at the age of 7 years. After GH replacement, he reached final height at the age of 18 within family target height. Pituitary image showed an ectopic posterior pituitary, hypoplastic anterior pituitary and thin pituitary stalk. SOX3 (c.912G>A/p.M304I) variant in hemizygous state was absent in populational data banks. In silico prediction algorithms SIFT, PolyPhen, and Mutation Assessor were predicted as damaging. Family segregation showed normal mother and sister carriers of the variant, while father, brother and uncle (from mother’s side), all phenotypically normal, did not harbor the variant. RNA In silico analysis pointed that the variant causes mRNA structure change. Protein stability dropped from 677.46 kcal/mol in wild type to 666.69 kcal/mol in p.M304I, making it less stable. Protein Interaction analysis with DNA binding motif (PDB 2LE4) required two times less energy in mutant (376.19 kcal/mol) than wild type protein (646.77 kcal/mol), leading to a less stable interaction. We conclude that one among 28 patients presented a rare novel variant in SOX3 associated to IGHD in a patient without mental retardation and compatible with an X-linked inheritance pattern.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS II

WFS1 Related Disorder in A 4-Month Old Girl
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MON-078
WFS1 related disorder in a 4-month old girl

Background: Idiopathic early-onset central diabetes insipidus (CDI) may be due to mutations of arginine vasopressin-neurophysin II (AVP-NPII (AVP)) or wolframin (WFS1/2) genes (1).

Clinical Case: A 4-month old girl presented to our pediatric endocrinology clinic due to severe polydipsia-polyphagia and normal pituitary stalk. Plasma and urine glucose and HbA1c were normal and 24h monitoring of urinary output was elevated (155 from 111 at 0 o'clock) with a goiter. Weight was 83 kg. Initial labs revealed TSH 6.8 mIU/L (0.3-4.7 mIU/L), free T4 2.0 ng/dL (0.8-1.7 ng/dL), free T3 491 pg/dL (222-383 pg/dL), and thyroid peroxidase antibody >600 IU/mL (<20 IU/mL). Additional work-up demonstrated elevated free T4 by equilibrium dialysis 2.5ng/dL (0.9-2.2 ng/dL) and elevated TSH with HAMA treatment 5.96 mIU/L (0.40-4.50 mIU/L), thereby ruling out familial dysalbuminemic hyperthyroxinemia and HAMA interference. Alpha-subunit of 0.30 ng/mL (<0.55 ng/mL) and normal pituitary MRI did not support a TSH-secreting adenoma. Quest Diagnostics RTH Gene Sequencing was negative for a mutation in the THRβ gene. The patient was subsequently diagnosed with nonTR-RTH.

Result: Two heterozygous variants were revealed: WFS1:NM_001145853: exon8c. G997A:p.R611H, WFS1:NM_001145853: exon8c.G1832A;p.R611H reported as possibly damaging in 1/6 and 4/6 prediction programs respectively. These variants will be checked in both parents to confirm the presumed compound heterozygosity pattern in the child.

Conclusion: We present a 4-month old girl with two heterozygous variants of WFS1 gene which may cause early-onset central diabetes insipidus and possibly a WFS1 related disorder (1).

Reference:
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Thyroid

THYROID DISORDERS CASE REPORTS III

A Case of Resistance to Thyroid Hormone with Concurrent Hashimoto’s Thyroiditis and Post-Surgical Hypothyroidism
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MON-472
Introduction: Resistance to thyroid hormone (RTH) is a rare defect that results in impaired sensitivity to thyroid hormone. While most commonly caused by mutations in the thyroid hormone receptor beta (THRβ) gene, in 15% of patients with the RTH phenotype, no mutation is identified. This entity is known as non-thyroid hormone receptor RTH (nonTR-RTH). Patients with RTH have an increased risk of autoimmune thyroid disease with a reported odds ratio of 2.36. Hashimoto’s thyroiditis or other etiologies of hypothyroidism add a layer of complexity to RTH as such individuals may require high doses of levothyroxine to overcome hormone resistance.

Clinical Case: A 36-year-old male was referred for abnormal thyroid function tests. He denied symptoms of thyroid dysfunction. Physical examination was notable for a goiter. Weight was 83 kg. Initial labs revealed TSH 6.8 mIU/mL (0.3-4.7 mIU/mL), free T4 2.0 ng/dL (0.8-1.7 ng/dL), free T3 491 pg/dL (222-383 pg/dL), and thyroid peroxidase antibody >600 IU/mL (<20 IU/mL). Additional work-up demonstrated elevated free T4 by equilibrium dialysis 2.5ng/dL (0.9-2.2 ng/dL) and elevated TSH with HAMA treatment 5.96 mIU/L (0.40-4.50 mIU/L), thereby ruling out familial dysalbuminemic hyperthyroxinemia and HAMA interference. Alpha-subunit of 0.30 ng/mL (<0.55 ng/mL) and normal pituitary MRI did not support a TSH-secreting adenoma. Quest Diagnostics RTH Gene Sequencing was negative for a mutation in the THRβ gene. The patient was subsequently diagnosed with nonTR-RTH.

Thyroid ultrasound showed multiple thyroid nodules,
including a 1.8 cm hypoechoic, complex nodule in the left inferior gland and a 1.7 cm isoechoic nodule in the right inferior gland. Fine needle aspiration of the left nodule was suspicious for papillary thyroid carcinoma and the right nodule showed lymphocytic thyroiditis. The patient under- went total thyroidectomy and pathology demonstrated a benign left nodule and an incidental 0.3 cm right papillary thyroid carcinoma. The patient started levothyroxine 150 mcg daily (1.8 mcg/kg) post-operatively with subsequent TSH of 18.1 mcU/mL. His dose was increased to 200 mcg daily (2.4 mcg/kg) and TSH was still elevated at 11.7 mcU/mL. His levothyroxine dose was subsequently increased to 250 mcg daily (3 mcg/kg) and TSH is outstanding.

Conclusions: This case highlights the diagnostic challenge in nonTR-RTH. It also demonstrates the complex management of patients with RTH and concurrent hypothyroidism. Such patients need close monitoring and aggressive titration of levothyroxine to achieve desired hormone levels.

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Thyroid

Thyroid Neoplasia and Cancer

Comorbidity of Primary Hyperparathyroidism and Papillary Thyroid Cancer: A Single Center Outcomes

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MON-489

Introduction: Concordance of primary hyperparathyroidism in patients with thyroid disease has been previously reported by several studies. However, comorbidity between primary hyperparathyroidism (PHPT) and papillary thyroid cancer (PTC) has been sparsely described by previous, mostly case-series studies, and is considered rare. Since pathophysiological mechanisms behind the two diseases are supposed to be different, any link between these diseases has not been explained as yet. Hypothesis: Aim of the study was to investigate the possible concurrence for the two diseases in people who underwent thyroidectomy for suspected thyroid nodules. Methodology: Retrospective observational study that included 2913 patients (24% men with mean age 49.82 yrs, 76% women mean aged 47.73 yrs), who underwent total thyroidectomy during the last 13 years (2005-2018) at the Department of Endocrine Surgery, Euroclinic Hospital, in Greece. The patient-groups were categorised according to histopathology criteria of the thyroid and/or parathyroid glands (in case of comorbidity of primary hyperparathyroidism (PHPT) diagnosed prior to surgery). Results: Statistical analysis revealed benign histopathology findings in 1945 patients (64%), while papillary cancer was found in 978 (32%). Among patients with non-malignancy, 16 (11 women/5 men) had PHPT, but in those with papillary cancer, PHPT was diagnosed in 38 (33 women/5 men) individuals. The relative risk for the concurrence of PHPT and PTC was 2.033 (95%CI 1.69 to 2.43, P<0.0001). Age groups between 30 and 60 yrs were associated with the highest relative frequency of comorbidity (82%). A significant positive correlation was observed between less aggressive PTC histopathology findings and PHPT concurrence (P<0.0001).

Conclusions: Our study found that the comorbidity between primary hyperparathyroidism and PTC may be considered as possible. Endocrinologist’s diagnostic approach may add serum calcium and parathormone levels in patients who undergo evaluation for suspected thyroid nodules. Patients with PHPT and PTC had mostly microcarcinomas, and histopathology findings showed a less aggressive PTC pattern. Further large cohorts as well as genetic studies, are needed to duplicate our results and further highlight possible common pathogenetic pathways behind PHPT and PTC concurrence.

Thyroid Cancer Case Reports II

Encapsulated Follicular-Variant of Micropapillary Carcinoma Presenting with Distant Bony Metastasis

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MON-434

INTRODUCTION: The incidence of thyroid cancer has risen steadily over the last decades, in part due to increasing diagnosis of apparently low-risk well-differentiated cancers. The outcomes of well-differentiated thyroid cancers, including follicular variant papillary thyroid carcinoma (PTC), are believed to be quite favorable, with a largely indolent benign course. We examine an encapsulated follicular-variant of micropapillary carcinoma presenting with distant bony metastasis. CASE: 55-year-old lady presented to clinic after biopsy of iliac crest (IC) mass revealed thyroid tissue. One year prior she started having dull pain at right hip, attributed to increased physical activity. She noticed a tender “lump” on her right hip. CT revealed destructive right iliac 8 cm mass with extraosseous soft tissue component, central necrosis, and eccentric calcifications; and right ovarian cyst. Right IC biopsy was consistent with thyroid tissue with positive Thyroglobulin and TTF-1 immunostains. Physical exam was normal, except for mild tachycardia, hypertension, right flank large rounded mass fixed to IC, tender to palpation without erythema or warmth on overlying skin. Thyroid ultrasound showed normal thyroid gland except 5.58 x 6.22 x 7.76 mm left lobe nodule without increased vascularity but with coarse peripheral calcification. FNA was unsatisfactory. Thyroid function tests revealed undetectable TSH, elevated FT4, FT3, and...