXEDEMA – A RARE EXTRATHYROIDAL MANIFESTATION OF GRAVES' DISEASE: TWO CASE REPORTS

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Introduction: Thyroid dermatopathy or pretibial myxedema (PTM) is a rare and late manifestation observed in Graves' disease (GD). It has a prevalence of 0.5%-4.3% and generally occurs concomitantly with Graves' orbitopathy (GO). Similar to what happens in GO, in PTM, glycosaminoglycans are secreted by fibroblasts stimulated by anti-TSH receptor antibodies (TRAb) and IGF-1, in addition to local cytokines. The elephantiasis form of MPT is rare (<1% of cases) and occurs in later stages due to deficiency in local lymphatic drainage. **Case report:** Case 1: Man, 45 yo, presented with weight loss (40 kg), sweating, insomnia, and diffuse goiter for 5 years. Laboratory tests confirmed thyrotoxicosis due to GD – TRAb > 40 U/L (ref < 1.75). He was treated with methimazole for 3 months and referred for total thyroidectomy due to a large goiter. Six months after surgery, he developed GO with inflammatory activity – Clinical Activity Score (CAS) of 5 – being treated with radiotherapy (2,000 cGy) and systemic corticosteroids. Alongside, he began to present skin thickening in pretibial region, like an orange peel, which progressed to the dorsum of his feet, with hard and noduliform appearance. Lymphoscintigraphy of the lower limbs revealed a bilateral lymphatic drainage deficit, confirming the elephantiasis form of MPT. Case 2: Woman, 69 yo, former smoker. Diagnosis of GD at the age of 42 (1997), TRAb > 400 IU/L (<1.22), presented with hepatitis secondary to anti-thyroid medication, and radioiodine was indicated. She developed hypothyroidism after 2 years and started on levothyroxine. Three years after diagnosis, the patient developed skin thickening in the pretibial region and GO in 2011 (CAS = 3). She was treated with radiotherapy (2,000 cGy) and systemic corticosteroids. A biopsy of the MPT region revealed interstitial mucin with blood vascular ectasia. Despite the use of multiple first-line therapies for MPT with intralesional, topical, and systemic corticosteroids, both cases evolved with an unsatisfactory response. They are currently undergoing immunomodulator therapy programming. **Conclusion:** GD complicated with MPT is rare. Treatment involves risk factor modifications and intralesional/topical or systemic corticosteroids. However, they are often poorly responsive, requiring evaluation of more specific therapies such as immunomodulators. These cases highlight the importance of continuous monitoring of GD complications after definitive treatment and maintenance of euthyroidism.

130364 – THYROID FUNCTION AND INCIDENCE OF INCREASED CAROTID INTIMA-MEDIA THICKNESS: RESULTS FROM ELSA-BRASIL COHORT STUDY

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Introduction: Recent literature highlights the intricate link between thyroid function and atherosclerosis, particularly emphasizing its influence on carotid intima-media thickness (cIMT). However, the studies yielded contradictory results in terms of subclinical thyroid dysfunction influencing atherogenesis and increased cardiovascular risk. **Objective:** Thus, we aimed to investigate the association between thyroid function and incidence of increased carotid intima-media thickness (cIMT) in men and women, euthyroid or with subclinical conditions, from the ELSA-Brasil study. **Methods:** This is a prospective cohort study using baseline and 8-year-follow-up data of men (n = 2,057, 48.1 ± 7.9 years old) and women (n = 2,857, 48.8 ± 7.7 years old), without history of cardiovascular disease. Fasting serum TSH, FT4, and FT3 were determined and quintiles were calculated. We included euthyroid participants (TSH 0.4-4.0 mIU/L and no use of levothyroxine and anti-thyroid medication), and participants with subclinical conditions. Baseline levels of cIMT ≥ 0.68 (75th percentile) were classified as "increased cIMT". Incidence of increased cIMT was defined as baseline cIMT0.05). Results remained the same in the sensitivity analyses, except for the association between FT3 and incident cIMT for euthyroid women. **Conclusions:** Individuals, especially women, with lower levels of TSH and FT3 were associated with higher risk of developing increased cIMT. The findings may suggest an influence of thyroid function on atherogenesis.

130515 – RELAPSE OF HYPERTHYROIDISM DUE TO GRAVES' DISEASE PRESENTING AS TOXIC ADENOMA

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Introduction: Toxic nodular goiter (TNG) and Graves' disease (GD) are frequent causes of subclinical hyperthyroidism. Besides antibodies against TSH receptor (TRAb), scintigraphy and radioisotope uptake scan are valuable tools for differential diagnosis. In GD, diffuse and high uptake are frequently seen, whereas in TNG, focal areas with hyper and hypofunction ("hot" and "cold") areas. Here we describe a patient with GD relapsed as TNG. **Case report:** A 70-year-old woman presented with palpitations, tachycardia, tremors, and unintentional weight loss over the past year, with no ophthalmopathy, goiter, or dermopathy. She has a past history of smoking and no familial history of thyroid disease. No amiodarone and other drugs that affect thyroid function were reported. Laboratory evaluation revealed subclinical hyperthyroidism: TSH < 0.02 µIU/mL (NR 0.27-4.2), normal free T4 (FT4) and T3 with positive TRAb 2.63 IU/L (NR < 1.75). Thyroid ultrasound (US) demonstrated heterogeneous parenchyma with diffuse increase in vascularization, normal volume, and an isoechogenic solid nodule in the upper third of the right lobe with well-defined margins and no calcifications measuring 0.6 x 0.4 x 0.3 cm. Scintigraphy identified diffuse and high uptake, reinforcing the diagnosis of GD. The patient was treated with methimazole (20 mg/d), with progressive reduction until suspension after three years when TSH and FT4 levels were normal, and negative TRAb. However, after six months, she relapsed to subclinical hyperthyroidism, with consistently negative TRAb. A new thyroid scintigraphy revealed a focal "hot" area in the middle third of the right lobe, suggestive of TNG. Thyroid US showed a solid-cystic, hypoechoic nodule with ill-defined margins and macrocalcifications measuring 1.4 x 1.2 x 0.9 cm corresponding to the "hot" nodule. The patient was submitted to radioiodine therapy with 29.8 mCi, and scintigraphy after 3 months demonstrated normal and homogeneous thyroid uptake. Levothyroxine treatment was initiated for hypothyroidism. **Discussion and conclusion:** Relapse of GD occurs in 25%-50% of cases after discontinuation of antithyroid drug treatment. Although there are documented cases of GD developing after radioiodine therapy for TNG, the opposite scenario has not been reported in the literature. Clinicians should be alert for hyperthyroidism relapse in patients with GD and perform an accurate differential diagnosis to provide the appropriate treatment.

130564 – EXPOSURE TO THE ORGANOCHLORINE PESTICIDE P,P'-DDE DURING THE INTRAUTERINE PERIOD DISRUPTS THE HYPOTHALAMUS-PITUITARY-THYROID AXIS FUNCTION OF THE OFFSPRING RATS DURING ADULTHOOD THROUGH EPIGENETIC MECHANISMS

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Introduction: Dichlorodiphenyldichloroethylene (DDE) is a persistent organic pollutant and the main metabolite of dichlorodiphenyltrichloroethane (DDT), which was banned in several countries, but is still used to control mosquitoes that spread malaria. DDE is an endocrine disruptor that impairs thyroid function in humans and rodents. However, the impact of DDE exposure during critical development periods on thyroid function programming was never reported. **Objective:** To investigate the effects of intrauterine exposure to DDE on the hypothalamus-pituitary-thyroid (HPT) axis gene expression and function of the adult offspring rats. **Methods:** Pregnant Wistar rats were orally exposed or not to 0.1 or 1 mg/kg/day of DDE throughout the gestation. Offspring rats were euthanized at postnatal day 90. The hypothalamus, pituitary, thyroid, and serum were collected. Gene and protein expression was evaluated by RT-qPCR and Western Blotting. Thyroid histology was assessed and T4 levels were measured by ELISA. **Results:** DDE exposure significantly decreased TRH gene/protein expression in the hypothalamus. DDE-exposed male rats presented increased Tshb mRNA expression but decreased TSHB protein content in the pituitary. In the females, Tshb mRNA and protein contents were reduced in DDE-exposed animals. Moreover, the genes/protein expression of two key proteins involved in thyroid hormone synthesis, NIS and TPO, was decreased in DDE-exposed animals. In agreement, T4 and T3 serum levels were reduced in these animals. Regarding thyroid morphology, DDE-treated animals exhibited both destroyed follicles and enlarged follicles with squamous cells filled with more, especially in the highest DDE treatment dose. Interestingly, the thyroid expression of enzymes involved DNA methylation (Dnmt3b), histone deacetylation (Hdac3), and histone methylation (Ezh2, Kdm5c) were increased in the DDE-exposed males. Conversely, thyroid expression of histone acetyltransferase (Hat1) and demethylase (Kdm6a) was decreased in these animals. In agreement, the thyroid of DDE-exposed animals presented increased levels of methylated histone H3 in the lysines 9 and 27 and reduced content of acetylated histone H3. These results are coherent with the decreased transcriptional activity observed in the thyroid. **Conclusion:** DDE exposure during a critical development period disrupted the HPT axis function and increased the susceptibility of the offspring rats to develop hypothyroidism during adult life.

130561 – POLYCHLORINATED BIPHENYLS EXPOSURE DURING THE INTRAUTERINE PERIOD DISRUPTS THE HYPOTHALAMIC-PITUITARY-THYROID AXIS OF F1 GENERATION RATS DURING ADULTHOOD THROUGH EPIGENETIC MECHANISMS

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Introduction: Polychlorinated biphenyls (PCBs) exposure disrupts the hypothalamic-pituitary-thyroid (HPT) axis function of exposed humans and rodents. However, the consequences of PCBs exposure during critical development windows have never been reported. **Objective:** To investigate the impact of intrauterine exposure to PCBs on the HPT axis programming and function of F1 generation animals during adulthood. **Methods:** Pregnant Wistar rats were orally treated with corn oil (control) or corn oil supplemented with 50 or 500 µg of Aroclor 1254 (a mixture of PCBs)/kg/day during the gestational period. Offspring rats were euthanized on PND90. The hypothalamus, pituitary, thyroid, and liver were collected. Gene and protein expression was evaluated by RT-qPCR and Western Blotting. Thyroid histological analysis was performed, and T3/T4 levels were measured by ELISA. **Results:** Intrauterine exposure to PCBs significantly reduced the mRNA/protein content of TRH and TSHB in the hypothalamus and pituitary, respectively, of male and female F1 offspring rats. PCB exposure has increased thyroid gene/protein expression of NIS, TPO, TG, and MCT8 in the thyroid of male and female F1 adult rats. In agreement, T4 and T3 levels were increased in PCB-exposed animals. Thyroid follicles of female and male PCB-exposed animals were enlarged and filled with higher amounts of TG than the follicles of the control rats. Inflammatory cell infiltration was also observed, especially in the female rats' thyroid. Interestingly, epigenetic alterations commonly involved in the activation of transcription, such as decreased DNA methylation, reduced content of trimethylated histone H3 at the lysine 9 and 27, and increased content of acetylated histones H3 and H4 were observed in the thyroid of PCB-exposed animals in comparison to the control group. The expression of Sult1e1, an enzyme involved in the peripheral degradation of thyroid hormones, was decreased in the liver of PCB-exposed offspring rats, while the expression of transthyretin, the main rat protein involved in the plasma transport of thyroid hormones, was reduced in the liver of PCB-exposed female F1 adult rats. **Conclusions:** Epigenetic mechanisms involved in the activation of transcription seem to be involved in the increased thyroid gene/protein content of PCB-exposed animals. Finally, the results suggest that intrauterine exposure to PCBs leads to hyperactivation of the HPT axis in F1 generation animals during adulthood.

130578 – CHILDHOOD HYPOTHYROIDISM AND ITS RELATIONSHIP WITH MOTOR DELAY AND MUSCLE WEAKNESS: CASE REPORT

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Introduction: Hypothyroidism is the clinical condition resulting from the insufficient production of thyroid hormones, which modulate the metabolism of almost all tissues in the body, playing a critical role in the child's development and growth. Therefore, prompt recognition and treatment of hypothyroidism in childhood is essential. **Case report:** Patient 3 years old, female, with negative heel prick test in neonatal screening. The mother reports that the child at birth showed no changes, but at six months of age she noticed that the child was unable to maintain balance and strength to sit, had difficulty keeping the tongue inside the mouth and did not respond to stimuli. When taking her to the pediatrician, tests were requested and a diagnosis was made of hypothyroidism, anemia, changes in liver enzymes and renal function enzymes and increased CPK. In addition, pituitary resonance imaging was performed, which did not detect changes, ruling out central hypothyroidism. Therapy with levothyroxine sodium, physiotherapy, hippotherapy, occupational therapy and swimming was immediately started. Therefore, with the set of stimuli associated with the medication, it was possible to reach the recommended level of thyroid hormones, but she still has high muscle weakness and motor delay. She was referred to a neurologist and after tests, neuromuscular syndromes and autism were ruled out and she had no genetic alterations. Over time, the child learned to sit, but had difficulty learning to speak and formulate sentences; he is a child who gets tired easily when playing. Today, at three and a half years old, he has a childish face, thin, short hair and a bulging abdomen. Upon reaching the age of four, the patient will undergo a growth hormone test. **Conclusion:** Hypothyroidism is a recurrent disease in pediatric routine. In this case, it is not yet known what caused the hypothyroidism, it is estimated that there is a problem linked to growth hormone, tests will still be carried out in order to discover the reasons for the child's motor delay and be able to provide them with a better quality of life.

130526 – THE ROLE OF OVERWEIGHT AND OBESITY IN THE QUANTIFICATION OF THYROID HORMONES IN AN OBSTETRIC INTENSIVE CARE UNIT

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Introduction: Thyroid hormone profile evaluation in intensive care unit (ICU) patients is not encouraged. In the context of pregnancy, this is even more complex due to the physiological changes that make the interpretation of these results even more difficult. However, in several everyday situations, this quantification is necessary. This work aimed to review all hospitalizations carried out in the obstetric ICU that led to the quantification of thyroid hormones. **Method:** The retrospective study evaluated 1,425 ICU hospitalizations. Of these, 160 participants who underwent hormone measurements during hospitalization and were not being treated for thyroid diseases were included. The clinical and laboratorial data were recorded, including complications during hospitalization and body mass index (BMI). TSH and free T4 (FT4) were measured with Cobas Roche Elecsys kits. The patients were divided into groups based on body mass index (BMI) and gestational age graphs with weight evolution curves during pregnancy. The groups of weight adequacy based on those criteria were low, normal, overweight, and obesity. Statistical analysis used Kruskal-Wallis's test, Spearman's correlation, Logistic Regression, and ROC curve to calculate the area under the curve (AUC). **Results:** After analyzing several associated factors, the patients were divided into groups, but three did not have their BMIs recorded. Of the 157 patients studied, 43 (27.4%) were classified as having an adequate BMI, 18 (11.5%) the BMI was low, 47 (29.9%) were overweight, and 49 (31.2%) were obese. The TSH values present differences among the groups: Low *vs.* Overweight (p: 0.013), Low *vs.* Obesity (p: 0.014), Normal *vs.* Overweight (p: 0.017), and Normal *vs.* Obesity (p: 0.018). No difference was observed in FT4. A correlation was found between BMI and TSH (rs: 0.261, p: <0.001) and with FT4 (rs: -0.191, p: 0.017). On subgroup analysis, only in the obese group, TSH presented the same pattern (rs: 0.283, p: 0.048). The combined analysis of BMI and FT4 reached an AUC of 0.993 in predicting fetal death, 0.927 for respiratory distress, and 0.868 for uterine bleeding. In contrast, when combined, TSH did not increase the isolated probability, except for the psychic disturbances (AUC: 0.801). **Conclusion:** Our results show that overweight and obesity represent a cause of elevated TSH in the Obstetric ICU, and is well known that they are highly prevalent in Brazil. The combined analysis suggests an incremental risk in the combined scenario.

130568 – PROGNOSTIC FACTORS OF RESPONSE TO RADIOIODINE THERAPY IN PATIENTS WITH GRAVES' DISEASE

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Introduction: Radioiodine (RAI) therapy is a definitive treatment option in Graves' disease (GD) with high success rates and lower complication rates. If hyperthyroidism due to GD persists after 6-12 months following RAI therapy, retreatment with this therapy may be required. **Objective:** To evaluate the clinical and laboratory characteristics of patients with GD who underwent RAI, as well as to identify prognostic factors related to the therapeutic response to RAI. **Methods:** An observational and retrospective study was conducted. Patients over 18 years old with GD followed at the outpatient clinic of a tertiary care service were selected. Patients diagnosed with hypothyroidism within 12 months after RAI therapy were considered responders. **Results:** A total of 59 patients were included in the study. The mean age at diagnosis was 43.5 years ± 14.4 years, with 50 (84.7%) women. Forty-eight (81.4%) patients responded to RAI therapy, while 11 (18.6%) patients did not. Most patients (87.5%) responded to RAI therapy with thyroid hormone replacement between 3 and 6 months. When the clinical-laboratory factors were compared between RAI non-responders *versus* responders, it was observed that the median of TrAb values 29.5 UI/L [7.5; 34.7] *vs.* 9 UI/L [2; 14.5], p-value = 0.02; and the thyroid volume on ultrasound 35 cm^3 [27.8; 49] *vs.* 22.5 cm^3 [15.3; 31.5], p-value = 0.018, were significant higher in non-responders patients. **Conclusion:** Our results confirm that RAI is an effective therapy for GD, leading to hypothyroidism within 3-6 months of therapy on the majority of patients. Higher thyroid volume and TrAb levels are the main risk factors for non-response to radioiodine therapy.

129452 – ALLAN-HERNDON-DUDLEY SYNDROME – A CASE REPORT

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Introduction: Allan-Herndon-Dudley syndrome (AHDS), linked to the X chromosome, is a deficiency of the thyroid hormone transporter monocarboxylate 8 (MCT8), due to mutation in the SLC16A2 gene. MCT8 is a specific thyroid hormone transporter that is crucial for transport of T3 and T4 into tissues. It's highly expressed in brain cells but heart, muscle, liver and kidneys express less MCT8. This results in central hypothyroidism and peripheral thyrotoxicosis. This syndrome is rare, affecting 1/70000 boys, with neurological deficiencies such as profound neurodevelopmental delay, intellectual motor disability, extrapyramidal signs, seizures and thyroid alterations. Peripheral thyrotoxicosis leads to tachycardia, hypermetabolism and progressive weight loss. **Case report:** 4 years and 10 months old, male, genetically diagnosed with AHDS (at the age of 3) due to muscle weakness and delayed cognitive and motor development. Pregnancy was uneventful. Inability to suck breast milk, tube fed for 8 days after birth. Follows objects, has a social smile, interacts with his eyes, doesn't crawl or sit. Parents deny seizures. Referred for assessment of thyroid function alterations. Weight 12.35 kg (-3SD); height 95 cm (- 3SD). No cardiovascular or respiratory alterations, no tachycardia, typical male genitalia. Generalized muscular hypotonia, no head support. TSH 8.990 mU/L (RV 0.4-5.2); total T3 336.7 ng/dL (RV 105-269); total T4 7.6 ng/dL (RV 5.95-14.7). Results confirmed in a second blood collection and antithyroid antibodies negative. It was intended to start triiodoacetic acid (Triac), a T3 analogue, with the objective to reduce the symptomatology of peripheral hyperthyroidism (absent in this patient) and impact the deficit on the development of the central nervous system. The access to this medication was not viable. **Conclusion:** AHDS requires multidisciplinary management. Its morbidity and mortality are high and imprecise, depending on its clinical evolution. There are few studies on progression, outcomes and treatments. In Triac use, the hormone is internalized into the cells without MCT8 action. Once inside the cell, the analogues minimize the actions of the hormones and carry out their physiological functions. However, there is little scientific evidence to support its clinical management, and more studies are needed on AHDS and its repercussions. As TSH levels are generally low, diagnosis by neonatal screening programs can fail when only TSH is used for screening.

129386 – NEONATAL HYPERTHYROIDISM INDUCED BY TRANSPLACENTAL PASSAGE OF TRAB: CASE REPORT

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Introduction: Neonatal hyperthyroidism (NH) is present in less than 5% of neonates born to mothers with Graves' disease (GD) due to transplacental passage of TRAb in the pregnancy's second half. The fetus' TSH receptors become responsive around the 20th gestational week. This may induce fetal hyperthyroidism (FH), which can lead to abortion, prematurity, intrauterine growth retardation, tachycardia, heart failure, hydropsis, bone maturity acceleration, craniosynostosis and goiter. TRAb levels may increase in pregnant GD patients treated with thyroidectomy, RAI or antithyroid drugs, however, the chance of ongoing production of TRAb is higher in those who received RAI when compared to surgery. **Case report:** The report addresses the case of a newborn male patient whose mother was diagnosed with GD 7 years prior to the pregnancy and submitted to treatment with methimazole (MMZ) and propranolol for two years. RAI was administered and she developed hypothyroidism, however, TRAb levels remained positive. Between the 23rd-24th gestational weeks fetal tachycardia and slightly enlarged thyroid were observed through ultrasound. As the mother presented TRAb levels 8 times the upper limit of the reference interval, the diagnosis of FH was established and propylthiouracil was initiated. The fetus evolved with improvement of the cardiac parameters and reduction of the goiter. Although the Cesarean section was performed without complications at 38 weeks, the baby developed upper gastrointestinal bleeding, gastric stasis, tachycardia and worsening of the respiratory status with the need of mechanical ventilation. As he presented TRAb positivity and hyperthyroidism, propranolol and MMZ (0,4 mg/kg/day) were initiated. MMZ dose was reduced to 0,2 mg/kg/day as his general condition improved and the drugs were suspended when hypothyroidism and TRAb negativity were reported on exams, however, after one week his thyroxine levels increased to 12 ng/dL and the initial MMZ dose was reintroduced. The patient is currently 3 months old and has been presenting an effective thyroid function so far. **Conclusion:** It's important to evaluate TRAb and thyroid function of pregnant women with history of GD, mainly on the first gestational trimester and after the 20th week, besides monitoring the fetus' parameters through ultrasound. Early diagnosis and proper treatment of FH are essential to avoid complications. Often NH is solved in 3-16 weeks after birth with elimination of maternal TRAb.

130325 – THYROID HORMONE HOMEOSTASIS LEVOTHYROXINE-TREATED PATIENTS: FINDINGS FROM ELSA-BRASIL

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Introduction: The effectiveness of levothyroxine (LT4) in restoring thyroid hormone (TH) homeostasis, particularly serum thyroxine (T4) and triiodothyronine (T3) levels, remains debatable. **Objective:** To assess TH homeostasis in LT4-treated individuals using data from the Longitudinal Study of Adult Health in Brazil (ELSA-Brasil) study. **Methods:** The ELSA-Brasil study follows 15,105 adult Brazilians (aged 35 to 74 years) over 8.2 years (2008-2019) with 3 observation points assessing health parameters including serum thyroid stimulating hormone (TSH), free T4 (FT4), and free T3 (FT3) levels. We analyzed 186 participants that initiated treatment with LT4 during the study, and 243 individuals continuously treated with LT4 therapy. **Results:** Initiation of therapy with LT4 resulted in a 11-19% decrease in TSH, a ~19% increase in FT4, and a 7% reduction in FT3 serum levels (FT3 dropped > 10% in ~40% of the LT4-treated patients). This was associated with an increase in triglyceride levels and utilization of hypolipidemic and anti-diabetic medications. Participants continuously treated with LT4 exhibited a stable elevation in serum FT4 and, a reduction in serum FT3 and TSH levels. While 115 participants (47.3%) had at least one serum FT4 levels above the control reference range (>1.52 ng/dL), 38 participants (15.6%) had at least one serum FT3 below the reference range (<0.23 ng/dL). **Conclusion:** The present results challenge the dogma that treatment with LT4 for hypothyroidism restores TH homeostasis in all patients. A substantial number of LT4-treated patients exhibit repeated FT4 and FT3 levels outside the normal reference range, despite normal TSH levels. Further studies are needed to define the clinical implications of these findings.

130288 – DUOX2 GENE VARIANTS IN CONGENITAL HYPOTHYROIDISM DUE TO THYROID DYSGENESIS: FUNCTIONAL AND *IN SILICO* ANALYSIS

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Introduction: Congenital hypothyroidism (CH) is the most common cause of preventable intellectual disability. Its etiology is divided into dyshormonogenesis and dysgenesis (TD). DUOX2 protein is located in the apical membrane of thyrocytes and, together with DUOXA2, is responsible for generating H2O2 for thyroid hormone (TH) synthesis. Previously, we identified five rare variants in the DUOX2 gene in patients with TD, four SNPs and one deletion which generates a smaller truncated protein. DUOX2 variants have recently been associated with TD. **Objective:** This study aimed to perform *in vitro* functional analysis and three-dimensional protein modeling of the five DUOX2 variants identified in CH patients with TD. **Methods:** The site-directed mutagenesis technique was used to introduce the variants (c.C1268T, c.G1547A, c.2895_2898del, c.G3367A and c.A3509C) into a plasmid containing the wild type WT-DUOX2 cDNA. The HEK293A cells were co-transfected along with mutated plasmids and DUOXA2 plasmid. After 48 hours, H2O2 generation was quantified using Amplex UltraRed reagent. As a control, plasmids containing WT-DUOX2 and DUOXA2 genes were also co-transfected. Softwares I-TASSER, ClusPro, and KFC2 were used for three-dimensional modeling and interaction patterns analysis. **Results:** All variants into the DUOX2 were confirmed by Sanger sequencing. Cells containing the deletion c.2895_2898del plasmid generated lower amount of H2O2 compared to the WT-DUOX2 transfected cells, while the amount of H2O2 generated by the c.C1268T, c.G1547A, c.G3367A and c.A3509C DUOX2 variants was like the control. *In silico* study showed a conformational change in all DUOX2-variants models compared to WT-DUOX2. Alterations in DUOX2/DUOXA2 interaction region and a decrease in hydrogen bonds number were also detected. **Conclusions:** The DUOX2 deletion variant may contribute to TD development due to its altered activity as well as the possible disturbance of three-dimensional structure and DUOXA2 interaction. Considering previous evidence that has shown the enrollment of DUOX2 in proliferation, migration, invasion metastasis and wing dysgenesis, the other variants also may contribute to TD development, considering the possible alterations observed through computational study, even if no change in hydrogen peroxide generation was observed. However, further functional tests are needed to confirm the real effect of DUOX2 variants in thyroid development.

130016 – CHANGES IN THE TREATMENT OF GRAVES' DISEASE, A 20-YEAR JOURNEY

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Graves' disease (GD), the most common cause of endogenous hyperthyroidism, can cause substantial morbidity. Despite about 60 years of experience in the use of antithyroid drugs (ATD) and therapeutic dose iodine (DTI) for the treatment of GD, the decision between therapies varies considerably within and between countries. The aim of this study was to analyze the change in the treatment strategy of GD patients followed up at a single institution in two consecutive periods: group A diagnosed between 2002 and 2010 and group B between 2011 and 2023 retrospectively. Variables such as DAT (methimazole) use, duration of use, maximum dose as well as DTI prescription, prescribed activity, time of DAT use until DTI were analyzed, and compared between the two groups studied. A total of 597 patients were diagnosed with GD during the study period. In group A, with 248 patients, the mean time of DAT use was 26.9 months, the maximum dose was 27.8 mg, and the time of DAT use before DTI was 26.9 months. In group B, with 316 patients, the mean time of DAT use was 30.1 months ($p < 0.002$), the mean maximum dose was 25.4 mg ($p < 0.04$), and the mean time of DAT use before DTI was 30.1 months ($p < 0.002$). Regarding the differences between the therapeutic modalities between the groups, in group A, 97.5% of the patients underwent DAT, 64% underwent DTI, and 4.7% underwent surgery. In group B, 99.7% of the patients underwent ATD, 14.6% underwent DTI, and 2.8% underwent surgery. When comparing which therapeutic modality was successful between the two groups, in group A, 73.2% achieved it through DTI and 23.2% through DAT. In group B, 32.7% by DTI and 59.3% by DAT ($p < 0.001$). In conclusion, there was a trend of change in the therapeutic approach to GD, characterized by the prolongation of the use of DAT at substantially lower doses, in contrast to the extension of the use of DTI among patients. In addition, there is a significant decrease in the prescription of DTI. These data show an inclination towards preference for the use of ATDs in the care of patients with GD.

130422 – HIGH THYROID STIMULATING HORMONE: A CASE OF HASHIMOTO'S THYROIDITIS ASSOCIATED WITH MACRO-TSH

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Introduction: Thyroid function evaluation is becoming increasingly frequent, and subclinical hypothyroidism is commonly diagnosed. Causes of interference in thyroid-stimulating hormone (TSH) measurement should be considered when faced with persistently elevated TSH and normal Free T4 (FT4), especially if associated with negative antibodies and absence of clinical symptoms, preventing the side effects of unnecessary treatment. **Case report:** A 47-year-old female patient with a diagnosis of primary hypothyroidism (Hashimoto's thyroiditis) in 2005, with TSH 112 µUI/mL and FT4 0.37 ng/dL (0.7-1.8) at the time, presented with clinical symptoms, elevated antibodies, and thyroid ultrasound showing signs of thyroiditis. She started treatment with levothyroxine (LT4) and had adequate control of TSH and thyroid hormones in the following years. In 2011, she had normal TSH and FT4 levels while on LT4. She was lost to follow-up with the specialist and returned in 2020 with TSH 70.4 and FT4 2.6 (0.7-1.8). She complained of fatigue, irritability, anxiety, and insomnia. Despite numerous titrations of LT4 doses and proper medication use, she maintained elevated TSH levels (50 to 150), without suppression even with FT4 above the normal reference range. Possible causes of difficult-to-control TSH were investigated, including a Macro-thyrotropin (macro-TSH) test: 35% (<40%: presence of macro TSH), in addition to a diagnosis of atrophic gastritis. **Conclusion:** Macro-TSH is caused by a large amount of monomeric TSH complexed with anti-TSH antibodies. Macro-TSH is a rare condition, resulting in persistently elevated TSH, but biologically inactive, not recommended for treatment. However, in this case, since the patient had a confirmed diagnosis of primary hypothyroidism for over a decade, levothyroxine use was maintained, and dose adjustment was made without considering the TSH value, aiming to keep FT4 in the upper half of the reference range, when the patient remained asymptomatic.

130404 – GESTATIONAL TRANSIENT THYROTOXICOSIS COMPLICATED BY THYROID STORM IN TWIN PREGNANCY: A CASE REPORT

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Introduction: Gestational transient thyrotoxicosis (GTT) is a condition characterized by reduced thyroid-stimulating hormone (TSH), with or without elevated free thyroxine (FT4). The elevation of human chorionic gonadotropin (hCG) at the beginning of pregnancy is the cause of thyroid stimulation, causing mild and transient hyperthyroidism, which may be associated with hyperemesis gravidarum. There is a greater risk for GTT in conditions of high concentration of hCG, such as twin pregnancy, hydatidiform mole and choriocarcinoma. **Case report:** A 27-year-old white woman with 13 weeks of twin pregnancy (primigravida) was brought to the emergency room due to suspected hyperemesis gravidarum, presenting with nausea and vomiting that had lasted two weeks, associated with the loss of 12 kilos during the period. Upon admission, the patient appeared sluggish, with crackling sounds on lung auscultation, in addition to jaundice and tachycardia (HR 139 bpm). Initial laboratory tests demonstrated total bilirubin 8.23 mg/dL (RR 0.2-1.20 mg/dL), TSH 5.0 ng/dL (RR 0.70-1.48 ng/dL), total T3 287.46 ng/dL (RR 64-152 ng/dL) with first trimester hCG of >15.000 mIU/mL. Graves' disease was initially suspected, it was diagnosed and managed as a thyrotoxic crisis. After 48 hours, there was clear clinical and biochemical improvement. Anti-TSH receptor antibodies (TRAb), thyroid peroxidase antibody (Anti-TPO) and antithyroglobulin antibodies (Anti-TG) were negative. Thyroid ultrasound did not show thyroid nodules. These findings ruled out thyrotoxicosis of autoimmune origin, toxic multinodular goiter and solitary toxic adenoma. PTU and beta-blockers were discontinued during hospitalization and the patient was discharged from hospital on the 11th day with TSH 0.12 mIU/mL and T4L 0.74 ng/dL. However, at 17 weeks of gestation, the patient suffered a spontaneous abortion. **Conclusion:** GTT is classically a temporary complication of the first trimester of pregnancy, characterized by suppressed serum TSH resulting from overstimulation of the TSH receptor by the hCG alpha subunit. GTT can be observed in states with significantly elevated hCG concentrations, as occurs in multiple pregnancies, trophoblastic disease and hyperemesis gravidarum. It can also occur in pregnant women without overproduction of hCG, but whose TSH receptors carry genetic mutations that make them particularly hypersensitive to hCG.

130389 – MATERNAL PROFILE AND PREGNANCY OUTCOMES IN HYPERTHYROID PREGNANT WOMEN

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Introduction: Hyperthyroidism is reported in approximately 0.2% of pregnant women, with Graves' disease identified as its main cause. When not adequately controlled during pregnancy, thyrotoxicosis is associated with a greater risk of adverse outcomes for both the mother and the fetus. **Objectives:** To evaluate the experience of a tertiary care university hospital in monitoring pregnant women with hyperthyroidism and to examine the impact of this condition and its treatment on maternal-fetal outcomes. **Methods:** Thirty-eight patients diagnosed with hyperthyroidism during pregnancy were retrospectively studied and compared regarding clinical-laboratory characteristics and maternal and fetal outcomes. The evaluation covers the period between August 2021 and January 2024. Results During the study period, 38 patients were included in the study. Of the total, 10 (26.3%) patients were diagnosed with transient thyrotoxicosis during pregnancy, 2 with toxic multinodular goiter (5.3%), and 26 (68.4%) had the diagnosis of Graves' disease confirmed. The average age was 30.2 years, with 84.2% of the pregnant women being multiparous, with 36.8% of them having other pre-pregnancy comorbidities. The average gestational age at the beginning of follow-up with endocrinology was 24 weeks, with a free T4 (FT4) level at the beginning of follow-up of 1.68 ng/dL. The hyperthyroidism etiology groups only differed in terms of the use of anti-thyroid drugs (ATD) during pregnancy and the use of ATD until the moment of delivery. When evaluating patients diagnosed with Graves' disease (GD), the cases were divided into two groups: one with pregnant women with compensated GD (DGC) and the other with decompensated GD (GDD), based on the average measurement of the serum level of free thyroxine (FT4) during pregnancy. Maternal complications, throughout the gestational period, occurred in 31 patients (81.5%), while fetal complications occurred in 17 (44.7%) of the total. When comparing the outcome of maternal and fetal complications in relation to the control of severe disease, there was no statistical difference in the groups evaluated. **Conclusion:** In our analysis, we observed no significant differences in maternal and fetal outcomes based on the cause of hyperthyroidism. Furthermore, among patients with Graves' disease, we found no differences in maternal and fetal outcomes in relation to disease control, when evaluated in relation to FT4 levels during pregnancy.

130053 – DIFFERENT SCHEDULING OPTIONS FOR LEVOTHYROXINE TREATMENT IN HYPOTHYROIDISM AND ITS IMPACT ON ADHERENCE: A COMPREHENSIVE REVIEW AND META-ANALYSIS

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Introduction: Hypothyroidism is a chronic condition caused by insufficient production of thyroid hormones and affects approximately 15% of the adult population. The treatment for hypothyroidism is long-term levothyroxine replacement therapy, which aims to restore thyroid hormone levels, control symptoms, and avoid complications. Medication adherence for hypothyroidism is a common challenge in clinical practice and it is essential to devise alternative strategies to enhance medication adherence. **Objective:** This systematic review aimed to assess different scheduling options to improve medication adherence in patients with hypothyroidism. **Methods:** We searched multiple databases (PubMed, EMBASE, SCOPUS, Web of Science, and CINAHL) using relevant terms related to hypothyroidism and medication adherence. Two independent reviewers conducted the selection, evaluation, and data extraction. The primary outcome was medication adherence, measured as thyrotropin (TSH) levels aggregated with inverse-variance methods meta-analysis. Trial sequential analysis (TSA) were conducted to assess the statistical reliability of the meta-analyses. **Results:** Twelve out of 706 studies initially identified met the inclusion criteria: eleven involved scheduling interventions such as evening administration (n = 8) and weekly administration (n = 3) of levothyroxine. In the comparison of evening *versus* morning administration of levothyroxine, there was no significant difference in the change in TSH levels (dTSH) between the two groups (dTSH 0.20; 95% confidence interval [95%CI] -0.04 to 0.44, P = 0.09). However, in the case of levothyroxine weekly administration, the TSH level was found to be higher in the experimental group (dTSH +1.82; 95% CI 1.34 to 2.29, P < 0.01), although the final TSH remained within the reference range in TSA indicated that the required information size was met in all studies. **Conclusion:** Daily timing and weekly administration of levothyroxine had no inferiority in maintaining medication adherence, maintaining TSH levels within the expected range for controlling hypothyroidism. Consequently, tailoring dosing schedules of levothyroxine to suit individual convenience and preferences could be considered.

130581 – LIFE-SAVING THERAPEUTIC PLASMA EXCHANGE IN THREE PATIENTS WITH THYROID STORM AND ACUTE LIVER FAILURE

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Introduction: Thyroid storm is a rare complication of hyperthyroidism characterized by multi-organ dysfunction. Treatment involves antithyroid drugs (ATD); however, when contra-indicated or severe complications require obtention of rapid euthyroidism, Therapeutic Plasma Exchange (TPE) is an effective treatment. **Case 1:** A 22-year-old female presented with a 10-day history of progressive jaundice. She had been self-medicating with *Valeriana officinalis* (*V. officinalis*). On admission, she was lethargic and febrile. Laboratory workup revealed AST = 1,908 U/L (reference value [RV] 14-36), ALT = 1,800 U/L (RV < 35), total bilirubin of 13.7 mg/dL (RV 0.2-1.3). Diagnosis of acute liver failure and thyroid storm were made, later confirmed by TSH < 0.008 µU/mL (RV 0.4-4.3) and free T4 = 8.66 ng/dL (RV 0.7-1.8). After investigation, diagnosis of toxic hepatitis due to *V. officinalis* was made. TPE was initiated and after the fourth session the patient was stable, allowing a successful thyroidectomy. **Case 2:** A 28-year-old female presented with a 20-day history of abdominal pain, jaundice and diarrhea. She also presented tachycardia and altered mental status, and was diagnosed with thyroid storm. Laboratory workup showed AST = 1,722 U/L and ALT = 1,821 U/L, indicating acute liver failure. TSH was 0.01 µU/mL and free T4 was 7.8 ng/dL; TRAb was positive. Further investigation revealed autoimmune hepatitis. She underwent four sessions of TPE followed by radioiodine therapy. The patient was discharged asymptomatic. **Case 3:** A 51-year-old female with type 1 diabetes and hyperthyroidism is admitted with diabetic ketoacidosis and a Burch-Wartofsky score of 70, culminating into cardiorespiratory arrest. After resuscitation, she presented heart and liver failure. Laboratory workup revealed TSH < 0,001 UI/mL and T4L 4,05 ng/dL. She was treated with two sessions of TPE, which allowed definitive treatment with radioiodine. **Conclusion:** Elevation of liver enzymes is an expected presentation of thyroid storm; however, acute liver failure is rare. When present, it should prompt investigation of other causes. Despite the cause, it is not advisable to use ATD when liver function is severely altered. In this setting, TPE must be considered since, besides being a treatment option for thyrotoxicosis, it is also therapeutic for toxic and autoimmune hepatitis. In this case series we report three cases of thyroid storm associated with liver failure, both conditions successfully treated with TPE.

132699 – THYROTOXIC PERIODIC PARALYSIS PRESENTING AS LIFE-THREATENING RESPIRATORY FAILURE – THE IMPORTANCE OF EARLY RECOGNITION AND TREATMENT OF THIS RARE DISORDER

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Introduction: Hypokalemic Periodic Paralysis is a rare disorder that manifests as sudden and reversible muscle weakness, associated with low potassium levels. It is a rare presentation of hyperthyroidism, when it is referred to as thyrotoxic periodic paralysis (TPP). TPP is a medical emergency that can rarely lead to respiratory failure as the case presented in this report. Mutations in KCNJ18, which encodes Kir2.6, a potassium ion channel, occur in up to 33% of patients. TPP resolves with the treatment of hyperthyroidism. **Case report:** A 55-year-old man without previous medical history presented to the emergency department with sudden onset areflexic paraplegia, tachycardia, potassium level of 1.7 mmol/L (reference value [RV]: 3.5-5.1), rapidly evolving to respiratory failure requiring orotracheal intubation and mechanical ventilation. He had a history of unprovoked transient episodes of lower limb weakness for the past year, and hypokalemia had already been identified. He had sought medical attention and received lumbar steroid injections for herniated discs. Furthermore, he had also been presenting palpitations, weight loss, and tremors for the past three months. On admission, TPP was considered and thyroid function showed TSH < 0.008 mIU/L (RV: 0.4-1.80) and FT4 5.59 ng/dL (RV: 0.70-1.80), confirming the diagnosis. Strongly positive thyroid antibodies and neck ultrasound showed heterogeneous thyroid echotexture with diffuse enlargement (total volume 30 cm^3). Treatment with antithyroid drugs and beta-blocker was initiated and after one week there was an elevation of hepatic enzymes, suggesting drug hepatotoxicity. Therefore, two sessions of Therapeutic Plasma Exchange were performed, along with iodine and lithium therapy, with resolution of clinical manifestations of thyrotoxicosis, which allowed subsequent definitive treatment with total thyroidectomy. The patient was discharged from the hospital asymptomatic and hasn't had a recurrence of the paralysis episodes ever since. We further analyzed the KCNJ18 gene using Sanger sequencing, and no germline pathogenic variants were found. **Conclusion:** TPP is a rare manifestation of hyperthyroidism that can lead to life-threatening consequences. Therefore, higher clinical suspicion is needed for prompt diagnosis and directed treatment.

129275 – QUALITY OF LIFE IN GRAVES DISEASE: DOES TYPE OF TREATMENT MATTER?

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Introduction: Graves' disease (GD) is the foremost cause of hyperthyroidism and antithyroid drugs (ATD) are the first choice for initial treatment, but about 40% of patients relapsed after drug withdrawal. Therefore, radioiodine treatment (RAI) or a second course of ATD is indicated. However, a few reports compare the influence of these two treatments on the quality of life (QoL). **Objectives:** Investigate QoL in GD patients on ATD and RAI Materials and methods Seventy-three patients with GD relapse were evaluated in the euthyroid state (normal TSH and free T levels), according to the Thy-PRO 39 questionnaire. Group 1 (n = 38, 54 ± 12 years; 86% was female) comprised patients on the second course of ATD, and Group 2 (n = 23, 57 ± 12 years; 82% was female) consisted of RAI treated patients (and levothyroxine replacement) while remission patients represented Group 3(n = 12, 57 ± 15 years; 91% was female). **Results:** There was no statistically significant difference ($p > 0.05$ by ANOVA) between the three groups with respect to age, sex, the mean clinical activity score (respectively 0.5 ± 0.9, 0.3 ± 0.6 and 0.2 ± 0.4), serum TSH, freeT4, freeT3, Total T4 and Total T3. The total of the Thy-Pro 39 questionnaire regarding patient symptoms about goiter, hypothyroidism, hyperthyroidism, eye symptoms, tiredness, cognitive complaints, anxiety, depression, emotional susceptibility, social impact, impact on daily life, and impact on appearance did not show any difference between the three groups either. Otherwise, Group 2 patients had a lower TT3/TT4 ratio (0.09 ± 0.02) than groups 1 and 3 (0.11 ± 0.03 and 0.13 ± 0.05, respectively; $p = 0.003$), but no correlation with symptoms in the ThyPro 39 questionnaire. **Conclusion:** Our results indicate that QoL in GD patients on ATD or RAI (with levothyroxine replacement) treatment is similar to remission patients.

129970 – WHAT IS THE BEST TREATMENT OPTION FOR GRAVES' DISEASE PATIENTS WHO HAVE RELAPSED?

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Introduction: Continuous low-dose antithyroid drugs (ATD) may be an alternative for Graves' disease (GD) relapsed patients. **Methods:** One hundred fifty-nine GD relapsed patients after following ATD withdrawal of ATD were studied (median follow-up 12-24 months). Forty-nine patients 87.2% female, mean age 45.10 ± 14.00 received treatment with Radioiodine (RAI) plus L-thyroxine (RAI Group). Forty-six patients 76.1% female, mean age 46.02 ± 13.34 were treated with continuous low-dose (2.5-5 mg/daily) Methimazole (MMI) (Continuous MMI Group), and 74 patients 87.8% female, mean age 46.04 ± 13.16 consisted of a second course of MMI (Second Course Group) for a period of 54.3 ± 44.7 months. Thyroid dysfunction, Graves' Ophthalmopathy (GO) evolution, quality of life (QoL), and body weight were evaluated during the follow-up. **Results:** The mean follow-up was 84.3 ± 36.7 months for the RAI Group, 85.2 ± 39.6 months for the Continuous MMI group, and 90.89 ± 35.52 for the Second Course Group. No important side effects were observed in either group. Euthyroidism was more frequent in the Continuous MMI group ($p < 0.006$). **Conclusions:** Continuous low doses of MMI may be an alternative choice for GD-relapsed patients, particularly in patients who refuse a definitive treatment.

130477 – SUBACUTE THYROIDITIS FROM COVID-19 INFECTION: CASE REPORT

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Introduction: The novel severe-acute-respiratory-syndrome-coronavirus-2 (SARS-CoV-2) virus has led to the ongoing Coronavirus disease 2019 (COVID-19) disease pandemic. There are increasing reports of extrapulmonary clinical features of COVID-19, either as initial presentations or sequelae of disease. Subacute thyroiditis precipitated by COVID-19 infection is rare and an uncommon cause of thyrotoxicosis. **Case report:** A 54-year-old woman presented with worsening pain and swelling of her anterior neck for 6 weeks and persistent fevers for 3 weeks. Four weeks prior to onset of symptoms, she experienced several days of fever, cough, and coryza. At that time, reverse transcriptase-PCR (rtPCR) by nasopharyngeal swab was positive for SARS-CoV-2, confirming COVID-19 infection. She reported complete resolution of symptoms after 7 days and supportive therapy. Ten days after symptom resolution, she noted a painful anterior neck mass associated with odynophagia. She endorsed a 4 kg unintentional weight loss, fatigue, heat intolerance, irritability, headaches, bilateral hand tremors, and palpitations. Thyroid function tests (TFTs) revealed TSH < 0.001 mU/L (NR: 0.4-4.3 mU/L) and fT4 2.23 ng/dL (NR: 0.7-1.48 ng/dL). Repeat TFTs confirmed low TSH < 0.001 mU/L and elevated thyroid hormone levels [fT4: 2,46 ng/dL; tT3: 226 ng/dL (NR: 40-180 ng/dL)], suggestive of thyrotoxicosis. Antibodies to autoimmunity were negative [TPO-Ab: 23 U/mL (NR: <60 U/mL); TRAb: 0.8 U/L (NR: <1.75 U/L)]. A thyroid ultrasound revealed a heterogenous thyroid gland (right lobe: 4.1 x 2.4 x 1.4 cm; left lobe 4.2 x 1.7 x 1.5 cm) with bilateral patchy ill-defined hypoechoic areas, suggestive of subacute thyroiditis. Due to persistent symptoms of odynophagia, neck swelling, and fevers, she was started on oral ibuprofen 600 mg every 6 h and prednisone 40 mg daily. On outpatient follow-up approximately 2 weeks later, she reported symptom resolution and improvement in TFTs (TSH: 0,18 mU/L; fT4: 1,52 ng/dL). She completed a 4-week corticosteroid taper and reported complete symptom resolution. **Conclusion:** Clinicians must be aware of the possibility of thyroid dysfunction and subacute thyroiditis after COVID-19 infection due to SARS-CoV-2. Early recognition and timely anti-inflammatory therapy can help in successful management of the disease.

130046 – CASE REPORT: GRAVES' DISEASE AND PSYCHOSIS IN A YOUNG PATIENT

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Introduction: Graves' disease (GD), an autoimmune condition affecting the thyroid gland, is a leading cause of hyperthyroidism, primarily impacting women between the ages of 30 to 50. In rare cases, psychiatric symptoms such as restlessness, irritability, behavior changes, and even psychosis may manifest. **Case report:** A 22-year-old female, African American, with no prior comorbidities presented to the clinic, complaining of insomnia for the past 11 days. She reported anxious symptoms, persecutory delusions, fear of sleeping and not waking up, and a recent suicide attempt with a sharp object the day before the visit. She mentioned recent job loss as a stressor. On physical examination, she appeared sweaty, with tachycardia (135 bpm), hand tremor, diffusely enlarged thyroid gland (3x), without palpable nodules, with thyroidal bruit. Orbital involvement with Clinical Activity Score of 1, eyelid edema (0-7), proptosis in the right/left eye at 23/22 mm (normal up to 20 mm), and divergent strabismus. The psychiatric evaluation suggested a possible organic origin, leading to a consultation with the Endocrinology Department. Laboratory results showed TSH: 0.01 µUI/L (reference range: 0.4 to 4.5 µUI/L), FT4: 7.77 ng/dL (reference range: 0,9-1,7 ng/dL), TRAb 33.37 UI/L (reference: <3.1 UI/L), and Thyroid US revealed an enlarged gland (total volume: 50.5 cm^3, normal range: 6-16 cm^3) with hyper-vascularization. The diagnostic conclusion was Graves' disease with psychosis. Treatment commenced with methimazole 40 mg/day and propranolol 120 mg/day. During hospitalization, clonazepam 10 drops were prescribed for psychiatric symptom control when the patient exhibited anxiety. After appropriate treatment of the underlying condition, there was a complete regression of psychiatric symptoms, and the patient was discharged with these medications after a 3-day hospital stay. **Conclusion:** Hormonal dysregulation can lead to overactivation of the adrenergic system, causing anxiety, fear, behavior changes, and aggression. It also affects neurotransmitters such as gamma-aminobutyric acid, dopamine, norepinephrine, and serotonin. In cases like this, addressing the organic cause is crucial, but antipsychotic medications may also be used to manage the crisis. This case underscores the importance of considering differential diagnosis for clinical conditions presenting with psychiatric symptoms.

130022 – ACTINIC THYROIDITIS AFTER RADIOIODINE FOR GRAVES' DISEASE EXACERBATED BY PREVIOUS LITHIUM USE

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Introduction: Lithium plays a role in radioiodine (RAI) retention in the thyroid gland, blocking organic iodine and thyroid hormone release without affecting RAI uptake. Hence, lithium has been used with RAI to increase its effectiveness, prevent acute increase of thyroid hormones, and decrease its dose. Here, we describe a case of actinic thyroiditis following RAI for Graves' disease (GD), exacerbated by previous lithium use. **Case report:** A 22-year-old female patient was diagnosed with GD and Graves' orbitopathy (GO) at the age of 19. She started treatment with methimazole (MTZ) 5 mg/day and beta-blocker without control of symptoms and hormonal levels after 3 years of treatment, despite the progressive increase in the dose of the antithyroid drug. Therefore, lithium carbonate was added, and she was referred for definitive treatment. At her first evaluation, she was on MTZ 90 mg/day, propranolol 40 mg 8/8h and lithium 300 mg 12/12h, remaining symptomatic, with TSH < 0.01 mIU/L (0.49-5.58), FT4 3.28 ng/dL (0.89-1.53) and TRAb 20 IU/L (<1.22). At this point, the MTZ dose was reduced to 40 mg/day, and she was referred for RAI treatment (activity of 30 mCi), with a prophylactic prescription of prednisone 20 mg/day due to GO. Five days post-RAI, the patient presented with increased cervical volume with hyperemia, local pain, dysphagia, and a diffuse pruritic skin rash. Current laboratory tests: TSH < 0.01 mIU/L and FT4 5.83 ng/dL. The Clinical Activity Score was zero. Cervical ultrasound showed a heterogeneous thyroid with pseudonodular outlines and a volume of 49 mL. Actinic thyroiditis was suspected, probably exacerbated by concurrent lithium use. Hence, the prednisone dose was increased to 40 mg/day (with gradual tapering) and initiated an antiallergic and MTZ 10 mg/day. The patient improved the thyrotoxicosis symptoms and allergic reaction and reduced thyroid volume to 13.8 mL. Five months post-RAI, she developed hypothyroidism, and levothyroxine 100 mcg/day (1.7 mcg/kg/day) was started. **Conclusion:** We report a case of a patient with GD refractory to drug treatment who developed actinic thyroiditis and an allergic skin reaction 5 days after RAI. It is known that lithium has the potential to concentrate in the thyroid and reduce the secretion of thyroid hormones and, therefore, can be used as an adjuvant treatment. However, as RAI retention in the thyroid increases, its actinic effect may also increase, mainly when high RAI activities are used, as observed in the present case.

130437 – TRANSSPHENOIDAL APPROACH TO URGENT DECOMPRESSION OF ACTIVE, SIGHT-THREATENING THYROID EYE DISEASE

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Introduction: The main extrathyroidal manifestation of Graves' disease (GD) is Thyroid Eye Disease (TED). Although it can be considered a rare condition, TED has a striking impact on patient's quality of life. Treatment depends on the severity and inflammatory state, the last assessed by Clinical Activity Score (CAS). If active, the physician should manage mild TED with local treatment and risk factors control. Intravenous (IV) glucocorticoid is the first-line treatment for active, moderate-to-severe TED. As second-line options, there are several medications depending on the remaining treatment goal (*e.g.*, teprotumumab, tocilizumab, rituximab, azathioprine, cyclosporin, oral prednisone, a second course of IV glucocorticoid or orbital radiotherapy). Sight-threatening TED should be managed with high-dose IV glucocorticoids (0,5-1g daily for 3 consecutive days) and referred to urgent orbital decompression if unresponsive to medical treatment. **Case description:** A 47-year-old female patient with a 10-month history of thyrotoxicosis, diagnosed with GD and treated with oral methimazole and beta-blockers, developed TED 3 months before admission. Visual acuity was progressively lowering when she presented to the Ophthalmology ER with sight-threatening orbitopathy (CAS = 6 and fundoscopy showing optic nerve compression on the left eye). The medical team initially opted for IV methylprednisolone 1 g for 3 days. However, there was no response, and visual acuity worsened even further. Thus, one week later, she was referred for orbital decompression surgery via a transsphenoidal approach. Weekly IV methylprednisolone 500 mg/week was continued, started oral cyclosporine, and orbital radiotherapy was scheduled within two months of the procedure. Before surgery, the patient had a CAS of 6, could only count fingers from 1 meter on the right eye (RE), and had light perception on the left eye (LE). Immediately after the procedure, visual acuity measured by the Snellen Scale was 20/25 on the RE and 20/160 on the LE. After one week of in-hospital admission, she presented a CAS of 3, and visual acuity was 20/25 on the RE and 20/40 on the LE. **Conclusions:** Sight-threatening TED unresponsive to clinical treatment is an urgent, challenging condition that requires close cooperation between medical and surgical teams. When accurately indicated, it presents excellent results, preserving the patient's vision and ensuring improvement in quality of life.

EPIDEMIOLOGIA

129906 – PERFIL CLÍNICO E LABORATORIAL DE PACIENTES COM CÂNCER DE TIREOIDE TRATADOS EM SERVIÇO TERCIÁRIO

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Introduction: Thyroid cancer is the most common endocrinological cancer and its incidence has increased significantly in the last decades. In Brazil, it is the 5th most common tumor in women, with 16,660 new cases/year. Differentiated thyroid cancer (DTC) represents 80%-90% of all cancers of the gland and usually presents a good prognosis. **Objectives:** To describe the clinical profile of patients with thyroid cancer treated in a private tertiary center. **Methods:** Descriptive, cross-sectional and retrospective study that evaluated patients with thyroid cancer treated at the thyroid diseases unit of a private tertiary center. We included patients 18 years or older, followed up between January 2022 and December 2023, with sufficient histopathological data. DTC was categorized according to the eighth edition of the American Joint Committee on Cancer (AJCC/TNM) cancer staging system. The data were obtained from the Institution's electronic medical record and the SPSS version 17.0 program was used for statistical analysis. **Results:** We had a total of 78 patients who qualified for inclusion. The mean age at diagnosis was 45 years (+/- 15.0 years) and 74.4% were females. Among the main risk factors, 17.9% of patients had Hashimoto's thyroiditis, 6.4% had a family history of thyroid cancer and 1.3% had a history of submission to radiation. Total thyroidectomy was the most common type of surgery (52.7%), followed by total thyroidectomy with neck dissection (41.9%) and partial thyroidectomy (5.4%). DTC comprised 91% of neoplasms and was primary represented by papillary carcinoma (85.9%). Multifocality was identified in 48.6% of the sample, microscopic extrathyroidal invasion in 36.4% and lymph node metastasis in 50%. Most of patients were classified at stage 1 (74.6%) and presented intermediate risk of recurrence and/or persistence of ATA (50%), with 23.6% being classified as high risk. A total of 72.4% underwent radioiodine therapy. Four patients have low-risk thyroid microcarcinoma and are under active surveillance and three patients had medullary thyroid carcinoma. **Conclusion:** Our sample obtained epidemiological data similar to the global estimate regarding gender prevalence, average age at diagnosis and most prevalent histological type. The high prevalence of patients classified as intermediate risk justifies the high percentage of patients undergoing total thyroidectomy and radioiodine therapy.

130524 – A FIVE-YEAR REVIEW OF THYROID CANCER EPIDEMIOLOGY IN BRAZIL

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A retrospective analysis using the Datasus database between 2019 and 2021 indicated that the pandemic has caused a significant reduction in thyroid cancer diagnostic and treatment procedures. However, temporal and demographic trends and patterns of diagnosis and treatment of thyroid cancer in different Brazilian regions with varying degrees of access to medical care are still lacking. To obtain a more comprehensive view of the condition across the country, we examined the DATASUS data collected from 2018 to 2023. We observed a 72% increase in the number of thyroid cancer diagnoses between 2018 (4370 cases) and 2019 (7520 cases), especially among women (73%) compared to men (69%), with a predominant age range of diagnosis between 45 and 64 years, confirming the increasing trend of incidence registered worldwide. In 2020, there was a marked reduction (13%) in diagnosis, particularly in the northeast region (25%) and among women (14%). However, the number of cases diagnosed bounced 22% from 2021 to 2020 and 43% by 2022, apparently resuming the upward trend in 2023 when 9015 cases of thyroid cancer were registered. The diagnosis was mostly carried out in the southeast (43.3%) and northeast (31.7%) regions, which also concentrated on the majority of surgeries (38% and 29% of surgeries registered in 2023, respectively). The northeast region suffered a reduction of only 8% in surgeries in 2020 compared to the 2019 data, in contrast to 20% and 29% in the southeast and south regions, respectively. Unfortunately, although SUS is the world's largest public health system and Datasus is based on reliable billing information, it does not include records from the private subsector or private health insurance subsector, and it is not a cancer registry system, lacking important information. Moreover, extensive missing data on treatment specifics and staging presents a critical challenge. This study highlights a notable increase in thyroid cancer cases in Brazil from 2018 to 2023, with an uneven temporary reduction in different regions of the country in 2020. The limitations of the Datasus system underscore the urgent need for improved data collection and more comprehensive epidemiological analyses. National guidelines outlining management strategies are urgently required to mitigate the impact of thyroid cancer on public health.

130611 – THYROID-STIMULATING HORMONE AND FREE T4 REFERENCE RANGES IN PREGNANT WOMAN: A STUDY FROM CURITIBA, BRAZIL

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Introduction: The assessment of thyroid function in pregnant women is essential for optimizing maternal-fetal health, with serum TSH as the principal indicator. TSH experiences physiological fluctuations throughout pregnancy and disparities in its values across populations, underscoring the impact of ethnic and geographical factors on its regulation. Given these factors, the American Thyroid Association (ATA) issued guidelines in 2017 for the Diagnosis and Management of Thyroid Dysfunction During Pregnancy, advocating for the adoption of population-specific reference ranges customized for each gestational trimester. **Objective:** This study aims to establish reference values for serum TSH during different trimesters of pregnancy in women from Curitiba. **Methods:** This prospective population-based study was conducted among pregnant women from Curitiba receiving prenatal care through Public Health System. Serum values of TSH, T4, FT4, TPOAb and urine iodine levels were analyzed. Women with a clinical or laboratory history of thyroid disease were excluded from the study. **Results:** A total of 222 pregnant women were included in the study, with a mean age of 27.8 ± 10.8 years. In the first trimester, 222 samples were analyzed, revealing a mean serum TSH value of 1.87 ± 1.42 µUI/mL, with an interquartile range of 1.02 to 2.54 µUI/mL and percentiles (2.5th and 97.5th) of 0.02 and 5.28 µUI/mL, respectively. Mean T4 levels were 10.6 ± 2.36 µUI/mL, and mean FT4 levels were 1.22 ± 0.24 µUI/mL. Ninety-five samples were analyzed in the second trimester, showing a mean serum TSH value of 2.33 ± 1.28 µUI/mL, with an interquartile range of 1.38 to 3.16 µUI/mL and percentiles of 0.16 and 5.42 µUI/mL, respectively. Mean T4 levels were 12.06 ± 1.98 µUI/mL, and mean FT4 levels were 1.16 ± 0.95 µUI/mL. Seventy-seven samples from the third trimester yielded a mean serum TSH value of 2.61 ± 1.46 µUI/mL, with an interquartile range of 1.64 to 3.26 µUI/mL and percentiles of 0.54 and 5.91 µUI/mL, respectively. Mean T4 levels were 12.02 ± 2.59 µUI/mL, and mean FT4 levels were 1.04 ± 0.13 µUI/mL. Urine iodine levels remained within the standard range. **Conclusion:** Our study reveals that healthy pregnant women in Curitiba exhibit higher TSH values compared to those established by the ATA, with an increase of T4 levels and decrease in FT4 throughout pregnancy. This data suggests the need to adjust the current TSH and FT4 reference values to prevent inappropriate diagnosis and treatment in this population.

130550 – UNDERSTANDING THYROID FUNCTION TESTS VARIATION AMONG AN ELDERLY POPULATION USING BIG DATA

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Introduction: Several research groups were consistently observing an increase in age-related TSH levels. The emergence of Big Data, characterized by an abundance of studies with extensive datasets, has alleviated past limitations regarding sample sizes. Consequently, the utilization of clinical laboratory databases for investigating the behavior of these tests has emerged as a viable and innovative approach. **Objective:** This study seeks to examine the patterns of TSH and free T4 (fT4) levels in individuals aged 60 years and above. The analysis is based on thyroid function test data obtained from a private clinical laboratory. **Methods:** A retrospective analysis was conducted on data from 8,694,807 blood samples. Initially, the data were filtered for TSH analysis based on fT4 concentration within the reference values, negative anti-thyroid antibodies and no medication usage. TSH assays were conducted using a Roche Platform, while fT4 assays were performed using Roche, Beckman, and Siemens platforms. Statistical analyses were conducted using methods such as Shapiro-Wilk, Kruskal-Wallis, Dunn's post-hoc test, Cohen's D test, among others. **Results:** From the initial group, 439,690 TSH samples, 79,928 Beckman fT4 (fT1b), 35,623 Siemens fT4 (fT4s), and 324,139 Roche fT4 (fT4r) samples were selected for analysis. The Kruskal-Wallis test (KWT) for TSH analyses revealed a significant difference between age groups (p-value < 2.2e-16), with the Cohen D test (CDT) indicating a small difference between the 18-59 and over-80 age groups. Similarly, significant differences were observed between age groups for fT4b analyses (p-value < 2.2e-16) in the KWT, with the CDT indicating the most significant difference between the 18-59 and over-80 age groups. For fT4s analyses, significant differences were found between age groups (p-value < 7.473e-09) in the KWT, with the CDT showing this difference only between the 18-59 and over-80 age groups. Finally, significant differences between age groups were observed for fT4s analyses (p-value < 2.2e-16) in the KWT, with the CDT indicating this difference only between the 18-59 and over-80 age groups. **Conclusion:** Analysis of this extensive dataset revealed significant age-related differences in both TSH and fT4 levels (across three different methods). These findings underscore the importance of establishing age-specific reference values to accurately assess thyroid function in this population and to prevent misdiagnosis of hypothyroidism.

130391 – ASSOCIATION BETWEEN THYROID CANCER AND BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Thyroid cancer (TC) and breast cancer (BC) represent common malignancies affecting mainly females, and intriguingly, there is growing evidence suggesting a higher-than-expected co-occurrence of these cancers within the same individuals. The purpose of this systematic review and meta-analysis was to evaluate the relationship between TC and BC and to examine the likelihood of developing BC following TC (TC1-BC2) and vice versa (BC1-TC2). **Methods:** A systematic search was performed using the PubMed and Embase databases. We searched for articles containing epidemiological evidence of TC after BC and vice-versa, published until 2021. In addition, for BC1-TC2 studies there was sufficient and comparable data for subgroup analysis regarding age at the time of BC diagnosis and the type of treatment, which included radiotherapy and chemotherapy. The type of chemotherapy received was not specified in the studies. The standardized incidence ratio (SIR) was used to calculate the risk of second primary malignancy. The MOOSE guidelines were followed, and the Newcastle-Ottawa Scale was used to assess the quality of the studies. **Results:** Fifteen articles were included in the meta-analysis of TC1-BC2, comprising 347,392 patients. An increased risk of developing BC was observed (SIR = 1.4, 95% CI 1.2-1.6, $p < 0.01$) in patients with previous TC when compared to the adjusted population risk. Moreover, for BC1-TC2, 24 articles were included, comprising 1,523,662 patients. An increased risk of developing TC following BC was also found (SIR = 1.6, 95% CI 1.3-1.9, $p < 0.01$). In addition, the risk of TC was higher for patients diagnosed with BC before the age of 50 (SIR = 2.1, 95% CI 1.6-2.6). Also, patients who received chemotherapy for BC had a higher risk of developing TC (SIR = 1.6, 95% CI 1.5-1.7). Radiotherapy for BC was not associated with increased risk of a secondary malignancy. **Conclusions:** This study demonstrated an increased risk of developing TC or BC as secondary malignancies. Further studies are needed to provide a more in-depth understanding of this association, which could have potential implications for patient follow-up and management strategies.

130171 – EPIDEMIOLOGICAL PROFILE OF PATIENTS UNDERGOING THYROID SCINTIGRAPHY AT A PUBLIC HOSPITAL IN THE STATE OF SÃO PAULO BETWEEN 2008 AND 2023

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Introduction: Thyroid scintigraphy (TS) is an important yet not routinely ordered exam in the differential diagnosis of hyper- and hypothyroidism, often following ultrasonography and fine-needle aspiration as diagnostic tools for thyroid disease. **Objectives:** The aim of this study is to characterize the epidemiological profile of patients undergoing thyroid scintigraphy in the outpatient setting at a public hospital in São Paulo. **Methods:** A cross-sectional study was conducted utilizing publicly available data from the *Departamento de Informática do Sistema Único de Saúde* (Datasus) database. Data pertaining to thyroid scintigraphy procedures at a public tertiary hospital in São Paulo from 2008 to 2023 were extracted, and variables including age, sex, city of origin, and diagnosis were analyzed. **Results:** A total of 2.465 patients were identified, the majority being female (81,54%, N = 2010), with a median age of 51. The most prevalent diagnoses for investigation were thyrotoxicosis with diffuse goiter (15,46%, N = 381), thyrotoxicosis with multinodular toxic goiter (14,89%, N = 367), followed by malignant neoplasia of the thyroid (14,0%, N = 345). The most prevalent age group was 51-55 (10,43%, N = 257), followed by 56-60 (9,61%, N = 237) and 61-65 (8,80%, N = 217). Prevalence increased with age, peaking at 51-55, then decreasing. Females predominated across all age groups, except for patients aged 1 to 5 (7,3%, N = 180), which had an even sex distribution (52,78% male, N = 95) and were mainly investigated for congenital hypothyroidism. Most patients (67,79%, N = 1671) were not residents of the city where the hospital is located. The number of scintigraphies performed per year decreased dramatically, from 287 in 2008 to 81 in 2023, with an average annual percent change of -3%. **Conclusion:** The results indicate an increase in TS with patient age, predominantly in females, consistent with the rising prevalence of thyroid nodular disease as age advances and in the female sex. While there is a trend of reduction in TSs performed annually, likely reflecting the increasing use of percutaneous aspiration biopsy of thyroid nodules, TS remains an important tool in the differential diagnosis of thyroid disease. This is particularly true for the diagnosis of congenital hypothyroidism, where TS remains a gold standard, as reflected by the substantial pediatric population undergoing the procedure in this study.

130158 – ASSESSMENT OF QUALITY OF LIFE IN PATIENTS WITH THYROID-ASSOCIATED ORBITOPATHY AND ITS RELATION TO DISEASE SEVERITY AND ACTIVITY

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Introduction: Graves' orbitopathy is the most frequent extrathyroidal manifestation of Graves' disease. Its clinical manifestation is varied and compromises the quality of life of the individual, both from a functional and aesthetic standpoint. **Objective:** To evaluate the quality of life and correlate it with the severity and activity of the disease in patients with thyroid-associated orbitopathy from a tertiary care center in São Paulo. **Methods:** A total of 164 patients with thyroid-associated orbitopathy were evaluated from the Ophthalmology Department between January 2018 and September 2023. A questionnaire (Graves Ophthalmopathy – Quality of Life) was administered, and the total functional and aesthetic scores were calculated for each patient (according to formula, as proposed by Terwee and colleagues: Total score = [(sum of items - n) / 2 x n] x 100, where "n" is the number of items responded to. The score ranges from 0 to 100, where 0 and 100 correspond to the highest and lowest impact, respectively. Patients were then divided into low (≥75), moderate (between 50 and 75), and high impact (≤50) for these two scores, as proposed by Cockerham and colleagues, to evaluate the main factors that could influence these scores, including clinical assessment (activity and severity) of orbitopathy using the CAS and EUGOGO classifications. **Results:** Worse functional scores in the QOL questionnaire were statistically significant when related to EUGOGO and CAS classifications ($p < 0.001$), presence of diplopia ($p < 0.001$), strabismus ($p < 0.001$), mean age, tomography classification and proptosis. No statistically relevant correlations were observed when comparing severity and activity classifications with aesthetic score. Female gender, mean age, palpebral asymmetry and retraction were negatively correlated with aesthetics. **Conclusion:** Thyroid-associated orbitopathy negatively impacts the quality of life of these patients. A correlation was observed between the severity and activity of thyroid-associated orbitopathy and the impact on functional score, whereas the same did not occur with aesthetic score.

130608 – ASSOCIATION BETWEEN IODINE STATUS AND METABOLIC SYNDROME PARAMETERS IN ADULTS MONITORED IN AN OUTPATIENT CLINIC SPECIALIZING IN THYROID DISEASES AT A HOSPITAL UNIVERSITY

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Iodine deficiency or excess affects thyroid function, altering the function of the gland. Currently, an association between obesity and iodine excess has been observed. Obesity is one of the main elements of metabolic syndrome, which, according to the NCEP (National Cholesterol Education Program and Adult Treatment), is characterized by the presence of three or more of the following criteria: central obesity (>102 cm in men and >88 cm in women), hypertriglyceridemia (>=150 mg/dL), low HDLc (<=50 mg/dL for women), arterial hypertension (AH) and dysglycemia (fasting blood glucose >=100 mg/dL or type 2 diabetes). The objective of this study is to evaluate the association between iodine status and metabolic syndrome parameters in women monitored on an outpatient basis. Ioduria was measured in a urinary sample using the ICP/MS method, fasting blood glucose and insulinemia, HDLc, triglycerides, HOMA-IR, weight and height for calculating BMI, waist circumference and presence of AH. This is a cross-sectional study with a convenience sample of 167 women treated at a thyroid disease outpatient clinic in a tertiary hospital. The patients were classified according to iodine and recommendations from the World Health Organization: 35.3% had iodine sufficiency 100-299 mcg/L, 19.8% insufficiency 300 mcg/L. The average age of the participants was 52 years and the frequency of metabolic syndrome was 30%. When analyzing HDLc, a higher frequency of low HDLc is noticeable in the groups with more than sufficient iodine (32.6%) and excessive iodine (60.7%) and a lower frequency in those with normal iodine (32.6%) and insufficient (30.8%); p = 0.023. It was observed that in the more than sufficient and excessive ioduria groups the median waist circumferences were higher (95 and 94 cm) than in the normal and insufficient groups (90 and 85 cm); p = 0.034. Regarding BMI, a lower median was observed in the group with insufficient ioduria (24 kg/m²) and a higher median for the groups with normal ioduria (27 kg/m²), more than sufficient (27 kg/m²) and excessive ioduria (27 kg/m²); p = 0.023. The present study suggests that low BMI values are associated with iodine deficiency, while high waist circumference and low HDLc values are associated with excess iodine, confirming the hypothesis of an association between metabolic syndrome and excess iodine.

130543 – DEVELOPMENT OF AN *IN VITRO* MODEL FOR THE SCREENING OF REDIFFERENTIATION DRUGS THROUGH NON-RADIOACTIVE IODIDE UPTAKE ASSAYS

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Introduction: During thyroid cancer (TC) progression, the dedifferentiation of the tissue and the loss of radioiodine (RAI) uptake is observed due to decreased NIS expression or NIS cytoplasmic retention. NIS is a plasma membrane protein responsible for the active transport of iodide into follicular cells. Clinical treatment of radioiodine refractory thyroid cancers is challenging. The recovery of radioiodine sensitivity has emerged as a therapeutic approach for the most aggressive thyroid tumors. **Objective:** To develop an *in vitro* model for the screening of redifferentiation drugs through a non-radioactive iodide uptake method. **Methods:** Papillary thyroid cancer (BCPAP; B), anaplastic cancer (HTH83; H), and non-tumor thyroid (NThyOri; N) cell lines were permanently transfected with a plasmid containing the human NIS gene using lipofectamine. Stable clones were selected with geneticin. NIS gene expression was determined by real-time PCR and a non-radioactive iodide uptake method was used to evaluate NIS activity in those cells. **Results:** Five stable clones (HH4, HH1, BE4, BF6, NH2) with higher NIS expression compared to the non-transfected cells (fold change: HH4: 14.73 au; HH1 au: 775.84 au; BE4: 55.01 au; BF6: 11.44 au; NH2: 49.63 au) were selected. The iodine uptake test was standardized and the transfected NthyOri cell (NH2) showed an increase in iodide uptake compared to the non-transfected cell N0. Interestingly, although we have observed increased levels of NIS expression, there were no significant alterations in the iodide uptake in the BCPAP and HTH83 transfected clones, suggesting impaired NIS translocation to the plasma membrane. **Conclusion:** We successfully standardized an *in vitro* model protocol to test the efficiency of redifferentiation drugs in the recovery of iodide uptake in normal and thyroid cancer cell lines. The ectopic expression of NIS in the NThyOri lineage increased iodine uptake, which was not observed in the transfected BCPAP and HTH83 cancer lines. These results may be a consequence of the NIS retention in the cytoplasm, as previously suggested in cancer tissues. This hypothesis will be confirmed soon.

130512 – ASSOCIATION BETWEEN IODINE URINARY, NODULAR GOITER, THYROID CANCER AND BRAFV600E MUTATION IN WOMEN ATTENDED AT A UNIVERSITY HOSPITAL LOCATED IN AN IODINE SUFFICIENT REGION

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Introduction: Nodular goiter (NG) and thyroid cancer depends on complex interaction between factors, including iodine status. BRAFV600E mutation is one of the hall markers of Papillary thyroid carcinoma (PTC) development and its association with excessive iodine exposure has been proposed. **Objectives:** To evaluate, in women attended at the outpatient unity of an university hospital located in an iodine sufficient region, the association between iodine status, NG and PTC. In addition, to investigate if excessive iodine status would be associated with BRAFV600E mutation. **Methods:** In this cross-sectional study, 133 women (67 with NG) were evaluated by clinical history, thyroid ultrasound, thyroid function and urinary iodine concentration (UIC) determination by the inductively coupled plasma mass spectrometry. PTC was defined by post-surgical histopathological report (n=20), and the presence of BRAF V600E mutation by immunohistochemistry. **Results:** The median UIC was higher in NG patients (207.1 µg/L *vs.* 158.0 µg/L; p = 0.022) and UIC > 200 µg/L was an independent risk factor for NG (OR = 2.90 CI = 1.06-7.95 p = 0.038). UIC > 300 µg/L was independently associated with PTC (RR = 4.67 CI = 1.26-17.34 p = 0.021). The frequency of excessive iodine status was higher in women with PTC compared to those without (40.0 *vs.* 17.0%; p = 0.032). BRAFV600E mutation was present in 33% of the studied PTCs. Within the iodine status spectrum in our population, the frequency of BRAFV600E mutations was 16.7%, 33.3% and 50.0% in the insufficient, adequate and more than adequate subgroups, respectively. The median UIC among patients with follicular subtype PTC was significantly higher than in the classical PTC subtype (318.1 µg/L x 207.1 µg/L; p = 0.048). This last subgroup of PTC had a higher frequency of excessive iodine status (71.4%). **Conclusion:** UIC > 200 µg/L was an independent risk factor for thyroid nodules and UIC > 300 µg/L increased the risk for PTC in the studied sample. Despite an absence of strong association between BRAFV600E mutation and higher UIC it was suggested an inverse u-shaped pattern of distribution of this mutation according to iodine status spectrum. Furthermore, follicular subtype of PTC was related to excessive iodine status despite absence of BRAFV600E mutation.

130429 – URINARY IODINE CONCENTRATION AND THYROID STATUS IN 880 PATIENTS FROM THE LONGITUDINAL ADULT HEALTH STUDY (ELSA-BRASIL)

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Introduction: Iodine is an essential micronutrient in the synthesis of thyroid hormones, directly affecting organic metabolic processes from the prenatal period to aging, including embryogenesis, growth and physical, neurological and cognitive development. Urinary iodine concentration (UIC), a marker of nutritional intake, is known to be a predictor of thyroid dysfunction. **Objectives:** This work aims to evaluate urinary iodine concentration in Brazilian adults from the Adult Health Study (ELSA-Brazil), correlating it with sociodemographic factors and thyroid status. **Method:** Analysis of 880 participants aged 35 to 74 years from six Brazilian capitals involving urinary iodine concentration and thyroid status assessed based on serum TSH and T4L levels. **Results:** Among the participants, 51.8% were women, the average age was 52.1 (9) years. According to the WHO classification, 523 (59%) have more than adequate levels of iodine, that is, between UIC > 200 and 299 mcg/L, 206 (23%) with excessive levels, and only 22 (2.5%) deficient (250 mcg/L). Participants who did not consume fruit daily (p 0.05), as well as vegetables (p 0.013) had a higher prevalence of excess iodine. No differences were detected in UIC according to thyroid status. **Conclusion:** The research confirms that Brazil reached the target for population iodine supplementation, including part of the population presenting excessive levels, however, without evidence of a direct link between iodine concentration and thyroid dysfunction. Of the participants who did not consume fruits and vegetables daily, 28% were in a situation of excess urinary iodine concentration, probably due to greater consumption of ultra-processed foods rich in added sodium.

129483 – LARGE TOXIC NODULAR GOITER WITH PEMBERTON'S SIGN AND SURGICAL CONTRAINDICATION: IS I131 AN ALTERNATIVE THERAPEUTIC OPTION?

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Introduction: Thyroid nodules are a common clinical issue, and the indiscriminate use of neck ultrasonography has led to an increase in their diagnosis. While most thyroid nodules are asymptomatic, rare thyroid enlargements can reach the mediastinum and cause venous obstruction, clinically manifested as facial plethora when lifting bilateral arms, characterizing Pemberton's sign. Differential diagnosis includes lymphoma, lung carcinoma, and aortic aneurysm. Careful evaluation for proper etiologic definition and treatment is essential. **Case report:** A 77 yo woman was referred to our service with a long-standing history of toxic multinodular goiter. She complained of slight difficulty swallowing but no dyspnea or hoarseness. Upon physical evaluation, the patient had an enlarged heterogeneous thyroid gland with impalpable lower poles, collateral circulation in the upper chest, and positive Pemberton's sign. The patient had undergone radioiodine (RAI) four years ago (40 mCi) without hyperthyroidism remission. 99mTc scintigraphy indicated persistent autonomous nodules. Non-contrast computed tomography revealed plunging goiter (222 mL) with tracheal shift, jugular compression, and prominent collateral circulation in the neck. The patient was already on methimazole and a recent introduction of amiodarone was also reported for arrhythmia. While thyroidectomy was considered, the extensive surgery combined with a high preoperative risk due to the patient's multiple comorbidities (heart failure + arrhythmia + hypertension + grade 2 obesity) contraindicated this approach. After a thorough review and discussion with cardiology, the decision was made to replace amiodarone with an alternative anti-arrhythmic drug, monitor urinary iodine clearance, and, upon achieving levels compatible with iodine discharge, another RAI would be pursued. **Conclusion:** When facing a voluminous toxic multinodular goiter with positive Pemberton's sign, surgery is the most common approach. However, when contraindicated, RAI is an alternative since it can lead to euthyroidism/hypothyroidism and significant gland volume reduction. However, this therapy efficacy is inversely correlated to initial gland volume (if > 100 mL, the volume reduction rate is around 35% after one year). Repeated courses of RAI therapy have been reported to result in more significant rates of goiter reduction. Therefore, since surgery was contraindicated for our patient, a second attempt with RAI is a reasonable alternative.

METABOLISMO E AÇÃO DOS HORMÔNIOS TIREOIDIANOS

130058 – RARE CASE OF THYROTOXICOSIS DUE TO HYDATIDIFORM MOLE – CASE REPORT

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Introduction: Gestational Trophoblastic Disease (GTD) is a rare condition that involves benign and malignant tumors originating from the placental trophoblast. These tumors produce human chorionic gonadotropin (hCG), which can induce hyperthyroidism due to cross-reactivity with the TSH receptor. Among benign tumors, the incidence of hydatidiform mole is 1 case per 200-400 pregnancies in Brazil. However, such statistics are based on data from tertiary hospitals and may reflect a false high incidence. **Case report:** A 49 years old, female patient, and without previous illness. Complaining of weight loss (18 kg in 2 months), anxiety attacks, insomnia, vomiting, palpitations, and amenorrhea. Three months later, she developed intense vaginal bleeding and sought emergency care. She received a diagnosis suggestive of molar pregnancy after an hCG test and pelvic ultrasound. At her first gynecology consultation, her BMI was 19 kg/m^2, HR 101 bpm, BP 140 x 80 mmHg, RR 35 rpm, and T 36.7 °C. Emaciated, anxious, and pale +/4+. Normal thyroid palpation. Fine tremor of extremities. Warm, clammy hands. Absence of orbitopathy, acropathy, and dermopathy. Globular abdomen, uterus at the umbilical scar, and painful on palpation. Admission tests: hCG > 10,000 mUI/mL (>25.0) / TSH 0.01 uUI/mL (0.27-4.20) / T4L 3.07 ng/dL (0.93-1.7) / T3T 2.23 ng/dL (0.70-2.04) / TRAb < 1.26 UI/mL (<3.10) / negative antithyroid antibodies / MRI pelvis: Uterus with increased dimensions, morphology and contours preserved, measuring 25.2 x 9.7 x 19.0 cm, with an estimated volume of 2,415.0 cm^3. Evaluated by the endocrinology that ruled out thyroid storm and initiated Methimazole 30 mg/day and Propranolol 120 mg/day. During hospitalization, hCG levels increased, reaching 975,296 mIU/mL. Absence of metastatic neoplastic involvement. Pan-Hysterectomy was performed and, based on immunohistochemical and pathological findings, a diagnosis of Complete Hydatidiform Mole was confirmed. She was discharged with T4L 1.11 ng/dL and hCG 68,235 mIU/mL, Methimazole being suspended and Propranolol dose reduced. Maintained regular follow-up in gynecology and endocrinology, with hCG negative and normal thyroid function. **Conclusion:** Identifying hyperthyroidism in GTD can be challenging, leading to delays in diagnosis and treatment. Early recognition and prompt therapeutic intervention are crucial in preventing the risk of hyperthyroidism and its complications, reducing morbidity and mortality from the disease.

130289 – TREATMENT WITH T3 PLUS HALF OF THE REPLACEMENT DOSE OF INSULIN AS A THERAPEUTIC TARGET FOR HEPATIC AND LIPID METABOLISM AND GLYCEMIC CONTROL IN DM1 RATS INDUCED BY ALLOXAN

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Type 1 *diabetes mellitus* (DM1) is an autoimmune disease characterized by chronic hyperglycemia, as a consequence of the increased hepatic gluconeogenesis (GNG), reduction of muscular glucose utilization and an imbalance of the lipid metabolism, due to defects in insulin synthesis and secretion. Previous studies of our laboratory have shown that DM1 induced by alloxan in rats led to hypothyroidism and an inflammatory state in the three main target tissues of insulin (liver, adipose tissue-AT and skeletal muscle), resulting in insulin resistance (IR). The treatment of these animals with T3 associated to half of the replacement dose of insulin (3U) restored the metabolic parameters studied to the values of the control group (non-diabetic), including the serum TSH levels. This study was aimed to evaluate the key proteins' content of the hepatic carbohydrate metabolism (GLUT2, Glucokinase-GK and enzymes of GNG-PEPCK and G6pase); AT lipid metabolism (Hexokinase-HK, lipoprotein lipase-LPL, triacylglycerol lipase-TAGL, Hormone-sensitive lipase (HSL) and Stearoyl-CoA desaturase1-SCD1), as well as the repercussion of the T3 treatment associated or not with insulin on these proteins and glycemic control of DM1 rats. To this end male Wistar rats were induced to *diabetes mellitus* by alloxan, a drug that destroys pancreatic beta cells, and treated with insulin (3 or 6U, sc) and/or T3 (1,5 µg/100g PC, ip) for 28 days. In addittion to the cited proteins expression. We evaluated the fasting blood glucose and the Insulin tolerance test (ITT). The DM1 rats presented increased fasting glycemia, IR, liver GLUT2, PEPCK, G6pase and AT TAGL, HSL and SCD1 content, in parallel to a reduction of hepatic GK, and AT HK and LPL content, reiterating the increase of GNG and lipolysis in this condition. The treatment with T3 and/or insulin promoted reduction of hepatic GNG and AT lipolysis, and increased glucose hepatic utilization and lipogenesis in the AT. The T3 associated to Insulin 3U treatment restored all the studied parameters to the values of the control (non-diabetic) group and to the diabetic group which received the replacement dose of insulin (6U). The present results indicate that lower doses of insulin could be administered when T3 is associated to DM1 rats, which would delay the IR resultant of its chronic use, avoiding the administration of higher insulin doses for the glycemic control, which could mitigate unfavourable side effects, like hypoglycaemia.

130602 – THE EXPOSURE TO ENDOCRINE DISRUPTORS DURING THE INTRAUTERINE PERIOD DYSREGULATES THE EXPRESSION OF ANTIOXIDANT ENZYMES AND THYROID HORMONE METABOLISM PROTEINS IN THE CORTEX OF ADULT F1 OFFSPRING RATS

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Introduction: Exposure to endocrine disruptors during critical periods of development, such as pregnancy and lactation, has been previously correlated with neuroinflammation and deleterious effects on the development and function of the central nervous system. **Objective:** To evaluate the impact of intrauterine exposure to dichlorodiphenyldichloroethylene (DDE) or polychlorinated biphenyls (PCBs) on the expression of genes involved in the regulation of oxidative stress and the peripheral transport and metabolism of thyroid hormones. **Methods:** Pregnant Wistar rats were orally exposed or not to 0.1 or 1 mg/kg/day of DDE, or to 50 or 500 µg of Aroclor 1254 (a mixture of PCBs)/kg/day during the gestational period. Female and male F1 offspring rats were euthanized at postnatal day 90. Cortex was collected, total RNA was extracted and the gene expression of catalase (Cat), superoxide dismutase 1 (Sod1), superoxide dismutase 2 (Sod2), deiodinase type 2 (Dio2), and monocarboxylate transporter 8 (Mct8) was evaluated by RT-qPCR. **Results:** The intrauterine exposure of female rats to both doses of DDE significantly reduced the expression of Cat, Sod1, Sod2, Dio2, and Mct8 in the cortex in comparison to the control animals. Nonetheless, the exposure of male rats to DDE only reduced the expression of Sod1, Dio2, and Mct8 mRNAs. Interestingly, intrauterine exposure to PCBs induced different effects in the cortex of male and female offspring rats. Indeed, the expression of Cat, Sod1, Sod2, and Mct8 mRNAs was increased in the cortex of PCB-exposed female rats, especially in the lowest dose of treatment. In the males, the PCB exposure induced increased expression of Cat, Sod2, Dio2, and Mct8 mRNAs, in both studied doses, in comparison to the control group. **Conclusion:** Different endocrine disruptors caused unique responses in the cortex of male and female adult offspring rats. Our results strongly suggest that the antioxidant control is impaired in the cortex of male and female adult rats exposed to DDE or PCBs during the intrauterine period. Moreover, the transport and the peripheral metabolism of thyroid hormones are impaired in the cortex of animals that were exposed to endocrine disruptors during this critical period of development.

130045 – EVALUATION OF DAILY OSCILLATIONS OF KIDNEY FUNCTION IN MALE AND FEMALE HYPOTHYROID RATS

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Introduction: Thyroid hormones (THs) play a crucial role in renal growth and development, directly influencing tubular metabolism. In humans, the hypofunction of the thyroid gland is associated with reduced glomerular filtration rate and renal hemodynamic alterations. In parallel, we have shown that THs modulate the circadian rhythmicity of clock genes and target transcripts in a tissue-dependent manner, as depicted in the heart and anterior pituitary. However, the effects of THs on the daily oscillations of kidney function have not been investigated yet. **Objectives:** This study aimed to characterize the effect of hypothyroidism on the daily regulation of renal function in both male and female mice. **Methods:** Male and female Wistar rats were equally divided into Control (C: euthyroid) and Hypothyroid (Tx) groups. Hypothyroidism was induced by thyroidectomy under deep anesthesia followed by methimazole (0.03%) and CaCl2 (4.5 mM) supplementation in drinking water for 21 days. Next, the animals were placed in metabolic cages, and after 48 h adaptation, the total volume of urine was collected, and the water intake and urinary volumes were measured up to 48 h, every 6 h. Urinary creatinine, glucosuria, and proteinuria were measured, and normalized by total urinary volume and body weight. At the end of the experiment, the animals were euthanized under deep anesthesia; the anterior pituitary gland was collected for Tshb mRNA expression analysis by RT-PCR. Temporal oscillations were analyzed through one-way ANOVA and 24 h cosine adjustment of the data. Overall, statistical significance was considered when $P < 0.05$. All protocols were approved by CEUA-UFMG 47/2020. **Results:** The increase of Tshb mRNA in anterior pituitary and reduction of heart/body weight ratio confirmed the hypothyroidism induction in both sexes. Urinary creatinine, glucosuria and proteinuria exhibited a well-defined circadian rhythmicity in the C group, independently of sex. Advance in the proteinuria's acrophase, and increases in glucosuria's mesor and amplitude were also observed in female Tx rats, while males exhibited a slightly reduction of proteinuria over the 24h. **Conclusion:** Our data showed that hypothyroidism impairs the daily pattern of kidney function and possibly the energy metabolism in a sex dependent manner, with females being more affected. Additionally, the kidney circadian clock seems to be another target for THs, highlighting their tissue-specific actions.

130292 – INCREASED PRO-INFLAMMATORY CYTOKINES EXPRESSION UNDERLIE THE DEVELOPMENT OF HYPOTHYROIDISM IN EXPERIMENTAL DIABETES: EFFECT OF T3 AND/OR INSULIN TREATMENT

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Besides hyperglycemia and subclinical chronic inflammation, diabetes mellitus (DM) also courses with alterations in thyroid function, with hypothyroidism being the most prevalent and of as yet unknown etiology. Previous studies have already shown a positive correlation between DM and hypothyroidism, limiting themselves to an autoimmune point of view. However, there is evidence that other factors are also at play, as demonstrated by our group's work, which detected primary hypothyroidism even in rats induced to DM1 by alloxan. It is therefore necessary to investigate other possibilities for understanding the causes of thyroid dysfunction in DM. To this end, the present study sought to assess whether increased inflammation is present in the thyroid of DM animals, while also observing its effects in the thyroid hormone synthesis pathway and the effect of T3 treatment, associated or not with insulin. Wistar rats were induced to DM1 through the administration of alloxan (150 mg/kg, ip) and subdivided into five groups: DM: treated with saline (0,9%, ip); T3: treated with T3 (1,5 µg/100 g BW, ip); I6: treated with replacement dose of insulin (6U, sc); I3: treated with insulin (3U, sc); and T3I3: treated with T3 (1,5 µg/100 g BW, ip) and insulin (3U, sc). Treatment lasted for 4 weeks. After euthanasia, the expression of the transcription factor NFκBp65, the cytokines TNF-α and IL-10, as well as TPO and NIS proteins were assessed in the thyroid gland. Serum TSH concentration, fasting glucose and glucose decay rate (kITT) were also assessed. Non-diabetic animals were used as control. The results of the study showed that DM animals had lower kITT, and higher fasting glucose and TSH levels. They also had an increased TNF-α and NF-κBp65 content, accompanied by a reduction of IL-10, NIS and TPO in the thyroid *versus* non-DM animals. In contrast, DM animals treated with T3I3 showed a reduction in fasting glucose, TSH levels and inflammation, with an increase in kITT and NIS and TPO content. NIS content was increased in I6 animals, however not to Control levels, as was the case with T3I3. These data point to a primary hypothyroidism that occurs with DM, caused by a loss of inflammatory control in the gland, resulting in a reduction of HT synthesis pathway's proteins. It is also clear that T3I3 treatment was the only one capable of restoring all variables, even while using half a dose of insulin, pointing to the potential of T3 as a therapeutic adjuvant in DM treatment.

130424 – METABOLOMIC PROFILE IDENTIFIES METABOLIC PATHWAYS ACTIVATED BY T3 IN ADIPOSE CELLS

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Introduction: Obesity, globally prevalent, results from the imbalance between calorie intake and expenditure, marked by excessive accumulation of adipose tissue (AT). This excess may be directly linked to the imbalanced production of reactive oxygen species (ROS) in obese individuals, triggering a chronic low-grade inflammatory process, which ultimately contributes to the development of comorbidities such as dyslipidemia, atherosclerosis, *diabetes mellitus* (DM), arterial hypertension (HTN), and insulin resistance (IR). AT, besides storing fat, is a complex endocrine organ capable of regulating various metabolic functions and releasing substances. Thyroid hormones, especially triiodothyronine (T3), profoundly influence AT metabolism. **Objective:** To identify, through the analysis of the metabolomic profile, the biochemical alterations caused by T3 in adipose cells. **Materials and methods:** Cell culture of 3T3-L1 preadipocytes was performed, divided into 2 groups: (C) adipocytes without treatment and (T3) adipocytes treated with a physiological dose of T3 (10 nM) for 24h. Metabolomic analyses were conducted by liquid chromatography followed by *in silico* analysis using systems biology software (Metaboanalyst 5.0), predictive power was determined using partial least squares discriminant analysis (PLS-DA), with a 95% confidence interval; univariate analyses (Student's t-test and Fold Change) were also performed using the VIP Scores method. **Results:** PLS-DA revealed a clear separation between groups C and T3. Volcano plot analysis was performed to select significant metabolites with m/z ratios with $p < 0.05$ and fold change ≥ 1.5 (Log2 (FC) ≥ 0.585). A heat map was developed, and seven biomarkers with statistically significant expression were identified, with glycine being particularly highlighted. **Conclusion:** T3 influences glycine metabolism, providing a possible protective role in inflammatory environments by reducing pro-inflammatory cytokines and free fatty acids, becoming a potential therapeutic target to reduce chronic low-grade inflammation caused by obesity.

130162 – DIO2 GENE THR92ALA POLYMORPHISM HETEROZYGOSITY IS ASSOCIATED WITH LOWER DOCUMENTED PREGNANCY LOSS IN WOMEN WITH UNEXPLAINED INFERTILITY

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Introduction: Unexplained infertility (UI) and low ovarian reserve (LOR) are challenging reproductive conditions that affect one-third of infertile women. DIO2 expression is high in reproductive organs, regulating local Thyroid hormone (TH) availability. The Dio2-deficient zebrafish model exhibits hypothyroidism, delayed sexual maturity, reduced reproductive capacity, fecundity, and fertilization. It is unknown if the DIO2 polymorphisms is associated with reproductive parameters in UI/LOR women. **Objective:** This study aimed to investigate the association of the Thr92Ala DIO2 variant with clinical and laboratory parameters among UI/LOR women. **Methods:** Clinical and reproductive data were collected. Genotyping for the Thr92Ala DIO2 polymorphism was performed using the TaqMan® SNP Genotyping method (7500 Real-Time PCR Systems, Applied Biosystems, CA). Laboratory tests included TSH, free T4, total T3, FSH, estradiol (E2), and Anti-Mullerian hormone (AMH). The association between the Thr92Ala DIO2 genotypes and UI/LOR women was analyzed using the Mann-Whitney and Chi-squared tests. Univariate and multivariate regression analyses were performed to evaluate the contribution of genetic polymorphisms to pregnancy loss. **Results:** A total of 89 UI/LOR women were included. The median [interquartile range (IQR)] age was 37 (34-40) years old. The overall pregnancy loss rate was 33.3%. Median (IQR) values for TSH, FSH, Estradiol, and Anti-Mullerian hormones were 1.33 (0.93-1.91) µIU/mL, 4.67 (3.41-6.41) mUI/mL, 89 (43-142) pg/mL, and 1.43 (0.56-2.38) ng/mL, respectively. Genotyping revealed that 35/89 (39%) patients were Thr/Ala, 21/89 (26%) were Ala/Ala, and 31/89 (35%) were homozygous for the Thr allele. Ala/Thr individuals experienced a lower rate of abortions (17.1%) compared to Thr/Thr (31%) or Ala/Ala (52.4%) (p= 0.01). Notably, the heterozygous genotype (Thr/Ala) was linked to a 76% diminished risk of abortion. Univariate and multivariate logistic regression analyses, adjusted for multiple covariates, demonstrated a consistent reduction ranging from 73% to 77%. All the other clinical and laboratory biomarkers tested were similar among the three genotypes. **Conclusion:** DIO2Thr92Ala heterozygosity was associated with lower documented pregnancy loss rates in UI/LOR women. TH action and metabolism modulation in the reproductive system, including genetic variants of crucial genes such as DIO2, should be better investigated in the future.

130157 – THE THR92ALA POLYMORPHISM IN THE TYPE 2 DEIODINASE GENE IS LINKED TO DEPRESSION IN COVID-19 PATIENTS AFTER HOSPITAL DISCHARGE

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Introduction: The Thr92Ala-DIO2 polymorphism has been associated with clinical outcomes in hospitalized COVID-19 patients and neuropsychiatric diseases. This study examines the impact of the Thr92Ala-DIO2 polymorphism on neuropsychological symptoms, particularly depressive symptoms, in patients who have had moderate to severe SARS-CoV-2 infection and were later discharged. **Methods:** Our prospective cohort study, conducted from June to August 2020, collected data from 273 patients hospitalized with COVID-19. This included thyroid function tests, inflammatory markers, hematologic indices, and genotyping of the Thr92Ala-DIO2 polymorphism. Post-discharge, we followed up with 68 patients over 30 to 45 days, dividing them into depressive (29 patients) and non-depressive (39 patients) groups based on their Beck Depression Inventory scores. **Results:** We categorized 68 patients into three groups based on their genotypes: Thr/Thr (22 patients), Thr/Ala (41 patients), and Ala/Ala (5 patients). Depressive symptoms were less frequent in the Thr/Ala group (29.3%) compared to the Thr/Thr (59.1%) and Ala/Ala (60%) groups (p = 0.048). The Thr/Ala heterozygous genotype correlated with a lower risk of post-COVID-19 depression, as shown by univariate and multivariate logistic regression analyses. These analyses, adjusted for various factors, indicated a 70% to 81% reduction in risk. **Conclusion:** Our findings appear to be the first to show that heterozygosity for Thr92Ala-DIO2 in COVID-19 patients may protect against post-COVID-19 depression symptoms up to two months after the illness.

130469 – THR92ALA-DIO2 HETEROZYGOSITY IS ASSOCIATED WITH SKELETAL MUSCLE MASS AND MYOSTEATOSIS IN PATIENTS WITH MODERATE TO SEVERE COVID-19

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Introduction: The type 2 deiodinase and its Thr92Ala-DIO2 polymorphism have been linked to clinical outcomes in acute lung injury and COVID-19. **Objective:** To identify a potential association between Thr92Ala-DIO2 polymorphism and body composition (appendicular muscle mass (MA), myoesteatosis, and fat distribution) and to determine whether they reflect the severity or mortality associated with the disease. **Methods:** In this prospective cohort study (June-August 2020), 181 patients hospitalized with moderate-to-severe COVID-19 underwent a non-contrast-enhanced CT of the thorax to assess body composition, laboratory tests, and genotyping for the Thr92Ala-DIO2 polymorphism. **Results:** 181 consecutive patients were stratified into three subgroups according to the genotype: Thr/Thr (n = 64), Thr/Ala (n = 96), and Ala/Ala (n = 21). The prevalence of low MA (< 92 cm^2) was 52.5 %. Low MA was less frequent in Ala/Thr patients (44.8%) than in Thr/Thr (60.9%) or Ala/Ala patients (61.9%) (p = 0.027). Multivariate logistic regression analysis confirmed that the Thr/Ala allele was associated with a reduced risk of low MA (41% to 69%) and myosteatosis (62% to 72%) compared with Thr/Thr + Ala/Ala (overdominant model). Kaplan-Meier curves showed that patients with low muscle mass and homozygosity had lower survival rates than the other groups. Notably, the heterozygotes with MA ≥ 92 cm^2 exhibited the best survival rate. **Conclusion:** Thr92Ala-DIO2 heterozygosity is associated with increased skeletal MA and less myosteatosis in patients with COVID-19. The protective effect of Thr92Ala-DIO2 heterozygosity on COVID-19 mortality is restricted to patients with reduced MA.

130570 – HEART FUNCTIONALITY AND PROTEIN EXPRESSION ARE PRESERVED IN ALLOXAN-INDUCED DIABETIC RATS BY T3 ASSOCIATED TO LOW DOSES (3U) OF INSULIN TREATMENT

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Introduction: Diabetes mellitus (DM) is one of the main risk factors for cardiac dysfunction. Instead, triiodothyronine (T3) induces positive inotropic and lusitropic effects, and the synthesis of proteins involved in these effects, which are decreased in the DM. Studies from our laboratory showed hypothyroidism in rats induced to DM by alloxan, and that the treatment with T3 (1,5 ug/100g, i.p.) plus half of the physiological replacement dose of insulin (3U, s.c.) reduced the glycemia and serum TSH to the control group values. **Objective:** Investigate the repercussions of this combined therapy on the function and protein expression of the left ventricle (LV) of DM rats. **Methods:** Wistar rats were divided into control (C); diabetic (D), (induced by alloxan [150 mg/kg]); D treated with insulin 3U, s.c. (DI3) or T3,1,5 µg/100g, i.p. (DT3); or T3 plus insulin (DT3I3) groups, in the same doses reported above. After 4 weeks, blood glucose and glucose decay rate, using the insulin tolerance test, were evaluated. Rats were then anesthetized (urethane, 1,6 mg/kg, i.p.) and subjected to catheterism for LV hemodynamic evaluation. Lastly, the rats were euthanized and T3 target proteins' expression was analysed by Western Blotting. **Results:** D rats presented hyperglycemia and insulin resistance *vs.* C. All treatments improved these parameters, but only DT3I3 reached the C values. LV weight was reduced in D *vs.* C, and T3I3 treatment was able to reverse it. Heart rate (HR) and cardiac function, evaluated by the LV systolic pressure (LVSP), initial and final diastolic pressure (LVIDP and LVFDP) and by cardiac contractility and relaxation indexes (dP/dt+ and dP/dt-), were not changed in the D and DI3 *vs.* C. The T3 and T3I3 treatment increased HR and reduced the LVIDV *vs.* D, without modifying any other parameter. The α and βMHC and the subunit α1Na+/K+ ATPase expression was not modified in D, while the SERCA2a/PLN ratio was reduced *vs.* C. I3 treatment increased the αMHC expression and the SERCA2a/PLN ratio *vs.* D. T3 treatment increased αMHC and α1Na+/K+ ATPase expression *vs.* D. Again, T3I3 treatment did not alter the expression of any evaluated protein (T3I3 = C). **Conclusion:** T3 associated to insulin (3U) treatment was able to preserve the LV weight, functionality and the expression of proteins related to cardiac mechanics of D rats to values of the C group, indicating that this treatment doesn't provoke any adverse effects on the heart, while improves glycemia control.

130513 – HYPERTHYROIDISM TREATMENT MODALITY CAN IMPACT WEIGHT GAIN IN PATIENTS WITH GRAVES' DISEASE – A LONGITUDINAL STUDY

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Introduction: Weight gain in patients with Graves' disease (GD) after clinical compensation has been reported and is a concern given the subsequent associated complications. Greater loss of lean mass and the severity of hyperthyroidism are possible factors associated. Some studies suggest that weight gain is greater in patients undergoing radioiodine therapy (RAI). **Objectives:** To compare the weight variation according to the definitive treatment modality selected; and to compare this variation with patients who received antithyroid drugs (ATD) until clinical remission and were followed by a similar period. Furthermore, to assess factors associated with the greatest percentage change in weight. **Methods:** A retrospective, descriptive longitudinal study evaluated 95 patients with GD from a universitary hospital who initially received treatment with ATD and subsequently progressed to: clinical remission with suspension of ATD (n = 42), surgery (n = 33) or RAI (n = 20). These patients had at least a minimum period of 24 months of follow-up for weight reassessment. Weight variations in the 3 different therapeutic modalities were compared. **Results:** Weight variation was greater ($p < 0.01$) in those who received RAI (+17.1% [IQR: +9.7% /+ 28.7%]) compared to those who underwent surgery (+7.8% [-4.7% / +19.2%]) and those who only used ATD (-0.3% [-4.8% /+ 4.6%]). The longer the time of ATD use, the lower the weight gain ($rs – 0.224$; $p = 0.05$). This fact was confirmed in those who were referred for RAI, since the duration of ATD use before definitive treatment was negatively correlated with weight gain ($rs -0.304$; $p = 0.08$). Other factors that were correlated with greater weight variation were the iodine uptake before RAI ($rs 0.717$; $p = 0.01$), the amount of radioiodine administered ($rs 0.609$; $p = 0.031$) and TSH at the end of the cohort ($rs 0.0289$ $p = 0.04$). Furthermore, those who were euthyroid at the end of the cohort had significantly ($p < 0.01$) less weight gain (1.2% [0.6%/+17.9%]) than those who were hypothyroid (+19.7% [9.8%/29.1%]). **Conclusion:** Weight gain in treated GD patients was greater in those undergoing RAI and was associated with greater uptake and dose of radioiodine used. The longer the time of ATD use, whether throughout the entire cohort or before RAI, was associated with less weight gain. The data reveal that the use of ATD for a prolonged period, greater than 4 years, is an option associated with clinical remission and less impact on weight.

MÉTODOS DE DIAGNÓSTICO

130591 – IN THYROID HEALTH AND HYPOTHYROIDISM, CIRCULATING MRNA OLFACTORY RECEPTOR EXPRESSION CORRELATES WITH KIDNEY AND PLACENTA TISSUE EXPRESSION

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Inttroduction: In a previous RNA-Seq study, we demonstrated that circulating olfactory receptors (ORs) ribonucleic acid (RNA) are differentially expressed in the peripheral blood of pregnant hypothyroid women. We also showed that ORs could predict preeclampsia. Nevertheless, every time we study the circulating RNA, a question arises: what is the relationship between what we observe in the blood and the physiology of this same gene in the tissues? However, the relationship between blood and tissues has not yet been investigated. To answer that, we analyzed the expression of the homologous ORs in euthyroid, hypothyroid, and hypothyroid rats undergoing levothyroxine treatment. **Methods:** This Project was approved by the Ethics Committee (nº 2750091219). The experimental model was constructed with pregnant Wistar rats (Rattus norvegicus). The hypothyroidism induction was carried out by the administration of Methimazole and iodine-deficient AIN-93G manipulated chow. The hypothyroid-treated group received 42 µg/kg of levothyroxine. The TSH, T4, and T3 measures confirmed the experimental adequacy. We selected the differential expressed genes (DEG) from our transcriptomic data (GSE157148/GSE 147527) available in the GEO database. The RT-qPCR amplifications of Olr519, Olr1576, Agtr1a, Pgf, and Oprm1 were performed with the 7500 Real-Time PCR System instrument. The expression in blood, heart, kidney, and placenta were analyzed. Statistical Analysis: RE values were log-transformed, and the correlation was used to calculate the Pearson and squared correlation coefficients (R2). We also performed a non-linear regression to estimate the R2 without the transformation. The highest R2 defined the mathematical model. IBM SPSS Statistics for Windows (version 23.0) was used for data analysis. **Results:** We found Olr519 and Olr1576 expressed in blood, kidney, and placenta, but we did not detect expression in the heart. In the blood, we identified a correlation between the two ORs and Agtr1a (r: 0.444, p: 0.044; r: 0.752, $p < 0.001$). There was also a correlation between the two ORs in the placenta and kidney, r: 0.848, $p < 0.001$, and r: 0.866, $p < 0.001$, respectively. Finally, the two ORs' blood expression correlate with the placenta in the hypothyroidism group. **Conclusion:** We ratified ORs homologous expression in blood and tissues. To validate OR as biomarkers, it was essential to confirm that the blood expression correlates with their tissue expression.

130243 – DEVELOPMENT OF A STRATEGIC BIOINFORMATIC PIPELINE DESIGNED TO INVESTIGATE GENE VARIANTS INVOLVED IN REDOX BALANCE WITH POTENTIAL DIAGNOSTIC AND PROGNOSTIC VALUE IN THYROID CANCER

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Thyroid cells rely on a robust oxidation-reduction (REDOX) system to safeguard against DNA damage from oxidative stress, stemming from high levels of reactive oxygen species. The crucial roles of SOD1, SOD2, GPX-1, and G6PD in the promotion and progression of various types of cancer as well as their influence on pathways frequently activated in thyroid cancer are widely recognized. However, studies of thyroid tumors have yielded controversial results. In order to identify potential biomarkers and therapeutic targets, our group developed a strategy for a thorough analysis of the entire coding region of these genes by combining open-source bioinformatics techniques, publicly accessible datasets, and molecular quantum chemistry with multiple analysis algorithms including 13 tools. Also, we investigated the frequency of genetic alterations and their association with protein expression levels, and validated our results using large cancer biological databases (cBioPortal, OncoPrint and PrognoScan). We amassed 1.885 nsSNPs from dbSNP, including 223 for SOD1, 593 for SOD2, 324 for GPX1, 389 for G6PD, and 356 for CYBA. Eleven nsSNPs (8 in SOD1, 1 in GPX1, 1 in G6PD, and 1 in CYBA) consistently exhibited detrimental forecasts across all 13 tools, demonstrating potential changes in protein function, structure, and stability, which can lead to perturbations in the REDOX balance. In addition, it was observed a robust interaction between G6PD and other proteins showing that its expression positively affects the expression of TP53 and HRAS, making G6PD a potential target for targeted therapy. Investigation of the frequency of genetic alterations and their association with protein expression levels was hindered by the low mutation rate found in 1.629 samples from patients with thyroid tumors in the database. Clinical databases indicated that SOD1, SOD2, GPX1, G6PD, and CYBA were associated with worse prognosis for several types of cancer, but our analysis did not reveal any significant impact on survival. Investigation of mRNA expression levels in the GEPIA database also did not show any impact of these genes on the overall survival of patients with thyroid cancer. In conclusion, we suggest that variations in these genes may influence antioxidant efficiency and play a role in the development and progression of thyroid cancer but not in its prognosis. Large-scale clinical studies in different ethnic populations and laboratory experiments are required to validate our results.

130576 – HIGH-RISK PREGNANCY IS ASSOCIATED WITH LOW URINARY SELENIUM CONCENTRATION

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Introduction: Selenium (Se) is a fundamental trace element during pregnancy and its deficiency is associated with negative maternal-fetal outcomes. Little is known about Se nutritional status in High-risk pregnancy women (HRPW). **Objective:** To analyze the nutritional status of Se in pregnant women (PW) screened in an important public maternity hospital in Brazil. **Methods:** In This cross-sectional study (May 2015- July 2016), 330 PW were investigated for Urinary Selenium Concentration (USeC) using the inductively coupled plasma mass spectrometry (ICP-MS) method. Socio-demographic, anthropometric data were collected and PW were classified by gestational risk according to the Ministry of Health. **Results:** 330 PW [median age: 29 (15-46) years] were divided into: (i) 226 HRPW and (ii) 104 Low risk pregnancy women (LRPW). The median USeC (MUSeC) was 25 µg/L (25th-75th percentile, 17-35.8 µg/L) and the mean was 28.4 ± 6.79 µg/L, indicating Se adequacy (SA). Low USeC (<15 µg/L) was detected in 20% PW. MUSeC levels were significantly lower in HRPW *vs.* LRPW [MUSeC: 24 (15.3-33.8) *vs.* 29.1 (20.2-40.6) µg/L, p = 0.0035]. Selenium Deficiency (SeD) rate was more observed in HRPW *vs.* LRPW [24.3% *vs.* 10.6%, p = 0.0037] [OR: 2,71 CI 1,4-5,7); P = 0.0048]. The adjusted odds ratio (OR) of HRP induced SeD was 3.38 (95% CI: 1.56-8.06, p = 0.003) after being adjusted for all the accepted confounders in multivariate logistic regression. **Conclusion:** This study reports USeC data on the largest number of HRPW, demonstrating an association between HRP and low USeC. This situation highlights the need for continuous nutritional monitoring of HRPW.

129887 – MEDULLARY THYROID CARCINOMA

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Introduction: Medullary thyroid carcinoma (MTC) corresponds to approximately 3% to 11% of thyroid tumours. It is a neoplasia of the parafollicular cells (or C cells), which produce the calcitonin hormone. Even though it can be sporadic, it is generally a hereditary cancer, being related to the RET proto-oncogene. MTC is an indolent tumour, with survival rates depending on which staging it was detected, and diagnosis generally made through cytology via fine needle aspiration (FNA), with immunohistochemistry being a possible aid for difficult cases. The sole possibility of cure is through chirurgical intervention; the 10 year survival rate varies according to the existence of lymph node metastasis, being approximately 95% in its absence and between 15% to 40% in its presence. Cervical ultrasonography is recommended for all patients with MTC suspicion, not only for the evaluation of the nodules and execution of the guided FNA, but also due to being the most sensible exam for cervical metastasis. Some of the characteristic findings of MTC to the ultrasound are hypoechogenicity, solidity, microcalcifications, irregular margins, and high vascularization on the Doppler, with prevalence of central vascularization over the peripheral. **Case report:** E.H.C., 56 years old, referred for thyroid FNA. At the USG examination, an isoechogenic nodule was found in the right lobe; it had a solid pattern and peripheral and central vascularization, the latter prevailing (Chammas IV/ TI-RADS 3). Its measurements were 2,92 x 1,84 x 2,27 cm, being wider than tall. The procedure was eventless. The cytopathological report favoured medullary carcinoma, showing groupments of plasmacytoid and spindle cells with abundant cytoplasm, round and eccentric nuclei, Bethesda category V. The patient underwent total thyroidectomy, and is in post-operative follow up, asymptomatic. **Conclusion:** In over 90% of MTC cases, the nodules are hypoechogenic, with intranodular calcification and no halo signal. However, in the presented case, the analysed nodule was isoechogenic, with no signs of calcification, being classified as ACR TI-RADS III. The aspiration was indicated due to the size of the nodule, without it having markedly malignant characteristics on the ultrasound. Thus, it's evident that attention to the ACR TI-RADS criteria are extremely important to the early detection of neoplasia.

130048 – EVALUATION OF FREE THYROXIN LEVELS IN PATIENTS WITH LOW THYROXIN BINDING GLOBULIN CONCENTRATIONS: IS THERE INTERFERENCE IN THE FT4 INDIRECT METHOD?

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Introduction: Thyroxine-binding globulin (TBG) is the major carrier of thyroid hormones in serum. Variations in the serum concentration of TBG determine proportional variations in the total serum concentrations of T4 and T3, without implying changes in function, as long as the free fraction remains normal. Several common clinical conditions lead to significant alterations in TBG levels, the most important factor behind low levels being genetic defects. As TBG is encoded by a gene located on the X chromosome, the defects are more easily manifested in males. Differences in FT4 concentrations were observed in sera from subjects with TBG abnormalities, when FT4 are measured by different immunoassays, specially at extremes of TBG concentrations. **Objective:** The objective of this study was to evaluate FT4 levels by indirect method in patients with low TBG concentrations. **Methods:** We analyzed blood samples requesting serum TBG, TSH and FT4 levels from patients admitted to a private reference clinical laboratory in Brazil, from 01/01/2017 to 12/31/2022. Anonymized data on laboratory tests was available from a database of the local Laboratory Information System. All the patients included had TSH within the reference range, 0.4 to 4.3 mUI/mL (ECLIA, Modular, Roche). FT4 was measured by ECLIA (0.7 to 1.8 ng/dL) and TBG by ICMA, Immulite, Siemens, 13 to 39 mcg/mL. **Results:** 357 patients with low TBG levels were evaluated, 220 (62%) men, 137 (38%) women; mean age 35 yrs (19 d to 88 yrs). They were divided in six groups according TBG levels (mcg/mL): < 3.5; 5.79 and 9.53 ng/mL, respectively. **Conclusion:** FT4 Indirect methods are developed taking into account the presence, in the serum, of a thyroxine binding capacity within the normal range, a fact that does not occur in individuals with extreme TBG deficiency. In this study, we found only one slightly elevated FT4 value among 17 patients with TBG values below 3.5 mcg/mL, suggesting little interference of very low TBG levels in this indirect free T4 method.

NÓDULOS E CÂNCER DE TIREOIDE

129716 – RECURRENT FOLLICULAR THYROID CARCINOMA WITH FUNCTIONING METASTASES, A CASE REPORT

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Introduction: Follicular thyroid carcinoma (FTC) is a malignant neoplasm derived from well-differentiated follicular epithelial cells. However, it can be aggressive, with distant metastases, mainly affecting bones and lungs, via hematogenous dissemination. **Case report:** A 71-year-old woman was admitted with an obstructive infraglottic tumor on 06/09/2023. In the last six months she developed hyporexia, nausea, rapid weight loss 10 kg, and severe low back pain, impairing deambulation. CT scan showed a L1 lytic lesion associated with pathological fracture and soft-tissue extension. She had a past history total thyroidectomy in 2017 due to FTC (Anatomopathology: FTC without capsular extension or vascular invasion), with subsequent use of levothyroxine (LT4) 100 mcg, recently requiring progressive dose reduction until discontinuation. A CT scan of the neck on 12/07/2023 showed an infiltrative formation, signs of erosion in the left vocal fold and irregularities in the adjacent cartilages. MRI of lumbosacral spine 23/09/2023: infiltrative lesion in thoracic and lumbar vertebrae, suggestive of bone metastases. In 02/10/23, she underwent emergency tracheostomy, fixation of the vertebral lesion, and biopsy of the infraglottic lesion, which revealed squamous metaplasia. One week later, laryngectomy with resection of part of base of the tongue and esophagus was performed, confirming metastatic follicular carcinoma in the larynx, primary of the thyroid. Laboratory tests showed persistently suppressed TSH, and free T4 initially elevated, and posteriorly normal, without levothyroxine replacement, and even after laryngectomy, suggesting autonomous production of thyroid hormone by the metastases. **Conclusion:** We report a case of recurrent FTC after total thyroidectomy, with functioning bone metastases. The recurrence of FTC, the occurrence of bone metastasis and the presence of vascular invasion draw attention, since the recurrence rate for well-differentiated carcinomas is around 35%, highlighting the need for regular post-operative follow-up and the evaluation of adjuvant therapies.

130582 – IMPORTANT METASTATIC REDUCTION OF FOLLICULAR THYROID CARCINOMA WITH LENVATINIB THERAPY

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Introduction: The use of systemic therapy with doxorubicin was the only therapeutic option available in Brazil for iodine-refractory differentiated thyroid carcinomas, with minimal efficacy and significant toxicity, until 2016, when Anvisa approved Lenvatinib, a tyrosine kinase inhibitor that acts in several signaling pathways involved in disease progression. This approval was based on data from the SELECT study, in which 261 patients treated with Lenvatinib experienced an average gain of 14.7 months in disease progression-free survival compared to patients using placebo. Furthermore, around 65% of patients developed not only a delay in progression, but also a regression in the size of the lesions. On the other hand, the occurrence of side effects was considerable, and had a negative impact on the maintenance of therapy. **Case report:** We followed a female patient, diagnosed with follicular thyroid carcinoma in 2013, at the age of 54, with locally advanced disease and the presence of lymph node and distant metastases in the lung. The patient underwent total thyroidectomy with removal of perithyroidal lymph nodes in 2013, followed by three doses of radioactive iodine between 2013 and 2016 (with a total dose of 750 mCi), left and right lung segmentectomy in 2018 for resection of metastases and recurrent emptying of the right in 2021, and maintained with suppressed TSH throughout the period. Despite all the interventions carried out, from 2019 onwards the disease evolved with a progressive increase in thyroglobulin and the size of the lung lesions (from 0.6 cm to 1.6 cm in 3 years). In July 2023, the patient started using Lenvatinib at a dose of 24 mg once a day. At the time, he had paratracheal lymph node enlargement of up to 2.0 cm and multiple pulmonary nodules, the largest measuring 1.7 cm. Just 2 months later, the medication was stopped due to severe mucositis, hypocalcemia (Ca 6.6) and hyponatremia (Na 106) as side effects of the drug. In the new chest tomography performed one week after stopping Lenvatinib, the largest paratracheal lymph node measured 1.8 cm and the largest pulmonary nodule 1.1 cm. **Conclusion:** Despite the short treatment period, the case described showed an excellent response to Lenvatinib, with a reduction of approximately 35% in the size of metastatic lesions.

130520 – V804M RET MUTATION AND FAMILIAL MEDULLARY THYROID CARCINOMA (FMTC): REPORT OF A BRAZILIAN FAMILY

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Introduction: The V804M RET mutation is the 3rd most common pathogenic variant associated with FMTC in Brazil. The 2015 revised ATA Medullary Thyroid Cancer (MTC) Guidelines placed such variant in the moderate-risk category, with the recommendation of thyroidectomy in heterozygous carriers in childhood by 5-10 years. However, there is some controversy in the literature regarding RET V804M phenotypic correlates, as well as the appropriate age for prophylactic thyroidectomy. None of the 15 Brazilian families carrying the variant V804M RET mutation has been described to date. **Objective:** To assess the penetrance and aggressiveness associated to RET-V804M mutation in a Brazilian family with MEN2A. **Methods:** Eleven members from three generations were evaluated. A RET proto-oncogene mutation, calcitonin (CT) measurement and thyroid ultrasound were performed on all individuals. RET mutation was performed by direct sequencing of PCR products from the entire RET coding region using DNA extracted from patients' whole blood samples. **Results:** The proband (female sex), diagnosed with MTC at 40 years of age, presented lymph node and lung metastasis in less than 10 years with indolent progress to date. Eleven members of three generations of the family were evaluated. Eight members (5 female) were positive for the RET V804M mutation (72.7% of penetrance), six of them underwent thyroidectomy. Only one (1st generation) of the eight patients was diagnosed with MTC at 40 year of age. Two members of the 2nd generation (20 and 27 years of age), and two members of the 3rd generation (3 and 6 years of age) were diagnosed with C-cell hyperplasia, all of them with normal CT levels before surgery. Only one member (2nd generation) had no thyroid gland alteration. Hyperparathyroidism or pheochromocytoma was not detected in any case. **Conclusion:** Our study revealed a high penetrance and low aggressiveness of the RET V804M mutation in the studied family. The data also suggest the need to review the recommendation for prophylactic surgery in children by 5- 10 years of age carrying the RET V804M mutation without taking into account the CT levels.

130051 – MALIGNANT STRUMA OVARII CONCOMITANT TO PRIMARY PAPILLIFEROUS THYROID CARCINOMA – CASE REPORT

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Introduction: Struma ovarii is a rare type of ovarian teratoma, composed of more than 50% mature thyroid tissue. It corresponds to 0.5% of ovarian tumors and has a 5% chance of malignancy. It rarely occurs concomitantly with Primary Thyroid Tumor. **Case report:** A 31-year-old female patient without previous disease underwent a tumorectomy of the right ovarian mass in 2018, revealing a mature teratoma in the histopathological examination. Lost medical follow-up until 2021, when presented pain and a progressive increase in abdominal volume. Nuclear magnetic resonance Imaging showed a solid-cystic ovarian lesion on the right, measuring 17 x 16 x 7.5 cm, extending to the epigastrium, associated with a small volume of ascites and signs of carcinomatosis. She underwent exploratory laparotomy for tumor excision, abdominal implants, and bilateral salpingo-oophorectomy. Confirmed primary malignant struma ovarii of the papillary thyroid carcinoma subtype. She was referred to the Endocrinology Service with normal thyroid function, Thyroglobulin 970 ng/mL (<38.5), and Thyroid Ultrasound with the presence of solid-cystic nodules, FNA reveled Bethesda V. Total thyroidectomy was performed on 03/22 evidencing Primary Papillary Thyroid Carcinoma. Radioiodine therapy (RIT) was indicated with a dose of 200mci of ^{131}I (iodine) at 6 and 12 months after thyroidectomy and whole-body scintigraphy (WBS) after doses under recombinant TSH stimulation. The result after 1st RIT + WBS (01/23): Bulky pelvic accumulation, multiple scattered abdominal areas, and two thoracic accumulation areas, TSH 41.81 uUI/mL (0.4-4) and thyroglobulin 11,854 ng/mL(< 38.5). After 2nd RIT + WBS (05/23): Reduction in pelvic mass and the number of abdominal foci and absence of focal areas of chest accumulation, TSH 61.31 uUI/mL (0.4-4) and thyroglobulin 3,165 ng/mL (<38.5). She is undergoing medical follow-up with hormonal replacement, aiming to suppress TSH. **Conclusion:** Malignant struma ovarii is more common in patients between 30 and 40 years old, and papillary thyroid carcinoma is the most common histological type. The concomitance with primary thyroid neoplasia is rare, with few cases reported. The scarcity of information about synchronous tumors makes it difficult to define treatment and post-surgical follow-up. The description of the current case provides relevant information that can help future decisions about the management of the disease, reflecting its prognosis.

128391 – ACTIVE SURVEILLANCE OF CERVICAL LYMPH NODE METASTASIS IN DIFFERENTIATED THYROID CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Cervical lymph nodes (LN) represent the most common site of recurrence in differentiated thyroid cancer (DTC), frequently requiring repeated surgical interventions that contribute to increase morbidity to a usually indolent disease. Data on active surveillance (AS) of cervical LN metastasis obtained from observational studies are limited. **Objectives:** To evaluate AS in cervical metastatic LN of DTC patients by performing a systematic review and meta-analysis. **Methods:** MEDLINE (PubMed), EMBASE, and Cochrane databases and gray literature were searched up to July 2023 for studies that included patients with DTC and metastatic cervical LN who were followed up with AS. Two independent reviewers performed the data extraction and methodological quality assessment (Newcastle-Ottawa scale). The primary outcome was disease progression, according to the study's definition. Additional outcomes were disease progression defined by LN enlargement ≥ 3 mm in any diameter or the occurrence of new cervical metastasis and conversion from AS to surgical treatment. The summarized data were analyzed using an inverse-variance weighting model. **Results:** The search identified 375 studies, and seven were included in the data synthesis, comprising 518 patients with metastatic nodal DTC. Most patients were female (70.5%) and had papillary thyroid cancer (99.8%). The mean AS follow-up period ranged from 28-86 months. Following each study's definition of disease progression, the pooled overall incidence was 26% [95% confidence interval (CI), 18%-35%], with significant statistical heterogeneity. The pooled overall incidence of LN growth ≥ 3 mm was 20% [95% CI, 17%-24%], with no statistical heterogeneity. Progression measured by the emergence of new LN sites had a pooled overall incidence of 19% [95% CI, 14%-25%] and no statistical heterogeneity. Combining growth of 3 mm and the emergence of new LN criteria, we found an overall incidence of 24% [95% CI, 19%-31%] with moderate statistical heterogeneity. The overall incidence of the indication for lymphadenectomy during AS was 19% [95% CI, 13%-26%], with elevated statistical heterogeneity. **Conclusions:** AS seems to be a suitable strategy for selected DTC patients with small cervical metastatic disease, avoiding or postponing surgical reintervention.

130580 – THE RISK OF THYROID MALIGNANCY ACCORDING TO THE AMERICAN COLLEGE OF RADIOLOGY THYROID IMAGING REPORTING AND DATA SYSTEM (ACR-TIRADS) CLASSIFICATION IN PEDIATRIC PATIENTS

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Introduction: Thyroid nodules (TN) are rare in children, although with a higher risk of malignancy compared to adults. The American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) is the best system for risk stratification and indication of fine needle aspiration biopsy (FNAB). However, the applicability of ACR-TIRADS in pediatric TN remains uncertain, and FNAB indication according to the ACR-TIRADS criteria for pediatrics has not yet been defined. **Objective:** Evaluate the performance of ACR-TIRADS classification in a cohort of pediatric patients with TN, correlating these features with biopsy results. **Methods:** We reviewed a retrospective cohort of pediatric patients ≤ 18 years who presented TN followed at a reference center from 2012 to 2023. All TN were independently classified according to the ACR-TIRADS by two blinded radiologists. We assessed the correlation between the ACR-TIRADS, dividing into 2 groups: TR1, TR2 and TR3 or TR4 and TR5 and the biopsy outcomes indicating benign or malignant status. **Results:** Our cohort consisted of 58 children and adolescents, comprising a total of 65 TN. The majority were female (70.7%), with a mean age of 14.0 (±3.4) years. The median size of the nodules was 1.45 [interquartile range (IQR): 0.78-3.15)] cm. The median TSH level was 1.96 (IQR: 1.17-3.67) mU/L. A history of previous cancer was evident in 17.2%, 13.8% had prior radiation exposure to the thyroid gland, and 13.8% had a positive family history of thyroid cancer. The malignancy rate was 20.7%, while 46 patients were diagnosed with benignity (20 of these were assumed to have benign conditions due to non-suspicious findings on thyroid US, with a median time of follow-up of 17 months, IQR: 4.5-38.0). Regarding the ACR-TIRADS evaluation, the interobserver agreement was high, with a kappa of 0.86 [95% confidence interval: 0.75, 0.97]. For predicting malignancy by using the cut-off of TR4 and TR5, we found rates of positive predictive value, negative predictive value, sensibility, and specificity of 50.0%, 97.6%, 87.5% and 85.4%, respectively. The area under the ROC curve could not find a cut-off for nodule size for predicting malignancy. **Conclusion:** In our cohort, ACR-TIRADS risk classification presented a high accuracy for predicting thyroid cancer in children and adolescents when using specifically the cut-off of TR4 and TR5. The US characteristics seem to be more important than the size of the nodules for prediction of malignancy.

130614 – PAPILLARY THYROID CARCINOMA IN A HIGH-RISK PATIENT WITH INCOMPLETE BIOCHEMICAL RESPONSE: CASE REPORT

MAIN AUTHOR: BRUNO DE FREITAS RICARDO PEREIRA

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Introduction: Papillary thyroid cancer (PTC) represents 80% of thyroid carcinoma cases, being the most common endocrine neoplasm. The most affected group are women aged 30 to 50, and its growth is generally slow with a good prognosis if treated. The spread of PTC occurs through the lymphatic system, with multicentric thyroid lesions, commonly cursing with lymph node involvement. Extrathyroidal invasion occurs in 20% of cases, and 5% of patients can have distant metastases, mainly to the lungs. **Case report:** M.R.F., 58 years old, diagnosed with PTC in 2016, treated with total thyroidectomy. The pathological analysis revealed diffuse sclerosing variant of the left lobe reaching regional muscle bundles, evidenced vascular invasion, parathyroid with discreet fatty infiltration of the parenchyma, and 3 compromised perithyroidal lymph nodes. After 6 months, a therapeutic dose of 150 mCi radioiodine (I131) was administered, followed by Whole Body Scintigraphy (WBS), indicating uptake in the thyroid site. During follow-up, she continued to present high levels of Thyroglobulin (TG) curve with TG = 68 and TSH = 90, which indicated incomplete biochemical response. A Chest Computed Tomography (CT) was requested to study the cause, finding an isolated nodular focus with ground-glass attenuation in the upper lingular segment, just within the fissure. She returned to the service in 2021, after discontinuing follow-up due to the COVID-19 pandemic, when new exams were repeated and the CT showed scattered tiny noncalcified centrilobular nodular opacities in the lateral segment of the middle lobe. It was decided to start a new therapeutic I131 (200 mCi), aiming to achieve biochemical response and treat the tomographic findings. Thus, the most recent WBS showed none iodine-avid tissue, just as the CT showed no residual abnormalities. The patient continues under follow-up using suppressive doses of levothyroxine, and still with high levels of TG (=10,7) and TSH = 0.06. **Conclusion:** An increase in the global incidence of PTC has been observed, which may be related to increased detection. However, current evidence suggests that there is a real increase in this neoplasm, which may be related to risk factors such as obesity, exposure to ionizing radiation, genetic factors, among others. Therefore, adequate follow-up is vital, in order to reach early and individualized treatment, as well as detect any sign of recurrence, ensuring the maintenance of the patient's quality of life.

129218 – CLINICAL PROFILE OF RAI-REFRACTORY DTC FOLLOWED AT A UNIVERSITY HOSPITAL ON THE NORTHEAST OF BRAZIL

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Introduction: Most DTC are curable with surgery followed or not by RAI and TSH suppression. However, local recurrence and/or distant metastases occur in approximately 15% of cases during follow-up and nearly two-thirds of these patients will become RAI-refractory with a poor prognosis. **Objectives:** to describe the prevalence, clinical and epidemiological profile of patients with RAI-Refractory DTC treated at the Endocrinology Service of HU-UFMA between January 2010 and December 2023. **Methods:** A total of 450 medical records were retrospectively evaluated. **Results:** there was a prevalence of 3.1% (n = 14/450) of RAI-refractory tumors. Most were women (n = 13; 92.8%) and mean age was 51.3 ± 13.9 years at diagnosis of DTC. PTC (n = 13; 92.8%) was the most common type of TC. Most cases were classified as stage I (n = 7; 50%) and high risk of recurrence at diagnosis (n = 10; 71,4%). During treatment, the average dose of RAI administered was 404.3 ± 177.7 mCi. At final medical appointment, 85.7% (n = 12) evolved with structural and there were 2 cases of biochemical disease. Lungs were the most common site of distant metastasis. The time for RAI-refractory diagnosis was 4.85 ± 2.82 years and the most frequent criteria was DTC with more than one metastatic lesion with at least one target lesion without radioiodine uptake. This was found in 42.9% (n = 6). Only two patients (14.28%) used MKI due to disease progression. **Conclusion:** RAI-Refractory DTC occurred in few patients. High risk patients may develop RAI-refractory disease more frequently but this needs to be confirmed in more studies.

129209 – CRIBIFORM MORULAR THYROID TUMORS MAY RECEIVE A DIFFERENT TREATMENT OF OTHER FORMS OF DIFFERENTIATED THYROID CANCERS

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Introduction: Tumors with papillary cribriform and morular architecture were initially considered to be variants of papillary thyroid carcinoma; however, recent observations have challenged this view and the new WHO classification names it as a thyroid tumor of uncertain histogenesis. **Case report:** A 32-years-old women underwent total thyroidectomy due to multinodular goiter. The biopsy showed a multifocal tumor with cribiform and morular architecture. The biggest nodule had 10,5cm and there was no vascular invasion and no extrathyroidal extension. Two linfonodes showed metastasis. Tumor was classified as pT3aN1aMx Intermediate risk of recurrence. The stimulated thyroglobulin (Tg) tested after surgery was 0,8 ng/d and the antibody anti-Tg was negative. The patient was submitted to RAI (150 mci 131 I) and the WBS was normal. During the follow up the patient had a femur pathological fracture. After that, she underwent a surgery and the biopsy showed thyroid cancer metastasis. **Conclusion:** Cribiform morular thyroid carcinoma is a distinct Entity and may not be treated as DTC. New strategies of follow-up and treatment may be used for these cases as Tg and WBS failed to demonstrate a metastasis in our patient.

130522 – HIRSCHSPRUNG'S DISEASE IN AN MEN2A PATIENT DUE TO A RET P.CYS609SER PATHOGENIC VARIANT: A RARE ASSOCIATION

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Introduction: Multiple Endocrine Neoplasia 2A (MEN2A) is an autosomal dominant genetic syndrome caused by germline RET mutations and is characterized by medullary thyroid carcinoma (MTC), pheochromocytoma (PHEO), and primary hyperparathyroidism (PHPT). Pathogenic variants in the exon 10 of the RET gene are considered predisposing to Hirschsprung's disease (HD). It was first described in a family with PHEO and reduced penetrance of MTC with p.Cys609Ser. **Case report:** A 43-year-old woman had a 1.5 cm thyroid nodule with a fine-needle aspiration biopsy suggesting follicular neoplasia. She underwent total thyroidectomy, and histopathology showed MTC. There is no family history of hypertension, nephrolithiasis or thyroid tumors. RET sequencing revealed the germline heterozygous variant p.Cys609Ser in exon 10. During follow-up, the patient remained with biochemical evidence of disease but with stable levels of tumor markers (calcitonin and CEA). She has not developed any evidence of PHPT or PHEO during 18 years of follow-up. The RET screening was negative for two brothers and one daughter. Her 25-year-old son carried the same RET variant. His initial evaluation showed a normal neck ultrasound, a serum calcitonin < 2 pg/mL, and serum calcium, PTH and 24-hour urine metanephrines values in the normal range. A prophylactic thyroidectomy revealed lymphocytic thyroiditis without MTC or C-cell hyperplasia. After 11 years of follow-up, he continues with undetectable calcitonin levels and no evidence of PHTP or PHEO. The granddaughter of the index case had a personal history of HD and surgery for intestinal obstruction at one week of age. At the age of six, RET screening was positive for the p.Cys609Ser variant. She underwent prophylactic thyroidectomy, and the histopathology showed only lymphocytic thyroiditis. She has 11 years of follow-up with undetectable calcitonin levels and no evidence of PHTP or PHEO. **Conclusion:** Herein, we report a variant in RET codon 609 in a patient with MTC and two relatives (son and granddaughter), one with HD presenting within the first week of life. This case is the only record in 1,081 screened familial MTC patients in our group with p.Cys609Ser presenting with Hirschsprung's disease. This case report is the first to describe the association of the p.Cys609Ser RET variant with MTC and Hirschsprung's in a family here in Brazil, reinforcing the importance of RET screening in MTC cases and the investigation of other symptoms.

130592 – EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH PAPILLARY THYROID CARCINOMA WITH UNEQUAL OUTCOME

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Introduction: Thyroid cancer is the most common malignancy among 16-33 year-olds, has a low morbidity and mortality and currently the incidence has increased by 313% in relation to the last 4 decades, mainly due to the excessive use of thyroid ultrasound and the use of studies using needle aspiration. Papillary thyroid carcinoma accounts for approximately 84% of all thyroid cancers. It is a well-differentiated malignant tumor originating from follicular cells. **Objective:** To evaluate the epidemiological profile of patients diagnosed with papillary thyroid carcinoma and unfavorable evolution. **Methods:** Descriptive analytical study, carried out through the analysis and collection of data from 12 medical records of patients being followed up at an endocrinology outpatient clinic of a public reference center in Bahia. All patients diagnosed with papillary thyroid carcinoma that progressed to distant metastasis, lymph node metastasis, incomplete biochemical response and incomplete structural response were included. **Results:** The patients' ages ranged from 37-65 years at diagnosis, with an average of 50 years, and were represented by 11 women and 1 man. All patients denied a family history of thyroid cancer. The most common histological type was the follicular variant, corresponding to 45.4% of patients. Only 3 patients had a tumor smaller than 1 cm, the largest being 5.5 x 4.5 cm. The average tumor size was 2.2 cm. Most patients had an intermediate risk of recurrence (41.6%). Total iodine doses ranged from 150-450 mci. More than 70% of patients developed lung metastasis Disease evolution: 27.2% with indeterminate response, 54.4% with incomplete structural response and one patient already indicated for levantinib at diagnosis **Conclusion:** The most common differentiated tumor is the papillary subtype. In the present study, unfavorable evolution occurs, in most cases, through tumor recurrence. The prevalence is in females, with an average age at diagnosis of 50 years, who have already undergone total thyroidectomy and iodine therapy.

130593 – REGULATORY NETWORK BETWEEN MAPK SIGNALING AND NEW TRANSCRIPTION FACTORS TO ACTIVATE EZH2 IN ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid carcinoma (ATC) is the most aggressive type of endocrine cancer, presenting undifferentiated cells that are resistant to radioiodine therapy. ATC oncogenesis is related to mutations in the MAPK pathway, in the TP53 gene and in the TERT promoter. In addition, ATC overexpresses EZH2, the catalytic subunit of the Polycomb 2 complex, responsible for promoting trimethylation of histone H3 at the lysine 27 (H3K27Me3) that leads to the formation of heterochromatin. Thus, EZH2 overexpression can lead to gene silencing, which can result in cell dedifferentiation and tumor progression. **Objectives:** Investigate the role of transcription factors (TFs) in EZH2 activation in ATC. **Methods:** TFs binding sites prediction in EZH2 promoter was performed on LASAGNA software and TFs with higher scores were chosen for gene expression analysis by qPCR in papillary thyroid cancer (PTC) cells, TPC-1 and BCPAP, and in ATC cell lines, KTC2, SW1736 and 8305C. Overexpression of TFs was performed in BCPAP using MSCV-puro plasmid and cells were submitted to cell viability, cell count, colony formation and luciferase assays. MAPK blockage was performed using U0126 inhibitor for 24 and 48h in ATC cells, and changes in TFs expression after treatment were analyzed through qPCR/WB. **Results:** Based on TF prediction for EZH2 promoter binding, we selected YY1, E2F1, NKX2.5, NFYA, SP1, GATA3, FOXM1 and KLF4 for gene expression analysis and found that the TFs were upregulated in ATC, while only KLF4 was down-regulated. Our previous data indicated that deletions of NFYA, YY1 and FOXM1 binding sites in EZH2 promoter reduced its activation in ATC cells. Hence, we decided to assess MAPK influence on these TFs, and the results showed that FOXM1 expression was reduced after MAPK blockage for 24/48h, while GATA3, NFYA, YY1 and SP1 were also modulated, showing a response only at 24h in general. YY1 protein expression and EZH2 gene and protein expression were also reduced in ATC after MAPK blockage. In addition, overexpression (OE) of NFYA and YY1 in BCPAP cells resulted in enhanced cell viability, proliferation rate, colony formation capability and enhanced EZH2 promoter activity for OE of NFYA, while YY1 OE did not induce EZH2 mRNA, but increased its protein expression, which could be due to posttranscriptional mechanisms that regulate EZH2 expression. **Conclusions:** NFYA, YY1 and FOXM1 are new TFs associated with EZH2 activation in ATC that are modulated by MAPK signaling.

130600 – VALIDATION OF A CRISPR INTERFERENCE SYSTEM TO BLOCK TERT TRANSCRIPTION IN ANAPLASTIC THYROID CANCER

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Introduction: Anaplastic thyroid carcinoma (ATC) is a rare but highly aggressive form of thyroid cancer that has a high mutation burden and is refractory to conventional treatment. ATC has a high prevalence of mutations in genes of the MAPK pathway as well as higher incidence of TP53 and TERT (Telomerase Reverse Transcriptase) gene mutations compared to other forms of thyroid cancer. Mutations in TERT gene promoter, frequent in aggressive forms of thyroid cancer, result in its overexpression and correlate with clinicopathological characteristics such as invasion and tumor recurrence, and reduced patient survival. Thus, developing new methods to block TERT overactivation in cancer cells could help improve the understanding of the roles of TERT in aggressive thyroid cancer. **Objective:** Investigate the applicability of a CRISPR interference (CRISPRi) method to block TERT transcription in t aggressive thyroid cancer. **Methods:** Chop-Chop software was used to design single-guide RNAs (sgRNAs) for CRISPRi in TERT proximal promoter. The sgRNAs 34, 42 and 46, targeting a region within -10 to -35 bases of the TERT transcription start site (TSS), were cloned in pLKO.1-puro plasmid using BfuAI restriction enzyme sites. An ATC cell line harboring a TERT promoter mutation, C643, was transfected with pCAG-dCas9-KRAB-Hyg using Lipofectamine 3000 and selected with hygromycin for 10 days, and then, transfected with pLKO.1-sgRNA-puro plasmids, containing TERT-targeting sgRNAs or a control neomycin-targeting sgRNA, and selected for 10 days with puromycin. Total RNA was extracted from cell lines and TERT expression was quantified by qPCR. Mitochondrial activity was measured by MTT assay. **Results:** C643 were transfected with dCas9-Hyg and pLKO-sgRNA-puro plasmids and after hygromycin and puromycin selection total RNA was extracted. TERT gene expression was reduced by 63%, 58% and 26%, respectively, in C643-dCas9-sg34, sg42 and sg46 cells in comparison to control C643-dCas9-sgNeo cells. Moreover, mitochondrial activity was reduced in 20%, 17% and 30% in sg34, sg42, and sg46, respectively, compared to control. **Conclusion:** CRISPRi system which uses a mutated version of Cas9 (dCas9) is effective in interfering with the transcription of TERT gene when individual sgRNAs target TERT proximal promoter region. The functional impact of TERT inhibition needs to be further investigated in those cells, and so the combinatorial effect of multiple sgRNAs targeting TERT promoter at once.

130562 – PHENOTYPIC EXPRESSION OF A FAMILY WITH FAMILIAL MEDULLARY THYROID CARCINOMA DUE TO MUTATION IN CODON 618 OF THE RET PROTO-ONCOGENE, IN THE AMAZON REGION

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Introduction: Medullary thyroid carcinoma (MTC) is a rare cancer, representing only 3 to 4% of malignant neoplasms of the gland. It can occur in sporadic or familial form, as part of multiple endocrine neoplasia syndrome type 2 (MEN 2). Its pathogenesis is associated with activating germline mutations in the RET proto-oncogene. The type of mutation in RET is associated with the biological behavior of CMT. Great clinical heterogeneity is observed in these patients, which may be related to polymorphisms and differences in ethnic and geographic origin. This study aimed to evaluate the phenotypic profile of patients diagnosed with MTC from the same family, carriers of a mutation in exon 618. **Case reports:** Four affected patients carrying the variant p.cys618gly were described. The screening for pheochromocytoma and hyperparathyroidism was negative in all patients. The age at diagnosis varied between the third and fifth decade of life. The majority of patients were classified as T3, according to the TNM classification. According to the dynamic risk stratification, one patient presented a symptomatic incomplete structural response with progressive disease, one patient developed an incomplete structural response with stable disease and two patients had an incomplete biochemical response. The only death occurred in the only male patient. Of the four first-degree relatives screened, two presented the mutation and underwent prophylactic thyroidectomy at age 12. One of them presented histopathologically with medullary microcarcinoma. **Conclusion:** This is the first study that presents a Brazilian family with hereditary MTC caused by the RET p.C618G variant. There was heterogeneity regarding the prognosis and evolution of the studied patients. The importance of genetic detection of the RET proto-oncogene for patients with MTC and the appropriate management of individuals after detection of RET mutations are highlighted.

130269 – INVESTIGATION OF METALLOPROTEINASE (MMP) AND METALLOPROTEINASE INHIBITOR (TIMP) GENES REVEALS THAT TWO MMP-9 SINGLE NUCLEOTIDE VARIANTS MAY BE CLINICALLY USEFUL IN THYROID CANCER PATIENTS

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Single nucleotide polymorphisms (SNPs) are useful biomarkers, however, the increasing number of documented gene variants poses challenges for their validation. Bioinformatics helps to identify SNPs that are most likely to influence a disease. Two matrix metalloproteinases, MMP2 and MMP9, are crucial mediators of processes closely associated with tumorigenesis, such as reorganization of the extracellular matrix, epithelial to mesenchymal transition, cell migration, angiogenesis, and immune response. MMP9 is even considered a target for targeted therapy. On the other hand, tissue inhibitors of metalloproteinases (TIMPs) control the activities of MMP, preserving the equilibrium of proteolytic pathways implicated in tumor invasion and metastasis. TIMP1 and TIMP3 are notable for controlling remodeling of the extracellular matrix and for their role in cancer progression. Seeking variants of potential clinical utility, we investigated the effects of polymorphisms for MMP2, MMP9, TIMP1, and TIMP3 on DNA and protein structures. Using data from dbSNP and Uniprot, we analyzed polymorphisms with MAF > 0,1 in 18 open-source bioinformatics tools. MMP2 analysis revealed two SNPs that did not promote amino acid changes, whereas MMP9 indicated 4 amino acid changes. rs17576 was considered deleterious in 50% of PredictSNP2.0 tools and was associated with decreased protein stability (MuPRO DDG: -0.414 and IStable DDG:0.596) and reduced molecular flexibility. The rs17577 variant was identified as harmful by the GWAVA tool and 37.5% of the PredictSNP1.0 consensus tools. The rs2250889 variant was considered deleterious by FUN and GWAVA of the Predict2.0 consensus but was considered neutral in all PredictSNP1.0 tools. rs2250889 leads to decreased protein stability and significant changes in binding to adjacent amino acids. TIMP1 analysis identified rs4898, which was considered neutral in all PredictSNP2.0 consensus tools and did not promote amino acid changes in the protein structure. Finally, TIMP3 examination indicated that the variant rs9862 was deleterious (CADD tool in Predict2.0), but a protein impact assessment was not possible due to a lack of amino acid exchange. The rs17576 and rs17577 MMP9 variants may affect DNA and the function, stability, and flexibility of the corresponding protein. Based on their function and location, these variants may be related to the development, progression, and migration of thyroid cancer, which deserves further investigation.

130420 – WHOLE EXOME SEQUENCING (WES) FOR GENETIC ANALYSIS AND MIRNA EXPRESSION PROFILING IN A FAMILY AFFECTED BY FAMILIAL NON-MEDULLARY THYROID CARCINOMA (FNMTC)

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Introduction: Familial non-medullary thyroid carcinoma (FNMTC) arises when 2 or more first-degree relatives develop thyroid cancer from follicular cells, comprising 3% of all thyroid cancer. FNMTC follows an autosomal dominant pattern with incomplete penetrance. However, genetic alterations and associated pathways underlying FNMTC remain unclear. Aim: Investigate genetic predispositions and tumor profiles in FNMTC individuals. **Material and methods:** We evaluated a family with 8 papillary thyroid carcinoma (PTC) patients: 5 in the 1st generation and 3 in the 2nd generation. Peripheral blood samples were collected for Whole Exome Sequencing (WES) analysis. DNA extraction utilized the Twist Human Core Exome Kit (TWIST Biosciences, San Francisco, CA, USA), followed by sequencing on Illumina HiSeq4000. VariantMaster facilitated subsequent analysis. For miRNA analyses, total RNA was extracted from the available paraffin blocks, comprising 2 from the 1st generation and 1 from the 2nd generation, using the RecoverAll Total Nucleic Acid Isolation Kit for FFPE (ThermoFisher). Following extraction, miRNA expression profiling was conducted utilizing the Nanostring nCounter® Human v3 miRNA Expression Assay (Nanostring). Later, data were analyzed using the nSolver Software. **Results:** Exome analysis did not reveal any pathogenic variants that segregate with PTC. Moreover, the miRNA expression in tumor patients resembled that of typical PTCs. While hsa-miR-146b-5p, hsa-miR-222-3, and hsa-miR-221-3p are significantly elevated, while hsa-miR-603, hsa-miR-451a, and hsa-miR-7-5p are less expressed in tumor samples in comparison to normal thyroid tissues. But upon comparison of the studied samples (FNMTC) with sporadic cases available in the Xena browser, the miR-21-5p, miR-181a-5p, miR-27b-3p, miR-24-3p, miR-126-3p, miR-145-5p, miR-148a-3p, miR-451a and miR-7-5p were detected differentially expressed only in familial samples. In addition, we revisited the exome data in light of the distinct miRNA expression profiles observed in FNMTC and sporadic cases. Despite this, our analysis did not reveal any notable polymorphisms within the microRNA genes referenced. **Conclusion:** These findings validate the PTC profile evident in the familial cases, while also highlighting distinct miRNA expression patterns within this studied family. This suggests that the differences in microRNA expression compared to sporadic cases might reflect a distinctive pattern specific to this FNMC family.

130585 – THYROID MASS WITH DIFFERENT DIAGNOSES THROUGHOUT THE BIOPSIES: A CASE REPORT

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Dysfunctions in thyroid gland may or may not cause symptoms, and can be either subclinical or clinical cases. However, all these patients are affected by the imbalance of such hormones, with mass effect being one of the causes. Therefore, this case report aims to analyze a patient with symptoms due to a thyroid mass, who has received multiple diagnoses throughout his life. A.S., male, 78 years old, came to the doctor's office in August 2021 presenting respiratory discomfort on exertion and limitations on sleeping, due to a cervicothoracic mass measuring 8.1 x 7.3 centimeters. From personal history, the patient was diagnosed with follicular thyroid carcinoma in 2013, with the cytology showing neoplastic Hurthle cells and oxilic cells, and surgery was recommended, nonetheless was not performed. A new biopsy was performed at this consultation in 2021, with a report of a plunging goiter in the sternum, along with subclinical hyperthyroidism in blood tests. Additionally, the doppler performed on the mass revealed a high vascularization. Tapazole and levothyroxine sodium were introduced to control subclinical hyperthyroidism, and surgery to remove the mass was contraindicated at this time due to the patient's advanced age and diabetes. Subclinical hyperthyroidism was controlled, but dyspnea symptoms remained constant. Thus, in January 2023, the case was discussed with radiology, and 16 sessions of radiotherapy were recommended to reduce the mass. Initially, there was a perception of worsened dyspnea, requiring the patient to use oxygen for some periods. After six months of radiotherapy, the patient's clinical condition improved visibly, being able to resume daily activities. Currently, the patient reports sleeping well, and absence of dyspnea. In 2024, during a reassessment consultation, tapazole and levothyroxine were maintained for hyperthyroidism control, and a new biopsy was performed, which showed a colloid goiter. This case illustrates that in 2003, despite surgery being indicated, the benefits should have been emphasized. The rejection of the surgical procedure could be a reason for the intensification of the clinical picture. The review of slides was not performed, and it may have been incorrectly diagnosed, since the patient's history does not resemble that of papillary thyroid carcinoma, as they have had a good outcome even without intervention. Thus, care for the patient should be carried out attentively, in order to avoid these multiple diagnoses.

129713 – SERUM MICRORNA ANALYSIS FACILITATE THE DECISION BETWEEN ACTIVE SURVEILLANCE AND IMMEDIATE SURGERY OF THYROID MICROCARCINOMA

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Introduction: The identification of thyroid microcarcinoma (TMC) with aggressive behavior is a challenge for the implementation of active surveillance (AS). **Objective:** To elaborate a serum expression test of miRNAs to differentiate TMC with aggressive from indolent behavior to help in recommending AS or surgery. **Methods:** This is a prospective observational study that included patients with malign thyroid nodules measuring 3 to 15 mm. Patients with low-risk TMC could opt for AS or surgery. Otherwise, they were referred for surgery. AS patients were followed up each 6 months for the first 2 years and annually thereafter and were referred for surgery in the occurrence of disease progression or at patient's request. Patients undergoing surgery were classified according to the risk of recurrence and/or persistence of ATA (RRP). We analyzed clinical, ultrasonographic and histological characteristics and the serum expression of miRNAs miR-146b-5p, miR-204, miR-221-3p, miR-222-3p and miR-21-5p. miR-16 was chosen as normalizer. The ROC curve was used to establish the cut-off value of miRNA expression able to differentiate the RRP into low or intermediate/high, considering the best value of the Youden Index. **Results:** 51 patients were included, 30 in the AS and 21 in the surgery group. Five patients in the AS group underwent surgery. Patients in the surgery group were younger (mean age of 41.9 ± 7.9 and 53.5 ± 12.6 years respectively; $p < 0.001$). The mean follow-up time in AS was 36.4 ± 25.8 months. The contact with thyroid capsule was the main reason for indicating surgery, followed by patient's choice. The group that preferred surgery or switched to it was composed of younger patients ($p < 0.001$). No patient experienced disease progression during AS. Molecular analysis of surgery group revealed that the upregulation of miR-146b-5p/miR-16 (≥0.1757) and the downregulation of miR-204/miR-16 (<0.02223) were associated with intermediate/high RRP ($p = 0.005$ and 0.006 respectively). The downregulation of miR-204/miR-16 presented sensitivity of 75% and NPV of 86.7% being considered a rule-out test. The combination of upregulation of miR-146b-5p/miR-16 with downregulation of miR-204/miR-16 had specificity and NPV of 100%, being a good rule-in test. The remaining miRNAs did not present good expression and were excluded. **Conclusion:** The serum analysis of miR-146b and miR-204 can be used to classify TMC in terms of its prognosis, allowing a more precise indication of AS or surgery.

130573 – POORLY DIFFERENTIATED THYROID CARCINOMA: ANALYSIS OF 36 CASES

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Introduction: Poorly differentiated thyroid carcinoma (PDTC) represents an intermediate stage within the spectrum of glandular neoplastic differentiation, posing challenges in its differential diagnosis with undifferentiated carcinoma and the solid variant of papillary carcinoma. Characterized by a loss of iodine uptake function in follicular cells and decreased reliance on thyroid-stimulating hormone for growth, PDTC retains immunohistochemical markers of epithelial differentiation with fewer mutational findings compared to undifferentiated carcinoma. Concurrent presentation with both differentiated and undifferentiated neoplasms further complicates prognosis. Surgical intervention remains the primary treatment modality, often supplemented by adjuvant radioiodine therapy. However, survival rates vary regionally, with 5-year rates ranging from 60% to 80% and 10-year rates hovering around 50%. **Objective:** Considering a single tertiary institution cohort of patients surgically treated on PDTC, the present study aimed to identify the profile of these individuals and observe their evolutions. **Patients and methods:** Thirty-six patients diagnosed with PDTC and undergoing thyroidectomy at a tertiary oncological center between May 2009 and December 2014 were included. Data, including demographics, pathological characteristics, treatment modalities, and follow-up information, were collected from electronic medical records. Statistical analyses were performed using SPSS version 26.0, including descriptive statistics and Kaplan-Meier survival analyses. **Results:** The cohort comprised 21 women and 15 men, with a mean age of 54.5 years. Pure PDTC was observed in 18 patients, while 18 exhibited mixed forms with histological variants. Notably, 15 patients presented with distant metastases at diagnosis. Surgical interventions included thyroidectomy with or without neck dissection. Disease progression was common, with 72.2% of patients experiencing structural disease evolution and resistance to additional therapies. The 5-year disease-free and overall survival rates were 49% and 44%, respectively. **Conclusion:** PDTC, while not highly prevalent, carries significant lethality, warranting careful consideration even in early-stage cases. This study underscores the importance of vigilance in managing PDTC to optimize patient outcomes.

130321 – METFORMIN ACTIVITY IN ANAPLASTIC THYROID CANCER CELLS, 3D MODELS AND THE INVOLVEMENT OF JAK/STAT PATHWAY

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Introduction: Differentiated thyroid cancer generally has a good prognosis, however 10%-15% of cases become aggressive and undifferentiated anaplastic carcinoma (ATC), although rare, is extremely aggressive with survival of 6-15 months. For these cases, multikinase therapies and targeted therapies are the only therapeutic options, as they are refractory to radioiodine, but most patients relapse or abandon the treatment due to severe side effects. To this end, there is a need to research new antitumor or adjuvant drugs for advanced thyroid cancer. Since the association of metformin with the decreased risk of cancer in patients with type 2 diabetes, its antitumor activity is being investigated in different cancer models. Metformin is able to block the JAK/STAT pathway, which has been related to cancer progression and metastases. The modulation of this pathway has not been widely explored in ATC and may be an alternative for disease control. In the search for new *in vitro* models that better represent the characteristics of tumors in drug tests, 3D cultures have been developed. **Objective:** This work aims to characterize the metformin antineoplastic activity in a 3D spheroid model of thyroid cancer (TC) cell lines and to investigate its action through JAK/STAT. **Methodology:** the ATC cells: KTC2 and HTH83, the non-tumoral cell NTHY-Ori were used. For the 3D models the "hanging drop" technique was used. Presto Blue reagent was used to evaluate cell viability in 2D and 3D cultures and morphological characterization was done by microscopy examination. Metformin was tested between 0.1 and 20 mM, in 72-h treatments, in 2D models. 3D models were treated with 0.5X to 4X of the 2D-IC50. An HTH83 strain with a deletion in STAT3 gene by CRISPR-CAS9 was constructed. **Results:** Metformin decreased cell viability in KTC2 and NTHY-Ori. KTC2 showed greater sensitivity in the 2D models than Nthy-Ori, IC50: KTC2 = 4.48 mM, Nthy-Ori = 10.77mM. In 3D models metformin reduced viability, the size of the spheroids, increased cells spread, and a necrotic region was observed. Spheroids were more resistant to metformin treatment. **Conclusion:** the cytotoxic activity of metformin, a cheap and safe drug, was observed in ATC cell in 2D and 3D models. Metformin activity in ATC through the JAK/STAT pathway is being investigated.

130517 – XENOTRANSPLANTATION OF TUMOR CELLS IN ZEBRAFISH (DANIO RERIO): A MEN2 MODEL TO STUDY MTC ONCOGENESIS

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Introduction: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor. Although most cases of MTC are sporadic, a quarter of cases have hereditary forms, often associated with Multiple Endocrine Neoplasia (MEN) syndromes type 2. MEN2 has an autosomal dominant inheritance pattern and is associated with activating mutations in the RET proto-oncogene. The MEN2 includes two clinically distinct forms: MEN type 2A (MEN2A) and MEN type 2B (MEN2B). The MTC cell lines, TT and MZ-CRC-1, characterized by the presence of p.C634W (MEN2A) and p.M918T (MEN2B) RET mutations. In TT, the prevalent RET mutation involves a cysteine substitution at codon 634, whereas in MZ-CRC-1, the mutations occur at codon 918 (with threonine replacing a methionine). Zebrafish (Danio rerio) is a potent animal model, playing a role in research for analyzing tumor growth and progression, exploring tumor-induced oncogenesis and metastasis formation through xenotransplantation of human cancer cells. **Objective:** Employ the zebrafish as an animal model to study MTC pathogenesis in MEN2. **Method:** The MTC cell lines, were xenotransplanted into zebrafish embryos by microinjection. The cells were trypsinized, counted, and stained. After 48 hours post-fertilization, the embryos were anesthetized with tricaine, and the cells were implanted into the perivitelline space. After injection, the xenotransplanted specimens are incubated at 34 °C and sorted into groups based on tumor size. Monitoring is conducted using a fluorescence microscope. **Results:** The microinjection enabled the monitoring of 72 embryos for 4 days, with 44 of them injected with TT and 28 with MZ-CRC-1. Of the embryos injected, it was possible to assess 31 tumor developments, with 9 from TT and 22 from MZ-CRC-1, resulting in tumor formation rates of 20% and 72%, survival rates of 88% for TT and 75% for MZ-CRC-1, and metastasis formation rates of 50% and 73%, respectively. Based on our experience, MZ-CRC-1 appears to be more aggressive, with great metastatic potential. **Conclusion:** Zebrafish as an animal model makes it possible to study the mechanisms involved in MTC carcinogenesis and the establishment of the tumor microenvironment. It also allows for new study perspectives to investigate how drugs interfere with colonization processes and tumor angiogenesis.

130547 – PAPILLARY THYROID CANCER IN A HYPERFUNCTIONING NODULE ASSOCIATED WITH GRAVES DISEASE – A CASE REPORT

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Introduction: Thyroid nodules are very common among adult women and its prevalence increases with aging. Hyperfunctioning nodules are rarely malignant, in less than 1% of cases. The coexistence of an autonomous hyperfunctioning thyroid nodule, named toxic nodule, and Graves disease (GD) is called Marine-Lenhart syndrome (MLS), a rare condition occurring in about 3% of cases. Papillary thyroid carcinoma is the most common thyroid cancer, occurring in about 10% of thyroid nodules and are rarely hyperfunctioning. Less than 5 cases of MLS and papillary thyroid carcinoma (PTC) have been reported. Here, we present a 48-year-old woman with GD and an AFTN which turned out to be a PTC. **Case report:** A 48-year-old Caucasian woman was diagnosed with thyroid nodules since the age of 16 years. After 20 years asymptomatic, she began to feel flutters, fatigue, and tremors and was referred to our service. Laboratory workup showed thyrotoxicosis (TSH < 0,1) and negative anti-thyroid peroxidase and anti-thyroglobulin antibodies. Ultrasound showed two solid nodules on the left lobe: one 1.7 cm hypoechoic nodule with peripheral calcifications on the lower left lobe – ACR TI-RADS 4 – and one isoechoic 0.7 cm nodule on the medium left lobe – ACR TI-RADS 3 - and no evidence of lymphadenopathy. Thyroid scintigraphy (99m-Tc pertechnetate) showed high heterogeneous uptake of 5,7% (reference 0,47-1,76%), with high concentration on the medium of the left lobe and lower uptake on the remaining thyroid tissue. Fine needle aspiration cytology of the two nodules was positive for malignancy, highly suggestive of papillary thyroid carcinoma (Bethesda VI). Total thyroidectomy was indicated. The procedure was performed successfully. **Conclusion:** We report the rare occurrence of papillary thyroid carcinoma in a toxic nodule, coexisting with Graves disease. This case reinforces the importance of carefully investigating thyroid nodules in the presence of thyrotoxicosis and that the finding of a toxic nodule and Graves disease cannot rule out a thyroid carcinoma.

130122 – CLINICAL AND MOLECULAR ANALYSIS OF A MEN2A KINDRED HARBORING THE RARE RET VARIANT P.SER904PHE

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Introduction: Medullary thyroid carcinoma (MTC) is a rare malignant tumor that originates from the thyroid C cells. MTC may occur sporadically (75%) or as part of cancer syndrome (hMTC). hMTC is associated with germline mutations in the RET proto-oncogene. The pathogenic variants at codon 634 were the most prevalent (30%-50%). Other pathogenic variants were found in less than 10% of MEN2A subjects. The rare RET variant p. Ser904Phe has been reported in only 3 kindreds worldwide and is currently classified as likely pathogenic. **Objectives:** To characterize the clinical and molecular features of the MEN 2A kindred with a variant at codon 904 and investigate its penetrance and risk of progression. **Methods:** Ascending, collateral, and descending relatives of subjects with p. Ser904Phe variant were invited to participate in this study. Molecular analysis was performed by Sanger sequencing of RET exon 15. **Results:** Of the 48 individuals screened, 31 (64.5%) harbored the mutation: 17 (54%) were women, and the median age was 34.4 ± 15.7 years. Thyroid ultrasound was performed on 24 subjects, revealing a nodule in 12 of them (0.8 ± 0.46 cm). All participants with thyroid nodules had high calcitonin levels (reference value up to 5ng/L). Twelve patients underwent total thyroidectomy (7 women and 5 men): 10 presented MTC (mean 1.06 cm), 1 had mixed MTC and papillary carcinoma (1.2 cm), and 1 had C cell hyperplasia with amyloid deposits (0.1 cm). Gene carriers without any evidence of clinical disease are being monitored. Twelve relatives are awaiting sample collection for molecular screening. **Conclusions:** This large hereditary MTC kindred with rare RET variant p. Ser904Phe indicate that this variant is associate with low aggressive tumor. Furthermore, the strong genotype-phenotype association indicate that it must be reclassified as pathogenic variant rather than likely pathogenic. Follow-up of these subjects will be necessary for a better understanding of the long-term behavior of the disease in carriers of this rare variant.

130539 – MIXED MEDULLARY FOLLICULAR THYROID CARCINOMA: A CASE REPORT

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Introduction: Papillary thyroid cancer (PTC) and medullary thyroid cancer (MTC) originate from follicular and neuroendocrine parafollicular C cells, respectively. Their co-occurrence in a patient is a rare phenomenon known as mixed medullary-follicular thyroid carcinoma (MMFTC). **Case report:** A 67-year-old female was referred to a tertiary hospital with a multinodular goiter and subclinical hyperthyroidism in October 2022. She had no apparent personal or family history of endocrine disorders. The patient underwent a thyroid ultrasound examination which indicated the presence of ACR TIRADS 4 nodule measuring 28 x 24 x 30 mm in the right lobe and ACR TIRADS 3 nodule measuring 48 x 19 x 45 mm in the left lobe. Technetium 99m pertechnetate thyroid scintigraphy was performed and revealed a heterogeneous pattern in the thyroid, with normal uptake and relative hyperconcentration of the radiopharmaceutical in the left lobe. Under suspicion of thyroid cancer, fine-needle aspiration (FNA) of both nodules was performed. The cytopathologic findings showed an unsatisfactory sample (The Bethesda System for Reporting Thyroid Cytopathology, category I) on the left lobe and Bethesda IV on the right nodule. Subsequent total thyroidectomy demonstrated lymphocytic thyroiditis and multinodular goiter in the right lobe and, in the left one (lower pole/transition with the isthmus), a nodule consisting of a component of classic PTC (16 mm) adjacent to an area of spindle-shaped to epithelioid cells. An immunohistochemical study was performed to confirm the diagnosis of associated MTC (11 mm). In the spindle/epithelioid cell component, there was diffuse positivity for calcitonin and synaptophysin and weak chromogranin staining, with a proliferative index (Ki-67) of 2%. After thyroidectomy, a cervical ultrasound was performed, and no lymph node enlargement was found. Additionally, laboratory tests showed normal levels of calcitonin, carcinoembryonic antigen, and thyroglobulin. The patient awaits the results of genetic research for the RET gene mutation and will continue monitoring with periodic measurements of calcitonin, CEA, and thyroglobulin. **Conclusion:** The co-occurrence of MTC and PTC in the same patient is a rare phenomenon. It is important to report this case to increase awareness and improve our understanding and management of these unusual carcinomas in the future.

130575 – AFTER LONG-TERM FOLLOW-UP, IS THERE AN IMPACT OF MINIMAL EXTRATHYROIDAL EXTENSION ON CLINICAL OUTCOMES IN DIFFERENTIATED THYROID CARCINOMA?

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Introduction: One of the criteria that defines risk of recurrence in Differentiated Thyroid Cancer (DTC) is the presence of extrathyroidal extension. According to the ATA (American Thyroid Association) guideline, the presence of minimal extrathyroidal extension (mETE) is considered as an intermediate risk with about 3%-9% risk for structural disease, but the relationship of minimal extension and clinical outcome still presents controversies. **Objective:** Evaluate the impact of mETE on clinical response in patients with differentiated thyroid carcinoma. **Methods:** Retrospective study with 400 patients who underwent follow-up of DTC. Patients were initially selected based on the presence of minimal extrathyroidal extension, and subsequently, intermediate-risk without mETE and low-risk of recurrence. For each patient, data evaluated were age, gender and tumor-related characteristics, serum stimulated thyroglobulin (sTg) and clinical response. Univariate and multivariate logistic regression models were used to investigate the association of clinical variables with acceptable and unacceptable (incomplete biochemical response and structural disease) responses. **Results:** Out of 400 patients, 358 were accurately selected. Clinical response was deemed acceptable in 256 patients (71.5%) and unacceptable in 102 (28.5%). Among 358 patients, 125 (35%) had mETE. The median follow up was 8,6 years. Histological aggressive subtype (odds radio [OD]: 10.8 [IC: 4.0-23.9], p = 0.001), vascular invasion (OD: 6.1, [IC: 3.5-10.9] p = 0.001), presence of lymph nodes (OD: 1.19, [IC: 1.08-1.3] p = 0.001), serum sTg (OD: 3.05, [IC: 1.7-5.2], p = 0.001) and mETE (OD:1.8, [IC:1.1-2.9] p = 0.01) were predictors of an unacceptable clinical outcome in univariate analysis. In contrast, the presence of minimal extension, as an independent criterion, was not a predictor of a worse clinical response. **Conclusion:** After long-term follow-up of patients with CDT, the presence of mETE was a histological finding for worse clinical outcomes only when combined with other criteria of intermediate risk of recurrence such as histological subtype, serum thyroglobulin, vascular invasion, and lymph node involvement.

130598 – OUTCOME ASSESSMENT IN PATIENTS WITH HIGH-RISK DIFFERENTIATED THYROID CARCINOMA AND ELEVATED THYROGLOBULIN LEVELS DURING THE FIRST YEAR AFTER INITIAL TREATMENT. A STUDY WITH A MEDIAN 7-YEAR FOLLOW-UP

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Introduction: The incidence of differentiated thyroid carcinoma (DTC) with more aggressive clinical presentation is rising, as its mortality rate. Thyroglobulin (Tg) is the most sensitive tumor marker, and its measurement is used to classify patients according to the response to initial treatment. **Objective:** To evaluate if there was a cutoff of thyroglobulin collected during the first year of follow-up in high-risk recurrence patients, which could be used as a predictor of treatment response. **Methods:** Data of 56 high risk patients were collected. All patients were treated with total thyroidectomy and radioiodine and had a minimum follow-up of 3 years from the time of diagnosis (median of 7 years). Thyroglobulin measurements were assessed before the first radioiodine treatment in hypothyroidism (Pre-ablation Tg); measurement under TSH suppression, 6 months after initial treatment (TgLT4); and one year after initial treatment in hypothyroidism (Tgs1). According to the outcome, patients were classified in acceptable response (excellent response and indeterminate response) and incomplete response (biochemical incomplete response and structural incomplete response) based on American Thyroid Association criteria. Thus, Pre-ablation Tg, TgLT4, and Tgs1 measurements were analyzed to determine which value correlated with the therapeutic response: acceptable or incomplete response. **Results:** Twenty patients (35.7%) had an acceptable response, and 36 patients (64.3%) had an incomplete response (p = 0.03). Considering TgLT4 and Tgs1 difference was found between the two groups (acceptable response and incomplete response), p = 0.01 to TgLT4 and p = 0.02 to Tgs1. Considering the Tg measurements the Pre-ablation Tg values greater than 24.65 ng/mL (sensitivity of 39% and specificity of 91%), TgLT4 greater than 1.44 ng/mL (sensitivity 59% and specificity 82%) and 2.25 ng/mL (sensitivity 65% and specificity 76%) and Tgs1 greater than 61.15 ng/mL (sensitivity 89% and specificity 45%) had a higher probability of an incomplete response in their outcome assessment. **Conclusion:** For high-risk DTC patients, the persistence of elevated thyroglobulin (TgLT4 > 1.44 ng/mL with higher specificity or > 2.25 ng/mL with higher sensitivity and Tgs1 > 61.15 ng/mL) during the first year of follow-up after initial treatment correlated with an incomplete response to treatment.

130566 – LONG-TERM OUTCOMES AND PROGNOSES OF 154 PATIENTS WITH DISTANT METASTASES FROM DIFFERENTIATED THYROID CANCER

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Introduction: Differentiated thyroid cancer (DTC) often follows an indolent course, but the diagnosis of distant metastases (DM) represents a critical turning point in the trajectory of the patient, influencing therapeutic strategies and the general prognosis. **Objectives:** To evaluate the clinical and tumor features of patients with DM from DTC. We explore risk factors for radioiodine (RAI) refractoriness, progression, and survival. **Methods:** Cohort review of DTC patients in two reference centers in the Southern Brazil. Patients aged ≥ 18 years at the time of DTC diagnosis, with DM identified at initial evaluation or follow-up were included. **Results:** Out of 1872 patients with DTC, 154 (69.5% women) were included, with mean age at diagnosis of 55.9 ± 15 years. The median follow-up time was 85.5 months. Eighty-eight patients (57.1%) had papillary cancer, 39 (25.3%) follicular cancer, 22 (14.3%) oncocytic carcinoma (OC) and 5 (3.2%) poorly differentiated thyroid cancer. Of these, 83 (53.9%) had lung metastases, 14 (9.1%) bone metastases, 46 (29.9%) lung and bone metastases and 11 (7.1%) in other sites. All patients underwent total thyroidectomy except three (1.9%) considered inoperable. RAI were utilized in 143 patients (92.9%), with a median total dose of 300 mCi. Eighty-seven cases (61.3%) were classified as radioiodine-refractory (RR)-DTC, 53 (60.9%) identified by no RAI uptake. Age at diagnosis ≥ 55 years, extrathyroidal invasion, aggressive histology including OC, TNM8 III/IV staging, lung and bone metastases and large volume of disease were risk factors for RR-DTC. These risk factors have also associated with progression, an outcome in 57.1% of patients. The prognosis was worse in patients with iodine-refractory metastases, with a survival rate of 10 years of 71.1% in iodorefractory patients, and 83.3% in iodosensitive patients. Notably, patients with DM discovered during follow-up (32.5%) were more classified as DTC-RR and with structural progression, being an independent prognostic factor for progression of distant metastasis. The 10-year a survival rate was 97.1% in patients who did not have progression and 59.4% in patients with metastatic disease progression. **Conclusion:** The present study contributes to expanding knowledge about the clinical evolution of patients with metastatic DTC, highlighting the importance to detect early metastatic involvement, especially in patients at high risk of RAI refractoriness and metastatic disease progression.

130521 – IMPACT OF EARLY *VERSUS* LATE RADIOIODINE THERAPY ON THE OUTCOME OF PATIENTS WITH PAPILLARY THYROID CARCINOMA AT INTERMEDIATE TO HIGH RISK OF RECURRENCE: RETROSPECTIVE COHORT STUDY

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Introduction: Although papillary thyroid carcinoma (PTC) evolves with low mortality, it persists/recurs in a considerable number of patients. For higher risk cases, total thyroidectomy (TT) followed by radioiodine therapy (RIT) has been indicated. However, it is not yet defined whether the period of time between these two approaches would influence the evolution of patients. **Objectives:** To evaluate, in patients with intermediate or high-risk PTC, treated with TT and RIT, whether the time between these two therapeutic approaches influences the evolution of the cases. **Methods:** This was a retrospective cohort study, with 163 patients with PTC, at intermediate or high risk of recurrence, who underwent TT followed by RIT. The main variable of interest was the time interval between TT and RIT and, according to this time, patients were divided into two groups: < or ≥4 months. $P < 0.05$ was considered significant. **Results:** No differences were observed between the groups < and ≥4 months regarding the outcomes excellent therapeutic response at 1 year [24 (40.7%) *versus* (*vs.*) 50 (48.1%); p = 0.3619], incomplete response at some point between 1 year after RIT and the last assessment [20 (33.8%) *vs.* 35 (33.6%); p = 0.97], disease-free survival time (34.03 ± 48.63 *vs.* 51.33 ± 55.92 months; p = 0.076) or excellent response to therapy at the last evaluation [36 (61.0%) *vs.* 60 (57.7%); p = 0.6784]. The Kaplan-Meier curves also showed no statistically significant differences ($p > 0.05$). **Conclusion:** In this study, with patients with PTC at intermediate or high recurrence risk, the time between thyroidectomy and RIT did not influence the evolution of the cases.

130525 – POTENTIAL NEW CANCER BIOMARKERS REVEALED BY QUANTUM CHEMISTRY ASSOCIATED WITH BIOINFORMATICS IN THE STUDY OF SELECTIN POLYMORPHISMS

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Introduction: Understanding the complex mechanisms involved in diseases caused by or related to important genetic variants has led to the development of clinically useful biomarkers and molecular therapy targets. However, the increasing number of described variants makes it difficult to identify variants worthy of investigation, and poses challenges to their validation. Selectins are important molecules in the cell adhesion process that play a fundamental role in the cancer metastasis process in addition to their role in the immune response. However, their role in thyroid cancer is still unclear. **Objective:** The aim of this study was to identify selectin variants with minor allele frequency > 0.1 which could become clinically useful markers. **Methods:** We combined publicly available datasets and open-source robust bioinformatics tools with molecular quantum chemistry methods to investigate missense single nucleotide variants (SNPs) in the intronic and UTR regions of SELL, SELP, SELE, and SELPLG genes and the effects of the amino acid changes produced by these variants. We then focused on thyroid cancer, seeking these SNPs potential as biomarkers for susceptibility, diagnosis, prognosis, and therapeutic targets. **Results:** We demonstrated that gene polymorphisms rs2229569, rs1131498, rs4987360, rs4987301 and rs2205849; polymorphisms rs3917777, rs2205894 and rs2205893 of SELP gene; rs7138370, rs7300972 and rs2228315 variants of SELPLG gene; and rs1534904 and rs5368 polymorphisms of SELE gene may produce important alterations in the DNA structure and consequent alterations in the morphology and function of the corresponding proteins. **Conclusion:** We developed a strategy that may save valuable time and resources in future investigations, as we were able to provide a solid foundation for the selection of 13 selectin gene variants that may become important biomarkers and deserve further investigation in cancer patients. Large-scale clinical studies in different ethnic populations and laboratory experiments are needed to validate our results.

130554 – MOLECULAR ANALYSIS IN FINE NEEDLE BIOPSIES OF THYROID NODULES: PRELIMINARY RESULTS FROM TWO BRAZILIANS SITES

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Introduction: A molecular profile, including the evaluation of BRAF and RAS mutations, is proposed as an accurate presurgical assessment for thyroid nodules, however its application may vary across centers and populations. **Objective:** This study aims to verify the prevalence of BRAF (V600E), NRAS, HRAS, and KRAS mutations in patients undergoing fine-needle aspiration under ultrasound (FNA-US) for thyroid nodules. **Methodology:** Consecutive FNA-US samples were prospectively collected and classified using the Bethesda cytological system. The extraction of DNA and total RNA was performed using Trizol, followed by the evaluation of the proportion of thyroid epithelial cells through the expression of the cytokeratin 7 gene. Point mutations were detected by DNA analysis using Sanger sequencing. **Results:** A total of 377 thyroid nodules in 347 patients were evaluated, (87.6% female, mean age of 56.2 ± 14.2). The cytological distribution was as follows: 5.3% (n = 20) nondiagnostic (Bethesda I); 66.6% (n = 251) benign (Bethesda II); 11.1% (n = 42) AUS/FLUS (Bethesda III); 9.0% (n = 34) FN/ SFN (Bethesda IV); 3.2% (n = 12) suspicious for malignancy (Bethesda V); and 4.8% (n = 18) malignant (Bethesda VI). Ninety-eight patients underwent surgery, resulting in 313 nodules with conclusive benign or malignant results by histology and/or cytology (BII or BVI). BRAF or RAS mutations were identified in 11.9% of the 193 samples evaluated. The frequency of the BRAF V600E mutation was 6.5%, detected in 8 out of 15 malignant nodules (53.3%) and in 3 out of 118 benign samples (2.5%). Mutations in RAS genes were distributed only in benign nodules: HRAS (4.8%), KRAS (2.5%), and NRAS (0.8%). There were 2 indeterminate cytology samples still without a definitive diagnosis, one involving HRAS and the other involving NRAS. No RAS mutations were detected in malignant nodules. When only the nodules of indeterminate cytology were considered (Bethesda III, IV, and V, n = 88), 11 mutations were detected, with 7 associated with benign histology (1 BRAF and 6 RAS), 2 with malignant histology (BRAF), and 2 were not yet operated on. **Conclusions:** The prevalence of the V600E BRAF mutation in malignant nodules aligns with literature. The occurrence of this mutation in benign nodules and the exclusive presence of RAS mutations in benign nodules warrant careful consideration in the molecular analysis of thyroid nodules and the importance of ongoing real-world studies of indeterminate nodules in various centers.

130519 – TERT PROMOTER MUTATION IN PAPILLARY THYROID CARCINOMA: INDEPENDENT RISK FACTOR FOR MACROSCOPIC EXTRATHYROIDAL EXTENSION WITH PROGNOSTIC IMPLICATIONS

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Introduction: Morbidity of papillary thyroid carcinoma (PTC) is related to locoregional recurrence and distant metastasis (DM). Despite recent acknowledgement that minimal extrathyroidal extension (mETE), corresponding to perithyroidal adipose tissue or microscopic strap muscle invasion, may not increase cancer-related mortality, the relationship between mETE and recurrence risk remains controversial. **Objective:** To evaluate outcomes associated with different degrees of ETE and molecular determinants of invasive differences. **Methods:** 352 PTC patients were analyzed and grouped based on ETE: 242 mETE, 81 macroscopic ETE to strap muscles (gETE) and 29 macroscopic ETE to other adjacent structures (gETE-T4). The groups were compared to determine risk of lymph node (LNM) or distant (DM) metastases, and recurrent/persistent disease (R/P). DNA sequencing of 96 PTC samples was performed by next-generation sequencing – 28 macroscopic and 68 microscopic ETE – to analyze the presence of BRAF V600E and TERT promoter variants (TERTp C228T and C250T). Multivariate logistic regression models were used to identify independent risk factors for macroscopic ETE, LNM, DM and R/P. **Results:** LNM were diagnosed in 52% mETE, 79% gETE and 97% gETE-T4 (p4 cm (OR 5.95, p = 0.012) and the presence of TERTp mutation (OR 3.1, p = 0.044) represented independent risk factors for macroscopic ETE. TERTp mutations were also associated with increased risk of DM (OR 5.7, p = 0.014). **Conclusion:** The degree of ETE is directly associated with unfavorable outcomes in PTC patients. Apart from the known association with DM, TERTp mutations also determine aggressive local invasion. The findings offer valuable insights into risk stratification and personalized treatment approaches for PTC.

130609 – UNRAVELING THE IMMUNOLOGICAL MICROENVIRONMENT OF MEDULLARY THYROID CARCINOMA: THE POTENTIAL ROLE OF TUMOR-ASSOCIATED MACROPHAGES

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Introduction: Cancer, accounting for approximately 3% to 10% of all thyroid cancers. Individuals diagnosed with MTC may be associated with multiple endocrine neoplasia type 2 (MEN2), a genetic disorder characterized by mutations in the RET gene. Progress in understanding immunological mechanisms has led to an increased interest in investigating the role of the immune system within the tumor microenvironment in MTC. **Objectives:** The main purpose of this study was to analyze both systemic and local immunological mechanisms in patients with MEN2 and MTC, using various available techniques and correlating them with clinical, laboratory, and histopathological data. **Methods:** We analyzed 26 patients who had histopathological confirmation of MTC. The tissues from these patients were re-examined to select the most representative areas, aiming to construct a tissue microarray (TMA). Immune cell markers were analyzed, including tumor-associated macrophages (CD68) and subgroups of tumor-infiltrating lymphocytes (CD3, CD4, CD8, CD20), as well as markers of immune activation (Granzyme-B, PD-L1). A statistical analysis was conducted to investigate potential associations between immunological markers and the clinical characteristics of the patients involved in the study. **Results:** The findings revealed that the presence of immune cells was more common in malignant tissues than in adjacent thyroid tissue. A significant correlation was observed between the expression of PD-L1 and CD68 in various areas, indicating a potential involvement of tumor-associated macrophages in the immune environment of MTC. The absence of CD68 cells was related to the absence of thyroiditis in several tissue regions, suggesting a mechanism by which MTC might evade immune detection. However, no significant associations were found between the presence of immunological markers and the clinical condition of patients during follow-up. **Conclusion:** This study provides insights into the immunological processes occurring within the tumor microenvironment of MTC, highlighting the potential influence of tumor-associated macrophages and their association with the presence of thyroiditis. However, further research is essential to fully understand the role of the immune system in MTC, as well as its clinical significance for the prognosis and therapeutic approach to patients.

130164 – 20 YEARS EXPERIENCE ON RET GENETIC SCREENING ON MEN2 IN A SINGLE CENTER: AN UPDATE ON THE PREVALENCE OF GERMLINE RET VARIANTS

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Introduction: Multiple endocrine neoplasia type 2 (MEN2) is an autosomal dominant hereditary cancer syndrome caused by pathogenic germline variants in the REarranged during Transfection (RET) gene. MEN2 comprises two distinct clinical entities: MEN2A and MEN2B, both involving a high risk for medullary thyroid carcinoma (MTC). Clinical recognition and accurate diagnosis of individuals and families at risk of harboring a RET pathogenic germline variant is critical since the earlier diagnosis and treatment increase the likelihood of MTC cure. Here, we describe the prevalence of the RET pathogenic germline variants screened at a reference center for molecular analyses. **Methods:** Genomic DNA was obtained from peripheral blood leukocytes by standardized procedures. Genetic screening for the RET gene was performed by Sanger sequencing. **Results:** From 2003 to 2023, we analyzed 1146 individuals; 182 (15.9%) presented sporadic MTC, while 576 (50.3%) carried germline variants in the RET gene [98 (8.6%) index cases and 478 (41.7%) family members positive for pathogenic alteration in RET]. Of the hereditary MTC patients, 562 (97.5%) presented MEN2A, and 14 (2.5%) MEN2B. Thirty-five individuals (3.1%) harbor variants of uncertain significance (VUS) and, 356 (30.8%) are family members with a negative result for RET screening. In total, 40 distinct germline variants were found (32 pathogenic variants and 8 VUS). The most frequent variants were p.Val804 [23.8%: p.V804M (15.9%), p.V804L (7.9%)]; p.C634 [23%: [p.C634Y (10.8%), p.C634R (9.2%), p.C634G (1.8%), p.C634W (1.0%), p.C634S (0.2%)]; p.M918 [14.4%: p.M918V (12.1%), p.M918T (2.3%)]; p.G533C (13.7%); p.S891A (4.6%). Less frequently, we also find the following alterations: G321R, p.A510V, G550E, p.C609R, p.C609G, p.C609S, p.C609W, p.C609Y, p.C611R, p.C611Y, p.C618R, p.C618G, p.C618F, p.C618S, p.C620R, p.C620F, p.C620S, p.C620Y, p.C630R, p.V648I, p.K666N, p.E768D, p.L790F, p.Y791N, pY791F, p.R886W. **Conclusion:** In our sample, there was great variability in the RET pathogenic variants compared to series published in Europe and other continents. The variants p.V804M (15.9%), p.M918V (12.1%), p.G533C (13.7%), p.C634Y (10.8%), p.V804L (7.9%), and p.S891A (4.6 %) were found in a higher prevalence, which reflects the proportion of the unique combination of European, Amerindian and African ancestries in the Brazilian genomic mosaic.

130590 – LIQUID BIOPSY ASSAY VALIDATION FOR DETECTION OF RET VARIANTS IN PATIENTS WITH MEDULLARY THYROID CARCINOMA

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Introduction: Multiple endocrine neoplasia type 2 (MEN2) is caused by pathogenic germline variants in the RET gene. Our lab has an interest in detecting circulating DNA (ctDNA) in a non-invasive manner to search for the presence of metastasis in medullary thyroid carcinoma (MTC). This strategy has been used in patients with pulmonary cancer in treatment with multikinase inhibitors (MTKI) to monitor resistant variants. Preliminary results for MTC indicate that somatic variants (p.V804L, p.V804M, p.Y806C, p.Y806N, p.G810C, and p.G810S) acquired during the MTKI treatment alter the RET structure leading to illness resistance and progression. Our objective is to validate a liquid biopsy assay to detect RET variants acquired along MTC progression. **Methods:** Peripheral blood samples were collected in Cell-Free DNA BCT® Streck tubes from patients with advanced MTC (sporadic or hereditary forms). ctDNA was extracted from plasma using a MagMax cell-free DNA Isolation Kit (Thermo Fisher Scientific, USA). The evaluation of variants on codons 630, 634, 804, 806, and 810 was done by dPCR QuantStudio (ThermoFisher Scientific) using TaqMan probes customized (FAM – for variant, VIC – wild-type, WT) and primers for each variant set, 1X QuantStudio 3D Digital PCR MasterMix v2 (Thermo Fisher). **Results:** We designed two strategies to detect the variants: "resistance probe double-WT," where the FAM probe links to the WT region next to the variants. When one of the RET variants is present, these probes lose this capacity. The VIC probe links to an adjacent area. With variation, just the VIC is detected. This strategy is used for codons 804, 806, and 810. In the second strategy, "degenerated probe" (applied to detect 634 variants), FAM and VIC link to the same region where the variants occur. However, VIC links just to the WT sequence while FAM to the altered one. Until now, we have collected samples of 15 patients with MTC and 8 control individuals (positive for RET germline variants). For p.M918T, 3 patients were positive. The probes for codons 630/634 and 804/806/810 are on validation in control samples. One patient, negative for germline RET variants, showed detection of the probe for 630/634. **Conclusion:** dPCR seems to be an efficient technology for monitoring patients with advanced MTC. Among the challenges in analyzing ctDNA are the variable amount of ctDNA between individuals, low concentration of tumor ctDNA, low ctDNA half-life, and high ctDNA fragmentation.

130588 – MOLECULAR DYNAMICS AND FUNCTIONAL STUDIES OF RET P.MET918VAL AND P.MET918THR VARIANTS DISCLOSE POTENTIAL UNDERLYING MECHANISMS FOR DISCORDANT PHENOTYPES IN MULTIPLE ENDOCRINE NEOPLASIA TYPE 2

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Introduction: Multiple Endocrine Neoplasia type 2 (MEN 2) is a rare syndrome triggered by pathogenic variants in the RET gene. Remarkably, two distinct variants within the same RET codon elicit different phenotypes. The classical p.Met918Thr RET variant, associated with the MEN 2B phenotype, stands as the highest risk factor for Medullary Thyroid Carcinoma (MTC) development. Conversely, the less common p.Met918Val RET variant corresponds to MEN 2A and triggers a lower MTC risk. The underlying molecular mechanisms driving MTC development under p.Met918Val influence remain elusive, as does the dynamic evaluation of the aggressive nature of the p.Met918Thr variant. Thus, this study seeks to elucidate these uncertainties by evaluating the wild type, p.Met918Val, and p.M918Thr variants through both *in vitro* and in silica designs. **Materials and methods:** In the *in vitro* study, we assessed both proliferative and migration abilities in HEK293 cells transfected with p.Met918Thr and p.Met918Val RET variants. For the *in silico* analysis, we employed a crystallized model (PDB: 4CKJ) and introduced our variants into the wild-type protein. Molecular Dynamics (MD) simulations were conducted in a TIP3P solvent box environment using AMBER FF14SB force field. Data analysis encompassed cpptraj for hydrogen bonds and loop movements, as well as MD analysis for PCA and RMSD using Python. **Results:** Cells expressing p.Met918Val showed the slowest migration compared to WT and p.M918Thr, while p.M918Thr exhibited faster migration ($p < 0.05$). MD-derived RMSD analysis indicated p.Met918Thr with the highest RMSD and p.Met918Val with the lowest. Notably, differences were observed in the 896-914 region adjacent to the ATP phosphorylation activation site, with p.Met918Val exhibiting a greater distance from the site compared to p.Met918Thr. Further distinctions emerged in the 915-916 region, with phi-psi analysis revealing significant angle changes for p.Met918Thr, while p.Met918Val and WT remained more stable. **Conclusion:** Our study, exploring our question in two distinct ways, revealed mechanisms that could explain such discrepant phenotypes. While p.Met918Thr is more aggressive in migration, the variant p.M918Val is slower in some scenarios and slower than the WT itself. To our knowledge, this is the first time p.Met918Thr and p.Met918Val are evaluated on both *in vitro* and *in silico* analysis using Molecular Dynamics approaches.

130544 – EVALUATION OF THE USE OF LOW DOSES AND THE DISPENSATION OF RADIOACTIVE IODINE IN PATIENTS WITH LOW OR INTERMEDIATE RISK OF PERSISTENCE AND RECURRENCE OF THYROID DIFFERENTIATED CARCINOMA BY THE AMERICAN THYROID ASSOCIATION

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Introduction: Differentiated thyroid carcinomas (DTC) typically undergo total thyroidectomy (TT) as the primary treatment modality, followed by risk stratification for recurrence to ascertain the necessity for radioiodine ablation (131I). This procedure is not routinely recommended for low-risk cases, and for those deemed to be at intermediate risk, its consideration is contingent upon specific clinical criteria, as delineated by the American Thyroid Association 2015 (ATA) guidelines. **Objectives:** To evaluate the recurrence rate and the requirement for additional therapy in patients with DTC larger than 1 cm, who underwent TT without subsequent ablation or received ablation using low doses of 131I. **Methods:** Observational analysis of a historical cohort, whose inclusion criteria were: patients with DTC greater than 1 cm, undergoing TT with low Thyroglobulin (Tg) postoperatively and not undergoing ablation with 131I or undergoing ablation with a low dose of radioiodine (30 mCi or 50 mCi). The outcomes assessed included the necessity for additional treatment, recurrence diagnosis, and current biochemical and structural responses. **Results:** Twenty-six patients with DTC were evaluated, who underwent TT with varying recurrence risks. All patients for whom 131I administration was waived were categorized as low risk by the ATA and demonstrated no recurrence during a median follow-up period of 30 months, with stable Tg concentrations and unchanged cervical ultrasound findings. Among the 14 patients submitted therapy with low doses of 131I, 6 were classified as low risk of recurrence, 7 as intermediate risk and 1 as high risk; for the last two groups, in accordance with institutional protocols, 131I therapy was administered. Two participants required additional treatment after confirmed recurrence, both exhibiting lymph node metastases, one initially classified as low risk of recurrence and the other as intermediate risk. **Conclusion:** The recurrence rate found in low-risk patients was 5.6% and in intermediate or high-risk patients treated with low-dose 131I, 12.5%. Such rates are similar to those found with more aggressive treatments and corroborate the approach of monitoring low-risk patients without adjuvant therapy or with a low dose of 131I and the use of the latter in intermediate-risk patients when biochemical and structural responses are complete.

130618 – METASTATIC MEDULLARY THYROID CANCER WITH INITIAL DIAGNOSIS OF PAPILLARY THYROID CARCINOMA

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Introduction: Medullary thyroid cancer (MTC) is a neuroendocrine tumor of the parafollicular or C cells of the thyroid gland. In diagnosis, there are numerous pitfalls, one of the reasons being the cytological pattern, which can be confused with Hürthle cell tumors, papillary carcinomas, undifferentiated carcinomas, or even cellular adenomas. **Case report:** A 50-year-old smoker underwent total thyroidectomy in 2013 due to thyroid neoplasm, with histopathological description of papillary carcinoma, measuring 6.5 cm. Adjuvant therapy was performed with 150 mCi radioiodine ablation in 2014, and post-dose whole-body scan showed uptake only in the anterior cervical region. Over the following years, there were 4 additional cervical lymph node dissections due to carcinoma metastases, with no significant elevation in serum thyroglobulin related to tumor recurrence. In 2019, a review of the histopathological slides was requested, with a new report compatible with poorly differentiated thyroid carcinoma with angiolymphatic invasion and capsular infiltration, immunohistochemistry compatible with medullary thyroid cancer, and elevated serum levels of calcitonin and carcinoembryonic antigen. Radiotherapy was performed between September and November 2020. Additional workup with magnetic resonance imaging showed the possibility of hepatic metastatic involvement, confirmed by biopsy with neoplastic infiltrate and immunohistochemistry compatible with MTC. Chemotherapy with Sunitinib was initiated and continued for approximately 1 year. Calcium kinetics, catecholamines and metanephrines were requested to exclude multiple endocrine neoplasia. Imaging follow-up showed a volume increase of lesions greater than 20%, meeting the criteria for disease progression according to the RECIST criteria. The decision was made to suspend chemotherapy and initiate treatment with Vandetanib, as a therapeutic option for the management of locally advanced or metastatic unresectable MTC. **Conclusion:** We illustrate with this case the importance of awareness for suspected cases of medullary thyroid neoplasm, as in the present case with the initial diagnosis of differentiated thyroid cancer but with atypical evolution due to presenting structural disease without compatible biochemical changes. Given a neoplasm with aggressive evolution characteristics like medullary thyroid cancer, factors such as tumor stage at diagnosis are extremely important in the patient's prognosis.

129890 – ANAPLASTIC THYROID CARCINOMA COEXISTING WITH PAPILLARY CARCINOMA

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Introduction: Anaplastic thyroid carcinoma is a rare (1,5% to 2%) and aggressive tumor, which mainly affects women over 60 years of age. It is believed that this tumor arises because of the loss of differentiation in well-differentiated thyroid carcinomas. The differential diagnosis of anaplastic carcinoma comprises medullary and poorly differentiated carcinomas, as well as sarcomas, squamous cell carcinoma, lymphomas and chronic fibrosing thyroiditis. **Case description:** M.C.R., 92 years old, referred for cervical ultrasound, due to an apparent nodulation in the right cervical region. She referred partial thyroidectomy 22 years ago, due to follicular thyroid carcinoma. On physical examination, there was a voluminous nodulation in the cervical region, with a stony consistency, and rounded contours. A cervical ultrasound was performed, wich showed a hypochoic nodular formation in the right thyroid fossa, with a solid pattern, imprecise limits, and a grossly heterogeneous texture; measured 4,0 x 3,0 × 3,2 cm, and had peripheral and central vascularization (CHAMMAS IV – TI-RADS 4). FNA (Fine Needle Aspiration)was performed, and the cytopathological diagnosis was 'Anaplastic carcinoma arising in papilliferous thyroid carcinoma", Bethesda category VI. Immunohistochemical analysis showed a change in the cell differentiation pattern during the course of the disease. **Conclusions:** The coexistence of a well-differentiated component and anaplastic carcinoma suggests disdifferentiation of a pre-existing, well-differentiated thyroid cancer through a multiphysics process of carcinogenesis. Most patients present with symptoms of extension of the carcinoma, such as dyspnea, dysphagia and cough. The median survival rate of this patients is five months, and almost 50% of cases have distant metastasis at the time of diagnosis.

130528 – A REAL-WORLD COMPARISON STUDY THE OF THE ANALYTICAL PERFORMANCE OF THE OLD V1 AND THE NEW IMPROVED V2 ALGORITHM OF A MICRORNA AND DNA-BASED MOLECULAR CLASSIFIER FOR INDETERMINATE THYROID NODULES

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[1] Onkos Molecular Diagnostics

Introduction: In 2018 we presented the first version (v1) of our microRNA-based algorithm for indeterminate thyroid nodules classification (mir-THYpe full), which was used in real-world clinical routine until recently, when a new optimized version (v2) was released using new machine learning techniques and combinating microRNA and DNA data. **Objective:** Our aim was to simulate and analyze what the performance of v2 algorithm would have been, if it had been used in the classification of the same samples originally classified by the v1. **Methods:** The cohort of this study was composed of microRNA and DNA data extracted from thyroid FNA smear slide of 1.718 nodules (from 1.687 patients who payed for the test) (945 Bethesda 3 and 773 Bethesda 4) that were originally classified by the v1 in real-world clinical routine and now were re-analyzed and classified by the new optimized v2 algorithm. The molecular analysis performed in the samples consisted of microRNA profile and DNA mutation analysis (BRAF V600E and pTERT C228T/C250T). From those, anatomopathological data was available for 329 nodules (112 benign and 217 malignant) and used to evaluate the performance of the v2. Due to the unrealistically high disease prevalence (66.0%), a real-world adjusted prevalence (32%) was performed based on Bayes' theorem. **Results:** When comparing the results of the v1 with the v2 version of the algorithm, 979 *vs.* 1.175 samples were classified as negative for malignancy (Benign Call Rate/BCR – 57.0% *vs.* 68.4%) and 739 *vs.* 543 samples as positive. In this simulation, the real-world performance of the new v2 would be: 94.5% of sensibility, 75.9% of specificity, 64.8% of positive predictive value (PPV), 96.7% of negative predictive value (NPV) and 81.8% of accuracy. **Conclusion:** The results show an BCR improvement in performance of v2 compared to v1, resulting in an increment of the number of cases that would have benefited from the test avoiding unnecessary diagnostic surgeries. The v2 also showed high PPV and NPV, suggesting that real-world performance for future tests will also be optimized.

130530 – EVALUATING THE PERFORMANCE OF THE NEW V2 ALGORITHM OF A MICRORNA AND DNA-BASED MOLECULAR CLASSIFIER TEST FOR CLASSIFICATION OF INDETERMINATE THYROID NODULES WITH FOCUS ON ONCOCYTIC SUBTYPES

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Introduction: In thyroid nodules, the presence of oncocytic cells poses a diagnostic challenge for both cytology and molecular analysis. This challenge arises from the distinctive morphological characteristics and molecular profile of these cells, making it difficult to differentiate between benign and cancerous conditions. **Objective:** To evaluate the performance of the v2 algorithm version of a microRNA and DNA-based molecular classifier test (mir-THYpe full) in oncocytic subtypes of thyroid nodules. **Methods:** The molecular data for nodule classification was obtained from preoperative FNA samples of 59 thyroid nodules (58 patients) (26 Bethesda-III; 32 Bethesda-IV; 1 Bethesda-V) with known post-surgery oncocytic lesions (45 oncocytic adenomas; 14 oncocytic carcinomas). The analysis of microRNA and DNA mutational data (BRAF V600E and pTERT C228T/C250T) were performed by qPCR. **Results:** The molecular test correctly classified as negative for malignancy 38/45 (84.4%) oncocytic adenomas (two false-positives had TERT C228T mutation) and as positive for malignancy 10/14 (71.4%) oncocytic carcinomas (four true-positives had TERT C228T mutation). Forty-eighth out of the 59 oncocytic samples were correctly classified (81% accuracy). The performance of the algorithm was: 71% of sensibility, 84% of specificity, 59% of positive predictive value, 91% of negative predictive value at 23.7% disease prevalence. **Conclusion:** Despite the diagnostic challenge imposed by oncocytic cells, the results showed that v2 version of the microRNA and DNA-based molecular test mir-THYpe full has an acceptable performance to early identification of benign and cancer oncocytic subtypes, when compared to Afirma and Thyroseq, that showed only 20% PPV on oncocytic lesions. Therefore, the molecular test has the potential to enhance prognostic insights by assessing pertinent mutations, thereby aiding in the prediction of patient outcomes.

130532 – THE NEW OPTIMIZED VERSION (V2) OF THE MICRORNA AND DNA-BASED MOLECULAR CLASSIFIER TEST: A LATIN AMERICAN MULTICENTER PERFORMANCE VALIDATION STUDY

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Introduction: Thyroid nodules are present in nearly 60% of the population, representing the most frequent endocrine disease. Fine-needle aspiration (FNA) cytopathology classifies 20%-30% of nodules as indeterminate (Bethesda 3 and 4), a scenario in which molecular tests are recommended aiming to avoid unnecessary diagnostic surgeries. **Objective:** The aim was to evaluate the diagnostic performance of the new v2 algorithm of mir-THYpe full molecular classifier test for preoperative diagnosis of cytologically indeterminate thyroid nodules, optimized by the use of new machine learning techniques, larger sample cohort size, multicentricity and association of DNA-mutation analysis. **Methods:** A multicenter validation study was conducted on a set of 2.372 thyroid nodules with Bethesda 3 and 4 cytology from 15 academic, community and private centers in Brazil, Argentina and Peru. Eligibility criteria were met in 510 nodules. The FNA smear slides were used to obtain and analyze microRNA expression and DNA mutations (BRAF V600E and pTERT C228/250T) by qPCR. Molecular data from 306 (150 benign/156 cancer+NIFTP) nodules were used to retrain and optimize the mir-THYpe v2 algorithm, using random forest, SVM and neural networks machine learning techniques. For final validation, molecular data from 204 (151 benign/53 cancer+NIFTP) thyroid nodules were used to measure diagnostic performance. Anatomopathological data were used as gold-standard for blinded comparison. **Results:** In the validation set, 61.8% of the samples were assigned as Bethesda 3 (126) and 38.2% as Bethesda 4 (78). The v2 algorithm had a specificity of 94% (95% Cl, 84-99), a sensitivity of 89% (95% Cl, 83-94) and an accuracy of 91% (95% Cl,86-94). At 26% cancer prevalence, the negative predictive value was 98% (95% Cl, 94-99) and the positive predictive value was 76% (95% Cl, 66-83) with a benign call rate of 68% (138/204). The v2 algorithm was able not only to classify but also to identify as medullary thyroid carcinoma (MTC) in all the MTC samples (5/5). **Conclusion:** The optimized classifier demonstrated a high diagnostic performance for identifying benign nodules, which may potentially obviate diagnostic surgery in 68% of patients with indeterminate nodules, and up to 89% of all benign nodules cytologically indeterminate. The BRAF and pTERT status analysis, added to the ability to rule-in cancer samples may help to guide prognostic decisions, including surgery extension and individualized treatments.

130533 – WHAT IS THE MOLECULAR PROFILE OF BRAZILIAN PATIENTS WITH INDETERMINATE THYROID NODULES? INSIGHTS FROM MIR-THYPE FULL MOLECULAR TEST SCREENING

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Introduction: Thyroid nodules are prevalent in up to 60% of the adult population, occurring in a ratio of 4:1 woman/man. Using fine needle aspiration (FNA), approximately 25%-30% of cases are categorized as "indeterminate", Bethesda 3 (B3) or Bethesda 4 (B4). In these cases, molecular tests, such as mir-THYpe full, can assist in diagnosis and prognosis, utilizing microRNA profiling and DNA analysis of mutations including BRAF V600E, pTERT C228T/C250T, RET M918T, C634Y/R, and V804L/M. **Objective:** To evaluate by a retrospective analysis of the molecular profile data of Brazilian patients submitted to the mir-THYpe full test. **Methods:** Molecular data from 3164 nodules (1812 B3 and 1352 B4) were analyzed, stratified by age (using a cut-off at 55 years), sex, mutation prevalence, and correlated with anatomopathological reports (APR) of patients who underwent surgery subsequent to the molecular test. **Results:** Out of the total 3,164 nodules, 64.2% (2,032/3,164) were classified negative and 35.8% (1,132/3,164) as positive for malignancy by mir-THYpe full test, being 75.5% (2,389/3,164) from female and 24.5% (775/3,164) from men. In the negative results cohort, no mutations were detected, of which 20 patients underwent surgery and in 18 benign lesions were confirmed by APRs. In contrast, in the molecular positive results cohort, mutations were detected in 22.4% (254/1,132) of the total cases, being: 232 BRAF V600E, 19 pTERT C228T, two RET M918T, and one RET C364R mutation. The pTERT C228T mutation was found in 5.2% (17/329) of the positive tests in individuals ≥ 55 years, compared to only 0.2% (2/803) in those < 55 years ($p < 0.0001$). Regarding the BRAF V600E mutation, it was detected in 17.9% (59/329) of individuals ≥ 55 years, compared to 21.5% (173/803) in those < 55 years ($p = 0.17$). Of all patients in the positive cohort, 207 APRs were accessible, confirming 127 cases of cancer/NIFTP. **Conclusion:** In our cohort, many clinical parameters were aligned with what is found in other cohorts from other countries, like woman/man ratio, BRAF V600E mutation prevalence (including distribution by age or in all cohort) and prevalence of TERT C228T over C250T. Interestingly, the TERT positivity rate when divided by age showed an increased rate in the ≥ 55 years Brazilian patients with indeterminate cytology, 90% of the patients, in other populations around 70% positivity on ≥ 55 years, suggesting acts as a risk factor for the occurrence of this mutation on indeterminate thyroid nodules.

130597 – A MICRO-RNA AND DNA-BASED THYROID MOLECULAR CLASSIFIER FOR GUIDING DIAGNOSIS AND TREATMENT OF INDETERMINATE THYROID NODULES: A REAL-WORLD, INDEPENDENT, RETROSPECTIVE, MULTICENTER STUDY

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Introduction: Thyroid nodules are a prevalent condition affecting approximately 50% of patients, according to autopsy findings. These nodules usually have benign characteristics and are often discovered incidentally. Following suspicious ultrasonography (USG), fine needle aspiration (FNA) may be necessary to better determine the risk of malignancy of a nodule. However, approximately 30% of nodules are classified as indeterminate by cytology. The development of molecular tests can refine the risk of malignancy of a thyroid nodule and reduce the need for diagnostic surgery. **Objectives:** This study sought to evaluate the performance of a microRNA and DNA-based molecular test (mir-THYpe full) in refining diagnosis and guiding treatment decisions for patients with indeterminate thyroid nodules. **Methods:** This is a retrospective, observational, and non-interventional study that evaluated patients who underwent the mir-THYpe full molecular test between February 2018 and December 2022 in the state of Santa Catarina, Brazil. **Results:** A total of 260 patients classified as Bethesda III/IV nodules were analyzed. The mir-THYpe full test was positive for malignancy in 91 patients and 82 (90.1%) were surgically treated. Among the 158 test-negative patients, 7 (4.43%) underwent thyroidectomy. We applied the sensitivity observed in the validation study based on Bayes' theorem, as we could not assume that all test-negative nodules were truly benign. The test performed a sensitivity of 0.8387 and a specificity of 0.8362; the positive predictive value observed was 0.6420 and the negative predictive value was 0.9367. In this study, the mir-THYpe full test supported 95.5% of clinical decisions when the test was negative for malignancy and 90.1% when the test was positive. The rate of surgery avoidance was 60.2% (151/251), excluding nine patients who were not treated surgically despite a positive test. **Discussion:** The integration of a microRNA and DNA-based molecular classifier into clinical practice has emerged as a valuable tool for guiding the management of thyroid nodules with indeterminate cytology, significantly reducing the need for thyroidectomies. Nevertheless, since the majority of benign molecular test results were not confirmed by the reference standard (histopathologic diagnosis), future studies with extended follow-up periods are warranted to accurately ascertain the rate of true negative nodules.

130439 – BRAIN METASTASES FROM DIFFERENTIATED THYROID CARCINOMA: A RETROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Brain metastases (BM) originating from differentiated thyroid carcinomas (DTC) are uncommon. Given the limited number of documented cases in the literature, the management of these patients remains uncertain. This study aimed to analyze the clinical features and outcomes of patients with DTC and BM. **Materials and methods:** We retrospectively analyzed 10 patients with DTC and radiologically confirmed BM retrieved from a cohort of patients who were followed up at a university teaching hospital in southern Brazil from 1986 to 2023. Data including demographic information, histology, treatment history, clinical and radiological features of BM, and outcomes were collected and analyzed. Overall survival was estimated from the date of BM diagnosis to the date of the last follow-up or death. Data extracted from electronic medical records were summarized using descriptive statistics. Moreover, we also evaluated tumor response to the first therapy using the RECIST criteria, version 1.1. **Results:** Of the 1532 patients, 10 (0.65%) had DTC-derived BM. The mean age was 54.3 years at DTC diagnosis and 58 years at BM diagnosis. Radiological features of BM included single lesions in 90% of cases and peritumoral brain edema in 80% of cases. All patients had distant metastases at other sites, including the lungs (n = 8, 80%), bones (n = 7, 70%), liver (n = 2, 20%), and adrenal glands (n = 1, 10%). Regarding the first treatment for BM, two patients underwent neurosurgery, four underwent stereotaxic radiosurgery, two received radioactive iodine and one was treated with a tyrosine kinase inhibitor. After receiving the first therapy, four patients evolved with disease progression and two patients had stable disease, one was not yet evaluated for tumor response, one patient had a partial response and only two patients had complete response. Remarkably, the two patients who achieved a complete response were the only individuals that underwent neurosurgery. Finally, the mean overall survival after BM diagnosis was 21.7 months (range, 1–72 months). **Conclusion:** BM is associated with a poor prognosis in patients with DTC. The disease burden is higher due to concomitant metastatic involvement of other sites, more frequently lungs. Therefore, further studies are needed to primarily assess the most effective treatment strategies for these patients, particularly for those exhibiting a good performance status and a heightened potential for undergoing aggressive therapeutic interventions.

130498 – SURVIVAL OUTCOMES IN THYROID CANCER PATIENTS WITH CO-OCCURRING BREAST CANCER: EVIDENCE OF MORTALITY RISK ATTENUATION

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Introduction: Previous studies have reported a strong correlation between thyroid cancer (TC) and breast cancer (BC). However, the oncological impact of this association is not yet fully understood. Here, we aimed to explore the differences in clinicopathological characteristics between TC patients with and without BC, and the effect of a history of BC on TC survival. **Materials and methods:** We retrospectively compared the characteristics and survival rates of patients with TC alone and those with TC and BC using two distinct cohorts. The primary cohort included 1,267 female patients diagnosed with TC between 1986 and 2020 and who were followed up at our university teaching hospital in southern Brazil. The second cohort used the Surveillance, Epidemiology, and End Results (SEER) database to select patients diagnosed with TC alone and with TC and BC between 2000-2016. In this cohort, a total of 3,542 patients with TC-BC and 109,446 patients with TC alone were identified. **Results:** In the primary cohort, 33 patients had a positive history of BC (2.6%) and these patients were older at the time of TC diagnosis (52.6 *vs.* 46.4 years). No differences were found between TC-BC and TC alone patients regarding tumor size, TNM stage or the ATA risk stratification. Further, survival rates were similar between TC alone and TC-BC patients. In the SEER cohort, we also found that TC-BC patients were older at the time of diagnosis. However, differences in TNM stage ($P < 0.001$) and disease extension ($P < 0.001$) were observed, with TC-BC patients exhibiting a higher proportion of advanced stages. Remarkably, using SEER data, we found that BC had a protective effect on TC and was associated with reduced TC mortality rates [hazard ratio (HR) = 0.72, 95% CI 0.57-0.92; $P = 0.026$]. Moreover, after stratifying TC patients according to the coexisting BC subtype (luminal, HER-2 enriched or triple negative), we found better survival rates only in patients with coexisting luminal A BC ($P = 0.015$). **Conclusion:** This study found mortality risk attenuation in TC patients with co-occurring BC. Importantly, this effect was restricted to TC patients with coexisting luminal A BC, which is a hormone receptor-positive tumor with absent HER-2 expression. These findings suggest that hormone pathways may play a role in TC-BC co-occurrence and impact survival. Therefore, further studies should be performed to confirm our findings and to elucidate these mechanisms in order to better understand this association.

130569 – EVALUATION OF THE TUMOR SUPPRESSOR ROLE OF MIR-665 IN PAPILLARY THYROID CARCINOMA

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Introduction: Thyroid cancer (TC) is the most prevalent type of cancer of the endocrine system. The most common mutations in papillary carcinomas are the BRAFT1799A point mutation and the RET/PTC rearrangements. MicroRNA (miRNA) dysregulation is another important event in the pathogenesis of PTC. In previous studies, our group identified the decreased expression of more than 50 miRNAs derived from the genomic region DLK1-DIO3 in human papillary carcinoma (PTC) samples. In bioinformatic analyses, miR-665 was highlighted as one of the most impactful miRNAs from this cluster, with potential role in development and progression in PTC. **Aims:** To evaluate the tumor suppressor activity of miR-665 *in vitro* functional assays. **Methods:** The PTC cell lines TPC-1(which carries the RET/PTC1 oncogene) and BCPAP (carrying the BRAFT1799A point mutation) were transfected with commercial miR-665 mimetic at concentrations of 10nM and 20nM, and then submitted to the monolayer cell migration assay. The given cell lines transfected only with the transfected reagent were used as control. **Results:** Our results show that overexpression of miR-665 led to a decreased migratory capacity ($p < 0.05$) only in the BRAF-mutated BCPAP cell line, which was not observed in the RET/PTC1-carrying-TPC-1 lineage. **Conclusion:** Although further analyses are needed, our results indicate that the role of miR-665 on cell migration might be dependent on the oncogene background. As BRAF-positive tumors display less differentiated and more aggressive phenotype than those bearing other MAPK signaling mutations, our results could lead to the development of therapeutic strategies against these types of tumors.

130112 – EXTRACELLULAR VESICLES AS A TOOL FOR THE DELIVERY OF TUMOR SUPPRESSOR MIRNAS IN THYROID CANCER

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Introduction: Thyroid cancer (TC) is the most common endocrine cancer in the world, and papillary thyroid carcinoma (PTC) is the most prevalent histotype. Extracellular vesicles (EVs), emerged as promising therapeutic tools, especially in cancer, as they have been proposed as new delivery vehicles for drugs and nucleic acids. In this context, the delivery of tumor suppressor miRNAs, small non-coding RNAs involved in the post-transcriptional regulation of oncogenes, could open perspectives for new therapeutic strategies in TC. However, the use of EVs as therapeutic tools for delivering miRNAs in TC remains to be characterized. **Aims:** To evaluate the potential of exosomes as a delivery tool for tumor suppressor miRNAs for TC. **Methods:** We used non-malignant thyroid cells (NThy-ORI) which overexpress miR-495-3p (previously characterized by our group as a tumor suppressor miRNA in TC) a as a source of EVs. We hypothesized NThy-ORI cells overexpressing miR-495 produce miR-495-3p-enriched EVs and deliver this tumor suppressor miRNA to the recipient tumor cells, subsequently modulating oncogenic pathways. Thus, EVs derived from the miR-495-3p-transfected cells (NThy-ORI-495) and control cells (NThy-ORI-Ø) were isolated by a combination of ultrafiltration and polymeric precipitation. The particle size and morphology of exosomes were characterized by nanoparticle tracking analysis and transmission electron microscopy. **Results:** Firstly, the expression of miR-495-3p was evaluated in the non-malignant cell line NThy-ORI, and the PTC cell lines TPC-1 and BCPAP. Although NThy-ORI cells exhibit higher basal levels of miR-495-3p expression than PTC cell lines, the overexpression of miR-495-3p in NThy-ORI cells resulted in increased miRNA levels in the Conditioned Medium (CM). Subsequently, the C.M. from N-Thy-ORI cells, transfected or not (Ø) with the miR-495-3p was used to treat TPC-1 and BCPAP cell lines. The TPC cells treated with C.M. derived from NThy-ORI-495 cells showed increased accumulation of this miRNA in the cytoplasm compared to those treated with C.M. from N-Thy-ORI-Ø or fresh medium. **Conclusion:** The results obtained so far suggest that EVs derived from NThy-ORI cells overexpressing miR-495-3p efficiently deliver this miRNA to target cancer cells. Further functional assays are necessary to characterize the therapeutic potential of this strategy.

130403 – THYROID CARCINOMA WITH HYPERFUNCTIONING NODULE ON SCINTIGRAPHY

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Introduction: This is an atypical case report of a patient with suppressed thyroid-stimulating hormone (TSH) and a hyperfunctioning thyroid nodule, with suspicious ultrasound characteristics and cytopathological results compatible with malignancy. Although malignancy in hyperfunctioning thyroid nodules is infrequent, it still occurs in about 3.1% of cases. Because they are rarely malignant, fine needle aspiration cytology (FNAC) may not be necessary under current guidelines. However, even if it appears on scintigraphy as a warm nodule, cytopathological analysis may be essential, considering the characteristics suggestive of malignancy of the nodule on US, as demonstrated in this clinical case. These characteristics include marked hypoechogenicity, irregular contours, height greater than width in the cross-section and presence of microcalcifications. **Case report:** Male, 51 years old, asymptomatic, sought care after routine tests revealed T4L 1.57 ng/dL (0.85-1.50), TSH 0.03 microIU/mL (0.48-5.60), thyroid stimulating hormone receptor antibodie (TRAB) 0.36 (<0.55). Thyroid scintigraphy and ultrasound (US) were requested for additional information. The US revealed an area in the middle third of the right lobe where the parenchima was heterogeneous and with a cluster of punctate hyperechoic foci, without nodule identification. The scintigraphy showed nodular areas with high uptake, one in the lower third of the right lobe/isthmus and another of greater extent in the upper two thirds of the right lobe. Given this situation, despite the changes found on scintigraphy, it was decided to perform a fine needle aspiration puncture (FNA) due to the characteristics on US, with aspects suggestive of malignancy. The pathological examination confirmed that it was a papillary thyroid carcinoma and the patient was referred to the surgery team for thyroidectomy. **Conclusions:** Papillary thyroid carcinoma, diagnosed in the case reported, presents the possibility of rapid progression to local lymph nodes, but responds satisfactorily to surgery, with the ten-year survival rate after intervention estimated at approximately 97%. Therefore, early detection and treatment of malignant thyroid diseases can be curative, highlighting the importance of an assertive approach to suspicious thyroid nodules on US, regardless of the hyperfunctioning characteristic on scintigraphy.

130324 – ZEBRAFISH AS AN ANIMAL MODEL FOR THYROID STUDIES: MAINTENANCE AND PROTOCOL DEVELOPMENT IN THESE SPECIALIZED BIOTERIUM FACILITIES

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Introduction: Currently, the zebrafish (Danio rerio) is widely utilized as an animal model for the study and research of thyroid diseases. Its advantages are numerous; among them, it is possible to highlight the high fecundity rate compared to other models. Zebrafish presents external embryonic development with transparent embryos, enabling real-time observation. Additionally, there is potential for generating transgenic animals that express fluorescent proteins in different tissues and organs, making them ideal for *in vivo* monitoring. Another significant advantage is the ability to perform xenotransplantation of human tumor cells without the need to suppress the zebrafish's immune system, as the immune system develops between 48-72 hours after fertilization. Thus, it facilitates the *in vivo* study of tumor-induced angiogenesis, observation of its invasion and neovascularization capabilities, along with the potential for conducting tests with antitumor drugs. **Objective:** Establish and prepare a specialized zebrafish facility dedicated to thyroid research. **Methods:** The maintenance of zebrafish lineages involves the implementation of specific protocols, from nutrition to the meticulous process of reproduction. The methods employed in conducting these studies strictly adhere to ethical guidelines and good research practices, as established by Resolution CONCEA nº 61, May 2nd, 2023. **Results:** Working with different zebrafish lineages requires a sufficient quantity of animals, in this way, reproduction protocol is one of the main maintenance protocols in the bioterium. Artemia, a small crustacean, is the primary live food used in zebrafish diets and is directly linked to reproductive success as it stimulates the animals. The protocol involves three feedings, with two of them consisting of artemia and one with dry food. To initiate the reproduction process, a pair of zebrafish is selected and placed in a divided aquarium, allowing a 10-hour period for courtship between them. After this period, the divider is removed, enabling the animals to come into contact. During this interaction, the eggs are fertilized and the female releases her eggs. **Conclusion:** In this manner, the establishment of a dedicated zebrafish facility for thyroid research, guided by meticulous protocols such as the zebrafish reproduction protocol, is extremely important to ensure the proper execution of all experiments with precision and reliability.

130371 – NEOADJUVANT THERAPY FOR INOPERABLE THYROID CANCER: CASE SERIES FROM REFERENCE CANCER CENTER

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Introduction: Neoadjuvant therapy for locally invasive thyroid cancers (TC) may enable resection of initially inoperable tumors and avoid morbid procedures in cases of extensive disease, such as laryngectomy or tracheal resection. Herein, we report a case series of neoadjuvant therapy with tyrosine-kinase inhibitor (TKI) for locally invasive TC in a cancer reference center. **Case report:** 6 patients had inoperable TC, 50% female with median age of 39 years (12-60), 2 of them had sporadic RET-negative medullary thyroid cancer (MTC) and 4 papillary thyroid cancer (PTC) – 2 classic, 1 columnar cell and 1 diffuse sclerosing subtypes. Criteria for unresecability were encasement of the common carotid artery or the brachiocephalic trunk, involvement of prevertebral fascia and extensive laryngeal invasion. Distant metastases were observed in 5 cases (83%). Neoadjuvant therapy was started to reduce the tumor for surgical viability, two cases had recurrent locally invasive TC, and four cases were newly diagnosed advanced TC. MTC patients received vandetanib without significant tumor reduction to proceed to surgery; the median duration of therapy was 60 months (54-66). PTC patients were treated with sorafenib with median duration therapy of 8 months (6-12), and 2 patients (50%) had tumor reduction enabling surgery: the first one, after 12 months of sorafenib, had total thyroidectomy with neck dissection and the second one, after 6 months of therapy, had lateral neck dissection of extensive lymph node recurrence. The drug was withdrawn 2 weeks and one day before surgery, respectively, with no surgical complication attributed to TKI. The other two PTC remained unresectable despite 13% and 20% reduction of largest tumor diameter. Local and distant metastatic disease remained stable in all patients during TKI treatment in a median follow-up period of 11 months (6-66). Side effects were observed with vandetanib in only one patient – QTc prolongation and uterine bleeding. Sorafenib was associated with hand-foot syndrome (75%), weight loss (50%), hypertension (50%), acneiform rash (25%) and glomus (25%). **Conclusion:** Neoadjuvant therapy with sorafenib was successful in tumor reduction to enable surgery in half of locally invasive PTC patients. However, vandetanib was not associated with significant tumor reduction. Despite remaining unresectable, local and distant metastatic diseases were stable during TKI therapy.

130446 – PAPILLARY THYROID MICROCARCINOMA: LARGE CASE SERIES AND OUTCOMES OVER UP TO 45 YEARS OF FOLLOW-UP

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Introduction: A significant increase in the incidence of papillary thyroid cancer, especially papillary thyroid microcarcinoma (mPTC),has been reported worldwide. Due to its indolent nature, excellent clinical outcomes have been reported for mPTC patients. **Objectives:** To evaluate the clinical characteristics and follow up of patients with a diagnosis of mPTC treated at a University Hospital over 45 years, correlating clinical and evolution data after the recommended treatment. **Methods:** Data base of 1,500 patients with thyroid carcinoma, 219 with mPTC were selected between the years 1978 and 2023. The BRAFV600E mutation analysis in cytological samples was introduced 16 years ago and evaluated in 78 (35.4%) patients. **Results:** 219 patients were selected (Female = 85.8%; Male = 14.2 %) with a median age of 48 years (15-78). At presentation, 42% (N = 92) had an initial diagnosis of multinodular goiter, 40.2% (N = 88) of uninodular goiter, 2.7% (N = 6) came due cervical adenomegaly and in 3.7% (N = 8) and 0.46% (N = 1) of cases, mPTC was found in the surgical specimens of patients operated on due Grave's disease and hyperparathyroidism, respectively. 36 were BRAFV600E positive and 42 BRAFV600E negative. 196 (89.5%) were submitted to total thyroidectomy, 22 (10%) to total thyroidectomy with neck dissection and only one patient to hemithyroidectomy. The mean tumor size was 0.6 cm (0.1-1.0 cm); 71 patients (32,4%) had multifocal tumor; subtypes identified were: 48.9% classical, 38.8% follicular, 2.7% oncocytic, 1.8% sclerosing, 0.5% trabecular and 7.3% mixed; 3.2% with vascular invasion; 15.1% (N = 33) with lymph node metastasis at biopsy. 49.8% were treated with 131I. The median follow-up was 8 years (1-41 years). Lymph node metastasis was observed in 7/36 (21.9%) BRAFV600E positive tumors and in 6/42 (14,3%) BRAFV600E negative tumors. 21 without BRAF analysis presented lymph node metastases. Nodal recurrence was observed in 5 patients of which 3 were BRAFV600E positive and 2 BRAFV600E negative (P = 0.66).Eighteen patients died, all from unrelated causes. 5.8% developed definitive postoperative hypoparathyroidism. **Conclusions:** In most cases, mPTC is a frequent finding in goiter surgery and it has an excellent prognosis. In our series, only 5 (2.3%) presented recurrences, all except one presenting nodal metastasis at initial diagnosis. Recurrence occurred despite total thyroidectomy and radioiodine therapy. No patient died from the disease. In this series, BRAFV600E was not associated with worse prognosis.

130412 – CLINICAL PROFILE AND FOLLOW-UP OF LOW AND INTERMEDIATE RISK DIFFERENTIATED THYROID CARCINOMAS IN NORTHEASTERN BRAZIL

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Introduction: Low and intermediate-risk differentiated thyroid carcinomas (DTC) are more common, and recent findings point to less invasive management options. Since this is a frequent cancer, it is important to look into possible regional specificity. **Objectives:** To analyze clinical-pathological characteristics and follow-up of low and intermediate-risk DTC. **Methods:** Retrospective longitudinal and observational study, based on chart reviews and interviews, that included low- and intermediate-risk DTC that underwent surgery and were followed in Sergipe, Brazil. **Results:** We assessed 180 patients, 86 low and 94 intermediate risk, 95% underwent total thyroidectomy, 96.1% papillary cancer, most frequent subtypes were classic (64.2%) and follicular (25%). Mean age at diagnosis 44.7 ± 13.4 years, 94.3% female, and mean follow-up 84.5 ± 28.8 months. There was no difference between groups regarding clinical features and comorbidities. Smoking was more frequent in intermediate-risk (12.7% *vs.* 3.2%; p = 0.048). Tumor size was similar in both groups (19.5 ± 14.5 *vs.* 17.3 ± 16 mm; p = 0.057). In intermediate-risk, there were 8.5% of aggressive subtypes, 47.8% of vascular invasion and 38.9% of microscopic extrathyroidal invasion. Microcarcinomas were more common in low-risk (47.7%), but it is worth mentioning that 18.3% of intermediate-risk were also microcarcinomas. Multicentricity and lymph node metastasis were more frequent in intermediate-risk (58.7% *vs.* 30.1%; 53.2% *vs.* 2.4%). Radioactive iodine treatment was used in 91.3% of intermediate and in 47.1% of low-risk subjects, and although uptake outside the neck was more commonly observed in intermediate group (32.9%), 15.4% of low risk presented this finding. Over 90% of cases were stage I, and main responses were excellent and indeterminate in both groups. There were 18 cases of local recurrence and 11 with a second dose of radioactive iodine in intermediate-risk, while in low risk, there were only two cases of local recurrence. There were no distant metastasis or death. **Conclusion:** Smoking was the only pre-operative characteristic that differed between groups. Even though over half intermediate-risk cases had local recurrence, both groups presented favorable outcomes. Besides, overtreatment might have occurred, since almost half of low-risk subjects received radiactive iodine therapy, and almost all of them underwent total thyroidectomy in this Northeastern cohort.

130418 – CLINICAL PROFILE AND FOLLOW-UP OF POSSIBLY OVERTREATED THYROID PAPILLARY MICROCARCINOMAS IN NORTHEASTERN BRAZIL

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Introduction: Although thyroid papillary microcarcinoma is an indolent malignancy in general, there is still a tendency towards an overtreatment in some regions. **Objectives:** To evaluate clinical profile of patients with papillary microcarcinoma that underwent surgical treatment in a reference center in Northeastern Brazil. **Methods:** This is a retrospective longitudinal and observational study, based on chart reviews and interviews, that included cases of thyroid papillary microcarcinomas that underwent surgery and were postoperatively referred to an Endocrinology reference center in Northeastern Brazil. **Results:** We evaluated 60 patients, mean age at diagnosis was 46.8 ± 11.3 years, 96.7% were female. All of these patients were referred to an endocrinologist after thyroid surgery had been performed. The most frequent comorbidities were hypertension (53.3%), obesity (36.7%) and diabetes (21.7%), and 21.6% had family history of thyroid cancer. Mean follow-up was 81.8 ± 60.6 months, and mean tumor size was 6.25 ± 2.7 mm. A total of 93.2% of patients underwent total thyroidectomy, in spite of only 42.4% of multicentricity. Papillary subtypes were: classic (64.2%), follicular (28.3%), diffuse sclerosing (7.5%) and oncocytic (5.7%). One third of cases had concomitant thyroiditis, while 12.3% had vascular invasion and 14% microscopic extrathyroidal extension. There were postoperative complications in 14% of cases. Lymph node metastasis occurred in 18.6% of patients, and 43.3% received radioactive iodine therapy. All cases were stage I. Regarding ATA recurrence risk, 68.3% were low and 26.6% intermediate-risk. Second thyroid surgery was indicated in 10 cases, and in 4 of them there was local recurrence and a second dose of radioactive iodine was used. The most common treatment responses were: excellent (61.4%) and indeterminate (28.1%). There was no distant metastasis or death. **Conclusion:** This Northeastern cohort corroborates the indolent behavior of papillary microcarcinomas, and points to possible overtreatment of these cases, since almost all of them underwent total thyroidectomy, and half received radioactive iodine treatment despite the favorable clinical presentation. Perhaps an earlier evaluation by an endocrinologist might have reduced indications for surgery.

130514 – THE IMPORTANCE OF GENETIC SEQUENCING OF FIRST-DEGREE RELATIVES FOLLOWING THE DETECTION OF AN INDEX CASE OF MTC

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Introduction: Medullary thyroid carcinoma (MTC) can manifest as either sporadic or hereditary, with the hereditary variants frequently linked to germline mutations in the RET proto-oncogene (97% of cases), encompassing multiple endocrine neoplasia types 2A and 2B, as well as the isolated familial form. **Case report:** We present a 12-year-old female patient referred for evaluation due to an altered genetic test (mutation in the RET exon 11 codon 634 TGC-> TAC p.Cys634Tyr). The patient's grandfather was diagnosed with MTC in his sixties and later tested positive for RET (index case). Two of his sisters also had a prior diagnosis of MTC, and revealed a positive genetic screening test later. Four of his daughters tested positive for the same mutation. As one of the affected at screening, the patient's mother underwent prophylactic total thyroidectomy (TT) at 27 years old, with MTC found in the surgical specimen. Genetic analysis of her children revealed a negative result for a 15-year-old boy and positive for a 10-year-old girl, the reported patient. At medical evaluation, no palpable thyroid nodule or cervical lymphadenopathy. Serum TSH and calcium in the normal range, and calcitonin: 26.2 (NR < 0.3 mm). The patient underwent TT in the subsequent year. Histopathology revealed an MTC of 0.3 x 0.2 cm in the left lobe and a focus of MTC adjacent to a colloid cyst in the right lobe, both with peripheral changes compatible with C cell hyperplasia. The patient showed an excellent biochemical and radiological response to treatment. **Discussion:** Approximately 25% of MTCs are hereditary. In this context, RET screening allows for the prevention of neoplasia progression through prophylactic TT and early diagnosis in patients without clinically manifest disease. In familial cases, C-cell hyperplasia is considered a pre-malignant lesion. The mutation presented by the patient is considered high risk by the ATA 2015, which recommends early prophylactic TT, preferably before five years of age. The patient underwent surgical treatment at 12 years old, 15 months after the genetic test, with a diagnosis of micro MTC. Her age was lower than all other cases in the family. This case underscores the importance of genetic sequencing of first-degree relatives following the detection of an index case, as well as the relevance of individualizing management based on the specific genetic mutation.

130507 – BONE METASTASIS IN THE THORACIC SPINE IN A YOUNG PATIENT WITH PAPILLARY THYROID CARCINOMA: CASE REPORT

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Introduction: Papillary thyroid carcinoma (PTC) accounts for 80% of malignant thyroid tumors, and the prognosis is usually good. Lymph node metastases are common in thyroid cancer, accounting for 30%-40% of the cases. However, distant metastases are rare, accounting for 1%-4%, and the bone ones occur with a frequency varying from 1.4% to 7%. **Case report:** A 39-year-old woman was referred by the head and neck surgeon for follow-up. She had been monitoring a thyroid nodule for 5 years and, 6 months ago, an increase in the nodule was observed (it went from 1.3 cm to 1.6 cm) and a change in characteristics (it went from TI-RADS 3 to TI-RADS 4). She underwent fine needle aspiration (FNA), which revealed a suspicious lesion of malignancy (Bethesda V). Therefore, she underwent a total thyroidectomy, whose histopathology revealed classic, non-encapsulated papillary thyroid carcinoma, measuring approximately 1.5 cm in diameter, with angiolymphatic invasion and perineural infiltration. Recurrent bilateral dissection revealed metastasis in 4 of 6 affected lymph nodes, with extralymph node extension. After surgery, she underwent USG of the total abdomen, without changes, and CT of the chest showed an expansive paravertebral formation on the right, with slight enhancement after contrast injection, measuring 2.7 x 2.1 cm, suggesting a secondary lesion. Laboratory tests revealed thyroglobulin (TG): 28 ng/mL (NR: 1.1-130 ng/mL) and anti-thyroglobulin (Anti-TG): 46 U/mL (NR: <115 U/mL). The patient then underwent iodine therapy with 150 mCI I131, with post-dose whole body examination (WBE) showing only iodine-capturing tissue in the anterior cervical region, related to thyroid remnants. MRI of the spine did not show more paravertebral expansive formation on the right. Thyroglobulin: 0.2 ng/mL (NR: 1.1-130 ng/mL) and anti-thyroglobulin: 17 U/mL (NR: <115 U/mL). **Conclusion:** Papillary thyroid carcinoma (PTC) is the most common thyroid carcinoma and generally has an excellent prognosis. However, there are few cases of distant metastasis, especially to the spine, which are associated with significantly worse outcomes. This case illustrates an atypical presentation of spinal metastasis in a patient with PTC and a good response to radioiodine treatment.

130529 – IMPACT OF TRANSITION OF CARE TO PRIMARY HEALTH CARE SUPPORTED BY TELEMEDICINE IN PATIENTS WITH DIFFERENTIATED THYROID CANCER: RANDOMIZED CLINICAL TRIAL

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Introduction: Differentiated thyroid cancer (DTC) has low recurrence rates (2%-5%). Despite this, the DTC guidelines recommend long-term follow-up with specialists without defining a maximum follow-up time. Telemedicine is a strategy that aims to optimize the transition of care for patients from tertiary care to primary health care (PHC) and can help in the follow-up of these patients. **Objective:** To evaluate the impact of the transition of care between specialized care and PHC for patients with DTC supported by telemedicine. **Methods:** Patients with DTC and excellent response to initial treatment were randomized to follow-up in-person consultations in a tertiary service or transfer of care with telemedicine support. This support was provided through telephone calls to patients and health units to ensure linkage in PHC and offer support through teleconsultations. The primary outcome was DTC recurrence, assessed in a face-to-face consultation through thyroglobulin measurement and neck ultrasound. Outcomes related to the use of the healthcare system and control of hypothyroidism were also evaluated. **Results:** To date, 206 patients have been included, the majority of whom are female (n = 175; 85%) and with papillary thyroid carcinoma (n = 176; 85.4%). Concerning the ATA risk classification, 110 patients were low risk (54.2%), 91 were intermediate risk (44.8%), and 2 were high risk (1.0%). All patients were treated with total thyroidectomy, and 133 (64.6%) received radioactive iodine. The median follow-up before randomization was 6 years (P25-P75 3-12). Both groups have similar demographic and oncological characteristics. One hundred and twenty-nine patients were reevaluated in face-to-face consultations with a median of 31 months (P25-P75 28-35) after randomization, 70 from the intervention group and 59 from the control group. In the intervention group, one patient presented DTC recurrence, and one presented indeterminate response. In the control group, three patients presented indeterminate response. The rates of euthyroidism in the control and intervention groups were 54.2% and 55.7%, respectively (P = 0.51). **Conclusion:** Transferring care to PHC for patients with DTC with excellent response after initial treatment appears to be safe, not increasing relapse rates or inadequate control of hypothyroidism. **Funding:** *Departamento de Tireoide da SBEM e Conselho Nacional de Desenvolvimento Científico e Tecnológico.*

129385 – IS HASHIMOTO THYROIDITIS PRESENCE ASSOCIATED WITH THE PROGRESSION OF PAPILLARY THYROID MICROCARCINOMAS?

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Introduction: The link between cancer and inflammation is well recognized and documented in several tumors, but the relationship of autoimmune thyroid diseases to the development and evolution of thyroid cancer is still a matter of controversy. Some authors have suggested that Hashimoto's thyroiditis, also called chronic lymphocytic thyroiditis (CLT), should be considered a precancerous lesion, while others have reported thyroiditis as protective against the appearance of thyroid cancer and the development of more aggressive tumors. Although the relationship between CLT and cancer is unclear, the simultaneous presence of these two diseases is common, particularly in patients with papillary thyroid carcinoma (PTC). However, data regarding its role in tumors < 1 cm, called papillary thyroid microcarcinomas (PTMC), are still scarce. We wondered if CLT could influence the progression of PTMC to larger and/or more aggressive tumors. **Methods:** We retrospectively evaluated 162 patients with thyroid nodules referred to the same service. The study group consisted of 141 women and 21 men aged between 18 and 63 years (40 ± 10 years). There were 66 benign nodules (48 goiters and 18 follicular adenomas) and 96 malignant nodules (65 PTC and 31 PTMC). All the patients underwent fine-needle aspiration for cytological examination. Patients with malignant nodules were submitted to thyroidectomy with eventual exploration of the lymph nodes, according to a standard protocol. Cytology and histology were performed by the same thyroid pathologist. **Results:** The incidence of CLT in malignant nodules was 27.08% (n = 26/96), in contrast to only 3.03% (n = 2/66) in benign nodules (p = 0.00078). CLT occurred in 18.44% of women and 9.52% of men (p = 0.3134). In the malignant nodule group, CLT was observed in 19 (29.23%) PTC and 7 (22.58%) PTMC (p = 0.493). Among cancer patients with CLT, multifocality was observed in 12.5% of patients with MPTC and in 28% of patients with PTC (p = 0.3732). Extrathyroid extension was observed in 14.28% of PTMC patients and 16.67% of PTC patients (p=0.8841). None of the patients with PTMC had lymph node metastases, whereas these occurred in 11% of the PTC cases (p = 0.3579). **Conclusion:** These data demonstrated that CLT is more frequent in malignant thyroid nodules. However, in this relatively small cohort of cases, CLT was not associated with patients' sex or with the characteristics of PTC aggressiveness, nor does it seem to be a predictor of progression in PTMC cases.

130540 – MEN 2A CASE REPORT – 20 YEARS OF FOLLOW-UP

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Introduction: Multiple endocrine neoplasia type 2 (MEN 2) is an autosomal dominant hereditary cancer syndrome due to germline variants in the rearranged during Transfection (RET) proto-oncogene. MEN 2A is characterized by the occurrence of medullary thyroid carcinoma (MTC) associating with pheochromocytoma (PC), parathyroid tumors, cutaneous amyloidotic lichen (up to 10%), and Hirschsprung's disease (less than 2%). The prevalence of MEN 2A is 13-24.000 and the incidence varies between 8-28.000 live births per year. RET sequencing is positive in 98% of cases. **Case report:** M. C. A., female, 55 years old, diagnosed with Hirschprung's disease at the age of 17 during her first pregnancy, who had undergone a resection of intestinal segments after giving birth. At the age of 34, showed an increase in the volume of some cervical lymph nodes and biopsy was performed found to be a metastatic neoplasia resembling medullary thyroid carcinoma. Immunohistochemistry was carried out, which concluded metastatic papillary thyroid tumor with medullary differentiation. After a total thyroidectomy, a genetic study verified the association between Hirschprung's disease and MTC, revealing the presence of a C618R (TGC --› CGC) mutation in the RET proto-oncogene, called MEN 2A. In 2019, an increase in her serum calcitonin level led us to request a PET/CT scan, which was negative for neoplasia. Tests were requested to investigate recurrence of the disease and/or distant metastasis due to progressive increase in serum calcitonin. PET-CT with DOTATOC-Ga68 revealed molecular overexpression of somatostatin receptors in the level IIA and V cervical lymph nodes on the left and bone focuses suggestive of recurrence/implants secondary to the underlying disease. Magnetic Resonance Imaging of the abdomen did not show any lesions. Cervical ultrasound was without abnormalities. Preventive research for MEN 2A was carried out on her descendants, where the same mutation (C618R; exon 10) was found in one of them whom has not undergone prophylactic thyroidectomy and has so far remained free of any manifestations of the disease, either clinically, biochemically or structurally. **Conclusion:** We present the case of a patient who initiated the condition with MEN 2A 20 years ago and underwent total thyroidectomy. She remains clinically well and structurally healed, with periodic monitoring of calcitonin and CEA levels.

130510 – MEDULLARY THYROID CARCINOMA ASSOCIATED WITH AN UNCOMMON VARIANT IN EXON 5 OF THE RET GENE

MAIN AUTHOR: SUSAN CHOW LINDSEY

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Introduction: RET genetic screening should be performed in all medullary thyroid carcinoma (MTC) cases, regardless of the clinical presentation. Routine RET sequencing usually involves exons 8, 10, 11, 13-16. Nevertheless, in 2014 we included exon 5 in the routine multiple endocrine neoplasia 2 screening. **Case report:** A 55-year-old woman was diagnosed with a 0.6-cm MTC after a total thyroidectomy due to a suspicious nodule. Subsequent investigation was negative for pheochromocytoma or hyperparathyroidism. The patient had no family history of MTC or other endocrine neoplasia. She underwent RET testing (Sanger sequencing – exons 5, 8, 10, 11, 13-16), and the variant p.Gly321Arg was identified in exon 5. Both of her daughters tested negative for this variant. The patient was later diagnosed with breast cancer and underwent a mastectomy. **Conclusion:** Herein, we report a variant in RET codon 321 in a patient with MTC. We have routinely been sequencing exon 5 along with the classical risk exons for index cases with MTC for the past 10 years and this is the only relevant finding so far. The minor allele frequency of this variant is < 0.0001. The variant occurs in a highly conserved calcium-binding site of the cadherin-like domain, and *in silico* investigations yielded conflicting results. This case report is the second one to describe the co-occurrence of the p.Gly321Arg RET variant and MTC. The previous report describes a Czech patient with MTC diagnosed at age 61 and her 42-year-old son with C-cell hyperplasia. In conclusion, it is possible that the growing use of gene panel sequencing reveals other cases of variants in exon 5 of RET but, so far, such variants in patients with MTC seem to be very rare in the Brazilian population.

130509 – MULTIPLE ENDOCRINE NEOPLASIA 2A IN A KINDRED WITH A NOVEL AMINO ACID SUBSTITUTION IN RET CODON 609

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Introduction: Management of multiple endocrine neoplasia (MEN2) is guided by RET sequencing, posing challenges when encountering variants of unknown significance. **Case report:** We present the case of a 43-year-old woman with an incidentally discovered suspicious thyroid nodule on ultrasound and a nondiagnostic FNA cytology. It lead to a total thyroidectomy and the diagnosis of bilateral medullary thyroid carcinoma (MTC), with the largest tumor measuring 2.7 cm. Physical examination and personal and family history were otherwise unremarkable. RET germline sequencing (Sanger) revealed a p.Cys609Trp variant. Previous reports have shown p.Cys609Trp only in Hirschsprung's patients with no thyroid phenotype. We performed *in silico* analyses that predicted a probably damaging/disease-causing impact for p.Cys609Trp. The patient's two children presented the same RET variant. The 9-yo daughter was asymptomatic with undetectable serum calcitonin. The 14-yo daughter had a borderline calcitonin level and a 0.2-cm thyroid nodule. Basal and calcium-stimulated calcitonin were 9.4 pg/mL (normal range ≤ 5) and 86.6 pg/mL, respectively. Total thyroidectomy was performed and pathology studies showed a 0.4-cm MTC and C-cell hyperplasia. Then, the youngest daughter underwent thyroidectomy, which revealed a 0.8-mm MTC. So far, the three patients have not developed pheochromocytoma, primary hyperparathyroidism or Hirschsprung's disease. **Conclusion:** This kindred with MEN2A presents a novel amino acid substitution in RET codon 609. This report confirms the deleterious prediction of tryptophan substitution in this codon and reinforces the pathogenic nature of this variant. While further studies are warranted, the current clinical presentation suggests that this variant behaves similarly to other codon 609 variants classified as moderate risk.

130601 – CONCOMITANT PAPILLARY AND MEDULLARY THYROID CARCINOMA: A CASE SERIES FROM AN ENDOCRINOLOGY REFERENCE CENTER AT SALVADOR, BAHIA

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Introduction: Thyroid cancer encompasses a clinical spectrum ranging from differentiated neoplasms, like papillary thyroid carcinoma (PTC), to neuroendocrine thyroid carcinomas such as medullary thyroid carcinoma (MTC). These distinct malignancies exhibit significant differences in embryological origin, histological characteristics, and clinical course. Consequently, the coexistence of PTC and MTC presents as a rare entity demanding tailored evaluation. **Objectives:** To present a case series of patients under the care of a specialized endocrinology reference center in Bahia (Cedeba, located in Salvador, Bahia) who harbor concurrent MTC and PTC. This report aims to delineate their demographic profiles, clinical progression, and outcomes. **Methods:** Patients diagnosed with both MCT and PTC who were followed at a thyroid cancer outpatient clinic in an endocrinology reference center were included in this study. Data were extracted from medical records ranging from 2009 to 2023, focusing on parameters such as age, gender, clinical manifestations, and histopathological findings. Exclusion criteria encompassed individuals with incomplete or missing clinical records. **Results:** We identified three female patients with concurrent MTC and PTC, aged between 39 and 64 years at diagnosis. In one case, the initial diagnosis was MTC, with incidental detection of PTC upon histopathological examination. Metastatic disease was observed in a single patient, identified via cervical lymph node biopsy with immunohistochemistry analysis indicative of MTC. PTC characteristics varied, with one case featuring a 0.1 cm lesion at the isthmus and another showing multifocal PTC (0.5 cm at the left lobe and 0.2 cm at the isthmus). Initial PTC risk was low in all cases, comprising two classic variants and one follicular variant. MCT dimensions ranged from 0.3 cm to 3.5 cm. Genetic testing for RET proto-oncogene mutation and screening for pheochromocytoma and hyperparathyroidism yielded negative results in all cases. All three patients exhibited a favorable clinical course with negative thyroglobulin, carcinoembryonic antigen (CEA), and calcitonin levels during the entire follow-up period. **Conclusion:** The coexistence of MTC and PTC presents a rare clinical scenario. Given the disparate prognoses and treatment modalities associated with these carcinomas, clinicians should remain vigilant regarding this possibility to facilitate personalized care for affected individuals.

130604 – EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH MEDULLARY THYROID CARCINOMA TREATED AT A BAHIA'S REFERENCE OUTPATIENT SERVICE

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Introduction: Medullary thyroid carcinoma (MTC) accounts for 5%-10% of thyroid carcinomas. It occurs sporadically (75%) or hereditary (MEN2), due to germline mutations in RET proto-oncogene. In most patients, there is already metastasis at the time of diagnosis. Approximately 70% have cervical lymph node involvement and approximately 5 to 10% have distant metastatic disease. **Objective:** To analyze the epidemiological profile of patients diagnosed with CMT treated at the SUS endocrinology reference outpatient clinic in Salvador, Bahia. **Methods:** Data were retrospectively collected from physical records of 11 patients diagnosed with MTC, during the period from 2015 to 2023. Age, sex, tumor size, presence of RET mutation and presence of metastasis were analyzed. **Results:** Patients were diagnosed with CMT aged between 37 and 64 years (average of 43.8 years). The majority through anatomopathological study after thyroidectomy (TT). Only two have already been diagnosed through fine needle aspiration cytology. In three cases, an immunohistochemical study was necessary for confirmation. A diagnosis was made years after TT, after requesting a slide review; another after cervical biopsy (soft tissue invasion). Regarding histology, there was concomitant papillary type in 27%; one case of MTC with a tubule follicular variant and the others with the classic form. Only one had multifocal carcinoma, while the others had a single lesion. Among the 11 patients, 4 were male (36%). Regarding tumor size: smaller than 2 cm in 36% (one of them microcarcinoma); between 2 and 4 cm in 36%; greater than 4 cm in 18% and irresectable lesion in 9%. Metastases were identified in 72% (9): cervical lymph node (7); lung (4); bone (1). Molecular analysis of the RET proto-oncogene was performed in 5 patients. All with negative results. Furthermore, no family history of MTC was identified, and screening for pheochromocytoma and hyperparathyroidism was negative in all patients. **Conclusion:** The profile of patients in this study is in agreement with the literature showing a predominance of the sporadic form of CMT. Knowing that surgery represents the only curative therapeutic strategy, early diagnosis is essential. However, in few cases sporadic MTC was diagnosed at an early stage, which makes the management of these patients with advanced disease more complex.

130268 – METHODOLOGICAL OPTIMIZATION OF CAPILLARY ELECTROPHORESIS FOR MOLECULAR ANCESTRY ASSESSMENT OF THE RET GENE

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Introduction: Medullary thyroid carcinoma (MTC) may be associated with Multiple Endocrine Neoplasia type 2 (MEN2) when arising from germline mutations in the RET gene. We are studying if the geographical spread of the pathogenic variants in the RET gene throughout Brazilian territory can be attributed to the founder effect. **Objectives:** To optimize a molecular and cost-effective methodology for analyzing the molecular ancestry of the RET gene. **Materials and methods:** This study investigated MEN2 in first-degree relatives of individuals with pathogenic variants in the RET gene or those exhibiting MTC. Peripheral blood was collected, and DNA was extracted, followed by Sanger sequencing of selected exons of the RET gene. For DNA amplification, four polymerase chain reaction (PCR) primers with fluorescent markers were employed. These primers corresponded to microsatellites flanking the RET gene, located at loci D10S196, D10S537, D10S1652, and D10S197, all on chromosome 10. Short Tandem Repeats (STRs) in the amplicons delimited by the primers were identified using the "Tandem Repeats Finder" software. Capillary electrophoresis was chosen over agarose gel due to its higher resolution. For analysis, the "GeneScan 500 LIZ dye Size Standard" molecular weight standard (0,25µL per well) was added to the DNA sample. The diluted PCR product and the marker were resuspended in highly deionized formamide to prevent ionic interferences. Plates were denatured and subjected to analysis using the SeqStudio Genetic Analyzer. **Results:** Pathogenic variants in codon 804 were selected for method standardization, covering three possible variants: c.2410G>A (p.Val804Met), c.2410G>T (p.Val804Leu), and c.2410G>C (p.Val804Leu). A total of 150 patients were studied, including 100 V804M, 40 V804L (G>C), and 10 V804L (G>T). Capillary electrophoresis provided superior resolution for STR analysis in the RET gene compared to agarose gel. Fluorescent primers allowed the reading of all four loci in a single run, optimizing time and resources. Using the "GeneScan 500 LIZ dye Size Standard" molecular weight standard ensured accuracy in allele size determination. The haplotype results have already been obtained, however, the analysis of molecular ancestry is still ongoing, with partial results. **Conclusion:** The methodology standardization proved appropriate, and the microsatellite markers flanking the RET gene at the studied loci were successfully employed to assess founder effects in the RET gene.

130587 – EVOLUTION OF A FINE NEEDLE ASPIRATION SERVICE (FNA) OF NODULAR THYROID LESIONS AT A UNIVERSITY HOSPITAL IN MATO GROSSO OVER A PERIOD OF 9 YEARS

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Introduction: Fine needle aspiration (FNA) is a widely used method in the diagnosis of patients with thyroid nodules. It has high sensitivity and precision, which reduces the number of thyroidectomies in patients with benign lesions, as well as adequately qualifying patients with malignant thyroid neoplasms for surgery using the Bethesda system. **Objective:** To compare the progress in obtaining epidemiological data regarding the performance of FNA in patients at a University Hospital in Cuiabá. **Methods:** A retrospective study was carried out, based on the analysis of data from medical records of patients who underwent the procedure between 2014 to 2019 and 2019 to 2023. By reading and interpreting the slides, the results were classified according to the Bethesda category, and grouped with the age and sex of the patients in a Microsoft Excel software database. **Results:** Between 2014 and 2019, 260 samples were collected from 175 patients, of which 167 (95,43%) were women and 8 (4,57%) were men, with an average age of 53,2 years. Regarding the samples, 112 (43,24%) are in Bethesda category I (indeterminate sample), 133 (51,35%) in category II (benign nodules), 2 (0,77%) in category III (atypia of undetermined significance), 5 (1,93%) in category IV (suspected follicular neoplasia), 2 (0,77%) in category V (suspected malignancy) and 1 (0,38%) in category VI (malignant). Between 2019 and 2023, 213 patients were evaluated, of which 204 (95,78%) were women and 9 (4,22%) were men, with an average age of 54,4 years. 245 samples were collected, of which the cytopathological examination classified 36 (14,69%) in Bethesda category I, 192 (78,36%) in category II, 4 (1,63%) in category III, 7 (2,85%) %) in category IV, 5 (2,04%) in category V and 1 in category VI (0,4%). In 8 patients who underwent post-FNA thyroidectomy, the anatomopathological results revealed malignant neoplasia in 87,5% of Bethesda ≥ III cases. **Conclusion:** Comparing data from the two periods, originating from the same institution and collected by the same examiner, a qualitative improvement in the acquisition process was observed, with greater detection of benign nodules and fewer unsatisfactory samples. The prevalence of nodules in females and people over 50 years of age remained. Furthermore, when FNA is positive for malignancy, there is a high probability that the nodule is malignant.

130559 – HYPERTHYROIDISM: A RARE COMPLICATION FOLLOWING THYROID PERCUTANEOUS ETHANOL INJECTION

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Case presentation: We present the case of a 52-year old female patient who was referred to us for treatment of a predominantly cystic thyroid nodule through Percutaneous Ethanol Injection (PEI). The patient refused surgery and felt extremely bothered by the presence of the "lump" in her neck. Thyroid ultrasound (9/30/2019) revealed a predominantly cystic, isoechoic, well-defined nodule, wider than tall, without calcifications, measuring 3 x 1.6 x 1.9 cm (volume 4.7 mL) located in the transition between the right lobe and the isthmus (TRADS 1). Laboratory evaluation showed (8/20/2019): TSH: 1.13 (VR: 0.4-4.5 µIU/mL) and T4L: 1.1 (VR: 0.70-1.48 ng/dL) with negative thyroid autoantibodies. In the next few months following her first visit, the patient underwent to three PEI sessions without complications and with excellent aesthetic result. There was a volumetric reduction of 62% (final nodular volume: 1.8 mL) and there was no longer a visible lump in the neck. Three years after the PEI sessions, the patient returned reporting an increase in intestinal rhythm, palpitations and fine tremors of the extremities. Subsequent laboratory evaluation showed that the patient was hyperthyroid: T4L 2.1, TSH 0.01 and negative TRAB. The patient denied taking medications that could interfere with thyroid hormone levels. The suspicion of nodular autonomy was raised and a scintigraphic study of the thyroid was requested. **Discussion:** Percutaneous ethanol treatment of cystic or predominantly cystic thyroid nodules under ultrasonography guidance has been used for more than twenty years and is an excellent, low cost and save non invasive outpatient method of treatment. However, like other mini-invasive procedures, PEI may have partial efficacy, possible adverse effects, and, eventually, mild complications. In the literature, cases of thyrotoxicosis due to Graves' disease have been identified subsequent to PEI. However, given a negative TRAB dosage, hyperthyroidism from another cause must be considered in the case of our patient, possibly due to a gain in nodular autonomy. To our knowledge, this is an extremely rare event, with only one other report of nodular autonomy gain subsequent to alcoholization reported in the literature. The mechanism of this gain-of-function mechanism has not yet been clarified.

REGULAÇÃO DA FUNÇÃO TIREOIDIANA

130549 – POLYCHLORINATED BIPHENYLS ACTIVATE THYROID GENE TRANSCRIPTION THROUGH EPIGENETIC MECHANISMS AND THE DYSREGULATION OF MAPK AND PKA SIGNALING PATHWAYS

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Introduction: Polychlorinated biphenyls (PCBs) are thyroid disruptors that alter thyroid hormones and TSH serum concentrations in exposed humans and rodents. However, the molecular mechanisms involved in thyroid function dysregulation by PCBs have never been reported. **Objective:** To evaluate the molecular mechanisms triggered by PCBs exposure in the disruption of thyrocytes gene/protein expression and function. **Methods:** PCCl3 cells were treated or not (control) for 24 h with 10-9 M Aroclor 1254, a mixture of PCBs. Gene and protein expression were evaluated by qPCR and Western Blotting, respectively. Transcriptional thyroid gene regulation by PCBs was evaluated in PCCl3 cells transiently transfected with plasmids containing NIS, TG, and TPO promoters' regions. The involvement of DNA methylation and histone acetylation/methylation alterations in the PCB-triggered effects was evaluated by using inhibitors of DNMT (Azacytidine), histone acetylation enzymes (A485), and H3K27 methyltransferase EZH2 (GSK343). The participation of the PKA/CREB and MAPK/ERK pathways was evaluated in cells exposed or not to PCBs and the inhibitors of PKA (H89) or MEK/ERK (PD0325901). **Results:** PCBs exposure significantly increased the gene/protein expression of TPO, NIS, and TSHR, but reduced TG expression. NIS and TPO promoter activity was increased in PCB-exposed cells, while TG promoter activity was reduced in these cells. PCB-exposed cells presented reduced expression of enzymes involved in DNA methylation and histone deacetylation. In agreement, PCB exposure increased the content of acetylated histones H3 and H4. PCB also augmented the expression of enzymes involved in histone demethylation and reduced the content of methylated lysines in the histone H3. DNMT, histone acetylation, and histone methylation inhibitors concomitantly with PCB treatment have abrogated some of the PCB-induced effects. Finally, PCB exposure increased CREB phosphorylation and decreased ERK phosphorylation, which is coherent with the activation of the thyroid differentiation markers expression. The use of H89 and PD0325901 reverted the effects of PCB on thyroid gene expression, except for the TG expression. **Conclusions:** Epigenetic mechanisms commonly involved in transcriptional activation are involved in the thyroid gene regulation induced by PCBs. PCBs stimulate the transcription of thyroid differentiation markers through the activation of the PKA and inhibition of the MAPK signaling pathways.

130595 – TRICLOSAN STIMULATES GENE/PROTEIN EXPRESSION IN THE THYROID THROUGH THE ACTIVATION OF THE PKA/CREB SIGNALING PATHWAY AND ENHANCED ACETYLATION OF HISTONES

MAIN AUTHOR: CAROLINE SERRANO DO NASCIMENTO

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Introduction: Triclosan (TCS) is an antifungal/bactericidal compound widely used in personal hygiene and cosmetic products. Previous studies from our group have shown that intrauterine exposure to TCS stimulates the transcription of differentiation genes in the embryonic thyroid gland. However, the molecular mechanisms involved in this effect have not been clarified. **Objectives:** To investigate the molecular mechanisms triggered by TCS that dysregulate the gene and protein expression of thyrocytes. **Methods:** PCCl3 cells were treated or not (control) for 24 h with TCS (10-6 and 10-7 M). Gene and protein expression were evaluated through qPCR and Western Blotting, respectively. The activity of the sodium-iodide symporter (NIS) was assessed through a non-radioactive iodine uptake assay. Transcriptional thyroid gene regulation by TCS was evaluated in PCCl3 cells transiently transfected with plasmids containing NIS, TG, and TPO promoters' regions. The participation of epigenetic mechanisms on TCS-induced effects was evaluated in cells concomitantly treated with TCS (10-7M) and A485 (10 µM), an inhibitor of histone acetylases. The participation of the PKA/CREB pathway was evaluated in cells exposed or not to TCS (10-7M) and the inhibitor of PKA (H89, 10 µM). **Results:** TCS exposure increased the expression of crucial genes/proteins involved in thyroid hormone synthesis, such as TPO, TG, and NIS, particularly at the lowest treatment dose. Consistently, NIS-mediated iodide uptake was increased in TCS-exposed cells compared to the control group. Furthermore, TCS exposure increased the transcriptional activity of NIS, TPO, and TG promoters. Interestingly, TCS exposure reduced the expression of histone deacetylases (Hdac1, Hdac3, Hdac6, Sirt1), as well as increased the expression of histone acetyltransferases (Hat). These effects were consistent with the augmented content of acetylated H3 and H4 histones in TCS-exposed cells compared to the control group. Interestingly, the use of the inhibitor A485 abrogated the stimulatory effects of TCS in thyroid differentiation markers. Finally, TCS treatment significantly increased CREB phosphorylation, and the use of H89 reverted the TCS-induced effects in thyroid gene expression. **Conclusion:** TCS activates the PKA/CREB signaling pathway and enhances chromatin accessibility through increased histone acetylation, thereby stimulating transcriptional activity in thyroid cells.

130062 – EXPLORING THE REGULATORY MECHANISMS OF PLACENTAL GENOMIC IMPRINTING AT THE DLK1-DIO3 LOCUS IN WOMEN WITH HYPOTHYROIDISM: ROLE OF THYROID HORMONE IN SUSCEPTIBILITY TO TYPE 2 DIABETES IN OFFSPRING

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Introduction: Metabolism regulation, crucial from fetal development to adulthood, is intrinsically attached to thyroid hormones. During the gestational period, deregulations that affect epigenetic control might predispose to metabolic pathologies, including *diabetes mellitus* type 2 (DM2). Despite theories on the reduction of deiodinase 3 (D3) expression and DNA methylation pattern changes, specifically in locus DLK1-DIO3, associated with glucose intolerance in DM2, the intricated mechanisms that bind the thyroid and pancreas remain inconclusive. Previous investigations indicate a significant increase in the methylation of MEG3-DMR zones in beta-pancreatic cells of diabetic patients, resulting in a decrease in microRNAs expression. In the present study, we investigated if hypothyroidism acts as a deregulator of placental imprinting mechanisms. Aim of the study: to investigate the mechanisms of epigenetic control that are responsible for the locus DLK1-DIO3 imprinting in the placentae of mothers with hypothyroidism. **Patients and methods:** 2 groups with 12 pregnant women each were selected: Healthy patients and Hypothyroidism patients and patients whose thyroid-stimulant hormone (TSH) value was equal to or higher than 4,5 UI/mL during the first gestational trimester. A comparative investigation of the methylation profile of placental DNA was conducted, by post-bisulfite pyrosequencing of zones I MEG3-DMR, IG-DMR-1, and IG-DMR2. Tukey Kramer statistic test was conducted, with a level of significance of 5%. **Results:** In the MEG3-DMR region, a statistical difference was found in the mean methylation profiles of the hypothyroidism group in comparison to the healthy group. This result indicates the epigenetic control mechanisms responsible for the DLK1-DIO3 locus imprinting. **Conclusion:** The hypermethylation of the zone responsible for the DIO3 expression in the placenta of mothers with hypothyroidism was observed. This observation confers the epigenetic mechanism involved in the relationship between hypothyroidism and glycemic metabolism and demonstrates the importance of alerting to the need for normal hormonal levels of pregnant patients with hyperthyroidism.

130508 – AMIODARONE-INDUCED THYROTOXICOSIS: CASE REPORT

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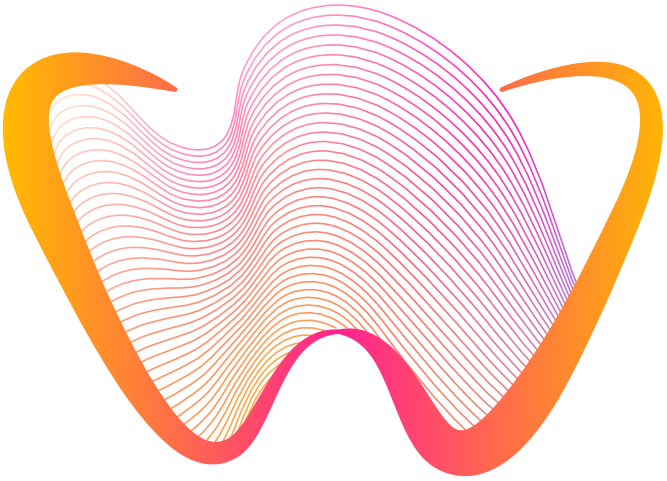
Introduction: Amiodarone is widely used in treating atrial and ventricular arrhythmias; however, due to its high iodine concentration, the chronic use of the drug can induce thyroid disorders. Amiodarone-induced thyrotoxicosis (AIT) can decompensate and exacerbate underlying cardiac abnormalities, leading to increased morbidity and mortality. **Case report:** A 60-year-old man presented with tachycardia, sweating and tremors of the extremities for 1 week. He had been using amiodarone for 3 months, prescribed for ventricular tachycardia and electrical instability due to chagasic heart disease. Thyroid function tests (TFTs) revealed TSH 0.01 mU/L (NR: 0.4-4.3 mU/L) and fT4 1.9 ng/dL (NR: 0.7-1.48 ng/dL). Repeat TFTs confirmed low TSH 0.01 mU/L and elevated thyroid hormone levels [fT4: 2.04 ng/dL; tT3: 192 ng/dL (NR: 40-180 ng/dL)], suggestive of thyrotoxicosis. Antibodies to autoimmunity were negative [TPO-Ab: 36 U/mL (NR: <60 U/mL); TRAb: 1.0 U/L (NR: <1.75 U/L)]. A thyroid ultrasound revealed normal volume with elevated parenchymal blood flow (right lobe: 4.3 x 2.3 x 1.6 cm; left lobe 4.4 x 1.6 x 1.2 cm) and there was RAIU at 24 hours <1%. Therefore, tapazole 10 mg/day was started and the patient regained euthyroidism after 6 months (TSH: 3.2 mU/L; fT4: 1.38 ng/dL), still using amiodarone. The cardiologist then suspended amiodarone, opted for implantable cardioverter defibrillator (ICD) implantation and the patient maintained normal thyroid function (TSH: 2.9 mU/L; fT4: 1.08 ng/dL). After that, it was also possible to withdraw tapazole and the patient maintained normal TFTs (TSH: 2.7 mU/L; fT4: 1.24 ng/dL). **Conclusion:** It is essential to carefully evaluate patients before and during amiodarone therapy. Careful analysis of the thyroid gland and determination of baseline TSH and free T4 values are recommended, which should also be measured after 3 months of therapy and, thereafter, every six months. Deterioration in cardiac function implies the suspicion of associated thyroid dysfunction, even in the absence of classic symptoms.



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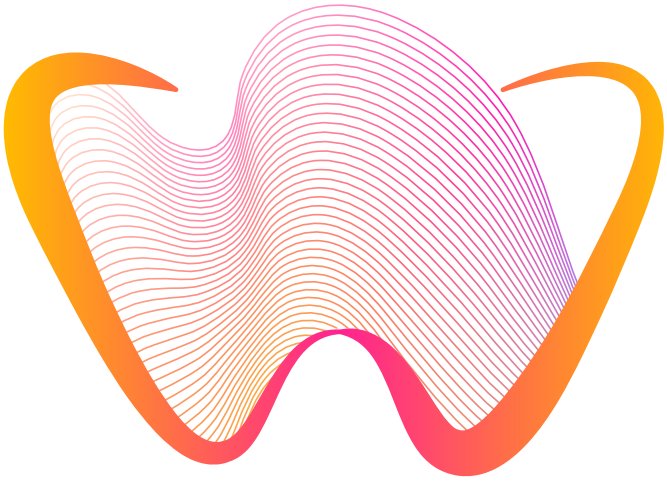

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