Glucose was consistently high, accompanied with polydipsia and polyuria. She was treated with metformin, despite persistent increase in her A1C, as well as fasting and random blood glucose. We performed GAD65 test which came back positive, hence we diagnosed her with latent autoimmune diabetes in adult. In the past three months, she experienced palpitations, tremor, diarrhea, diaphoresis, and unexplainable weight loss. No exophthalmos was found, but she complained of an enlargement around her neck. We run thyroid hormone test, her TSHs was <0.003 (0.35-4.94 μIU/mL) and FT4 was 4.17 (0.70-1.48 ng/mL). Her ultrasound revealed diffuse enlargement of both thyroid with increased vascularization. We diagnosed her with Graves’ disease and treated her with methimazole and propranolol.

Discussion: This case highlighted the rare co-occurrence of four autoimmune diseases. The underlying genetic predisposition of individual with autoimmune disease, will make them prone to develop multiple defect in their self-tolerance mechanism. However, the strict criteria of APS or MAS constrained us from putting all her autoimmunities into one big umbrella. Based on epidemiological data, hyperthyroidism in female productive age, with diffuse thyroid enlargement, is commonly due to Graves’ disease. However, this diagnosis needs to be further evaluated with thyroid scintigraphy and confirmed with TSH-receptor antibody test. Conclusion: Improvement in medical diagnostic tools as well as better understanding of the underlying pathophysiology will make it inevitable to find more autoimmunity co-occurrence in the future. In order to keep up with this progress, the traditional classification of APS or MAS should be reviewed to allow clinician to see the case in one big entity. Keywords: GD, LADA, SLE, UC

Thyroid

THYROID DISORDERS CASE REPORT

Oscillating Hypo-Hyperthyroidism; a Rare Type of Autoimmune Thyroiditis in Adolescence
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Background: Spontaneous conversion of hypothyroidism to hyperthyroidism and vice versa is a unique autoimmune entity characterized by the oscillating activity of thyrotropin blocking inhibiting immunoglobulin (TBII) and thyroid-stimulating immunoglobulin (TSM). The simultaneous presence of both antibodies is a rare phenomenon in children. Clinical Case: At 11 years of age a female with Trisomy 21 and mild developmental delay had elevated TSH 5.4uIU/mL (0.4-4.5), normal thyroxine (T4), negative thyroglobulin peroxide antibody (anti-TPO), and thyroglobulin antibody (Anti-Tg). Levothyroxine (LT4) 1.2mg/kg/day was started. At 12 years of age, she relocated, and the same treatment was continued. About 7 months later, she was referred for weight loss of 8lbs, tachycardia, high BP, suppressed TSH <0.015uIU/mL, high total T4 15.9mg/dL (4.5-12.0), and anti-TPO 38 IU/mL (<9). She was diagnosed with hyperthyroidism and LT4 was discontinued. Repeat lab showed persistently undetectable TSH, high T4, TBII 70 (normal <16%), and TSI 698 (<140 %). Methimazole (MMD) 0.38mg/kg/day and Atenolol 25mg daily was started for Grave’s disease. At 15 years of age, she presented with symptoms of hypothyroidism; 10lb weight gain in 2months, high TSH

Case: At 11 years of age a female with Trisomy 21 and mild developmental delay had elevated TSH 5.4uIU/mL (0.4-4.5), normal thyroxine (T4), negative thyroglobulin peroxide antibody (anti-TPO), and thyroglobulin antibody (Anti-Tg). Levothyroxine (LT4) 1.2mg/kg/day was started. At 12 years of age, she relocated, and the same treatment was continued. About 7 months later, she was referred for weight loss of 8lbs, tachycardia, high BP, suppressed TSH <0.015uIU/mL, high total T4 15.9mg/dL (4.5-12.0), and anti-TPO 38 IU/mL (<9). She was diagnosed with hyperthyroidism and LT4 was discontinued. Repeat lab showed persistently undetectable TSH, high T4, TBII 70 (normal <16%), and TSI 698 (<140 %). Methimazole (MMD) 0.38mg/kg/day and Atenolol 25mg daily was started for Grave’s disease. At 15 years of age, she presented with symptoms of hypothyroidism; 10lb weight gain in 2months, high TSH
>150mIU/L, low FreeT4 0.12ng/dl (0.8-2), anti-TPO 95 IU/mL, and TSI 2.1 IU/L (0.0 - 0.55). MMI was discontinued and she was started on LT4 0.9mcg/kg/day. Repeat TFT’s 5 weeks later showed a normal TSH and Free T4. Thyroid ultrasound showed a diffusely enlarged gland; right lobe - 3.9 x 2.0 x 2.0 cm (volume of: 7.6 mL) and left lobe 4.5 x 1.6 x 2.4 cm (volume: 8.6 mL) with increased vascularity on color Doppler consistent with diffuse thyroiditis. A year later, she developed hyperthyroid symptoms for the second time with 6lb weight loss, tachycardia, suppressed TSH <0.015uIU/mL, elevated free T4 >6.9ng/dl, TBI 8.6 U/L (<1.0), and TSI 12 IU/L. However, this time her TSI level was significantly higher than when she was hypothyroid. She was treated with MMI 0.15mg/kg/day which was increased to 0.3mg/kg/day, and 3 months later she reverted to hypothyroidism; TSH 17.5uIU/mL, Low free T4 0.54ng/dl, normal total T3, with 15lb weight gain. Her MMI dose was lowered to 0.15mg/kg/day, however more definitive treatment options including thyroidectomy and radioactive iodine ablation was discussed with the family. Conclusion: The spectrum of autoimmune thyroid disorders span between extremes of Hashimoto’s thyroiditis and Graves’ disease, but rarely in adolescents, these conditions can co-exist, and management can be challenging and tedious to the patient, family, and physician. Since autoantibody status/titer may not always predict the clinical course, it is important for clinicians to keep a high index of suspicion of this process when the clinical course is atypical. Definitive therapy with thyroidectomy or radioactive iodine ablation may be a suitable option in these cases.

Thyroid

THYROID DISORDERS CASE REPORT

Outcome of Teprotumumab Treatment for Graves Orbitopathy After Multiple Attempts at Orbital Decompression Surgery

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Background: Graves’ Orbitopathy, also known as Thyroid Eye Disease (TED) is a severe ocular manifestation of Graves’ Disease. It manifests as an autoantibody mediated reaction to the thyroid hormone stimulating receptor (TSH-R), these receptors are closely linked with the insulin-like growth factor-1 receptors (IGF-1R). The TSH-R antibodies play a major role in the pathogenesis of TED. The activation of the TSH-R and IGF-1R on orbital fibroblasts and adipocytes lead to IGF-1 expression. This initiates inflammation, fibroblast proliferation and accumulation of glycosaminoglycans in the orbital tissue. Treatment modalities include glucocorticoids, orbital radiation and orbital decompressions. Recent understanding of the molecular basis of TED has resulted in targeted therapy with Teprotumumab, an inhibitory monoclonal antibody against IGF-1R. There is limited literature on the outcomes of Teprotumumab use after orbital decompression surgery. Clinical Case: 43-year-old female presented with symptoms of diplopia, periorbital pain, dry eyes and tremor. Ocular exam: Vision was correctable to 20/20 in each eye, restricted motility, bilateral lid edema, lid retraction with superior scleral show and conjunctival injection. Clinical Activity Score > 4. Diagnostic tests: TSH 0.00 undetectable (N:0.5-5.0mIU/L) FT4 3.19 (N:0.7-1.9ng/dl) TSI thyroid stimulating immunoglobulin 490% of baseline (N: 130% of baseline). Diagnosis of Graves’ disease with associated orbitopathy was made. In addition to medical management for Graves’ thyroid disease she was referred to ophthalmology. She was treated with high dose steroids for 4 weeks with no resolution of symptoms. She was then referred to an oculoplastic surgeon for bilateral orbital decompressions which resulted in mild improvement in diplopia but a residual proptosis. The decision was made to treat with teprotumumab, which had recently been FDA approved. Patient reported improved symptoms without complicate enophthalmos. Review confirmed improved proptosis on Hertel Exophthalmometry. The right eye improved from 22 mm to 16 mm and the left eye from 21 mm to 17 mm (N <20.1 mm Caucasian females) with preserved visual acuity, improved lid retraction, resolved conjunctival chemosis and decreased periorbital pain after 6 doses of Teprotumumab therapy.

Conclusion: Graves’ orbitopathy can result in debilitating symptoms affecting quality of life. Targeted molecular therapy such as teprotumumab is an effective treatment even after orbital decompression.

Reference: Ting, M., Ezra, D.G. Teprotumumab: a disease modifying treatment for Graves’ orbitopathy. Thyroid Res 13, 12 (2020). https://doi.org/10.1186/s13044-020-00086-7

Thyroid

THYROID DISORDERS CASE REPORT

Overt Hypothyroidism Induced by Prolonged Therapy With Imatinib

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Background: Imatinib, a tyrosine kinase inhibitor (TKI), is commonly used to treat chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors. TKI-induced thyroid dysfunction is recognized as an adverse class effect with most cases occurring between six to twelve months after treatment initiation.

Clinical Case: 76-year-old man with hypertension and CML on Imatinib that had been started twenty months prior was admitted for confusion. The patient also reported constipation, cold intolerance, and weight gain despite no change in diet, appetite, or physical activity. On evaluation, his responses to questioning were noticeably delayed, however he was not lethargic. His vital signs were normal and his temperature was 99.5°F (37.5°C) with a heart rate of 78 beats per minute and a blood pressure of 116/70 mmHg. He had a 9 cm goiter with right lobe at 4 cm. His neck was supple and he had no cervical bruit. His lungs were clear to auscultation and his abdomen was soft with normal bowel sounds. His extremities were cool and non-pitting. His right lower extremity was edematous. His thyroid function tests showed a TSH of 94.7 (0.4 - 4.2 uIU/mL), Free T4 0.4 (0.8 - 1.5 ng/dL), and Total T3 30 (87 - 178 ng/dL). Thyrogblobulin antibody was 1016 (0.0 - 4.1 uIU/mL) and TPO antibody was >2000 (0.0 - 5.6 IU/mL). A TSH checked two months before admission was 1.1. Antibody levels had not been checked previously. Thyroid ultrasound demonstrated a hyperemic and heterogeneous thyroid, consistent with thyroiditis. Levothyroxine at a dose of 50 mcg daily was advised, due to patient’s advanced age as well as history of arrhythmia. The patient’s confusion resolved on hospital day three. Repeat thyroid function tests will be checked four to six weeks after Levothyroxine initiation.