with a HbA1c of 9.6% and was transitioned to long-acting insulin once daily and liraglutide 0.6 mg once daily which was subsequently titrated to 1.8 mg once daily over 3 weeks. The patient tolerated this well and has been off short acting insulin since December 2018, with notable improvement in his HbA1c to 5.9% and marked improvement in his post-prandial glycemic control. To our knowledge this is the first report demonstrating the benefits of GLP-1 RA therapy in patients with the HNF4A mutations (MODY-1). Based on this report, it appears that GLP-1 RA therapy could be an effective therapy in patients with MODY-1.

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# Reproductive Endocrinology

## FEMALE REPRODUCTION: BASIC MECHANISMS

### *Activin a Increases Human Trophoblast Invasion by Up-Regulating Integrinb1 Through ALK4*

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**MON-025**

**Activin A Increases Human Trophoblast Invasion by Up-regulating Integrin β1 Through ALK4**

**Abstract:**

Following implantation, extravillous trophoblast cells (EVTs) derived from trophectoderm invade into the maternal decidua to a certain extent, which is tightly regulated by a variety of factors. Activin A, a member of the TGF-β superfamily, has been shown to stimulate the invasion of human trophoblasts (1). Integrin β1 has been implicated in cancer cell invasion and is consistently expressed in human preimplantation embryos (2). However, whether integrin β1 is integrated in activin A signaling and mediates activin A increased-human trophoblast invasion remain unknown. The objective of our study was to investigate the possible mediation role of integrin β1 in the pro-invasive effect of activin A on trophoblasts and illustrate the underlying molecular mechanisms. Primary and immortalized (HTR8/SVneo) cultures of human trophoblast cells were employed as study models. Real-time qPCR, Western blot, and small interfering RNA (siRNA)-mediated knockdown approaches were used to investigate the molecular determinants of activin A-mediated functions. The integrin β1 protein levels in poorly invasive BeWo,JAR and JEG-3 human choriocarcinoma cells were lower than that in highly invasive HTR8/SVneo cells and primary human EVTs, suggesting the possible essential role of integrin β1 in mediating human trophoblast invasion. The expression levels of integrin β1 were up-regulated in a time-dependent manner after activin A treatment in HTR8/SVneo cells. Importantly, siRNA-mediated down-regulation of integrin β1 significantly attenuated both basal and activin A-induced cell invasion in HTR8/SVneo cells as measured by transwell invasion assay. Interestingly, the TGF-β type I receptors (ALK4/5/7) inhibitor SB431542 abolished activin A-induced activation of SMAD2/SMAD3 as well as activin

A-up-regulated integrin 1 expression. Moreover, siRNA-mediated down-regulation of ALK4 or SMAD4 attenuated activin A-up-regulated integrin β1 in both HTR8/SVneo cells and human primary EVT cells. These results reveal that activin A promotes human trophoblast cell invasion by up-regulating integrin β1 expression through ALK4-activated SMAD2/3-SMAD4 signaling pathway.

Reference: (1) Bearfield et al., Eur J Endocrinol 2005;152:909–16. (2) Campbell et al., Hum Reprod 1995;10:1571–8.

# Thyroid

## THYROID DISORDERS CASE REPORTS III

### *Novel Thyroid Hormone β Mutation L266s Causes Atrial Fibrillation & Cerebral Infarction*

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**MON-465**

Background: Resistance against thyroid hormone β (RTHβ) is characterized by reduced tissue sensitivity to thyroid hormone. Patients with RTHβ resistance typically demonstrate increases in FT3 and FT4 accompanied by inappropriately elevated TSH. Mutations in the TRβ gene are the most common genetic disorder in thyroid hormone resistance and result in impaired thyroid receptor functions due to a dominant negative effect. Here, we describe a case with a novel TRβ mutation, presenting atrial fibrillation and cerebral infarction.

Clinical case: A 55-year-old man presented chronic atrial fibrillation and tachycardia as the onset of cerebral infarction. Because blood tests revealed 5.6 pg/ml FT3 (reference range: 2.36–4.06), 3.39 ng/ml FT4 (0.71–1.5), 0.98 TSH μIU/ml (0.541–4.261), and negative TRAb, suggesting inappropriate secretion of TSH (SITSH). He was referred to our department for further investigation. All three test kits, including LUMIPULSE, ECLusys, and TOSOH, showed

an unsuppressed TSH value despite hyperthyroxinemia, demonstrating genuine SITSH. His family history was unclear, but his father had died of heart disease. A pituitary MRI suggested microadenoma, but TSH-secreting pituitary adenoma was excluded because of a negative α subunit and responsiveness to a TRH stimulation test. The TRβ gene was analyzed with informed consent from the patient, and a novel mutation replacing the 266$^{th}$ amino acid serine (TCG) with leucine (TTG) in the 8$^{th}$ exon was found, confirming the diagnosis of RTHβ. Tachycardia and atrial fibrillation were considered to be caused by thyrotoxicosis in heart, which dominantly expresses TRα rather than TRβ. Therefore, β-blockers and anticoagulants, were continued.
Conclusion: This is the first report of a case of RTHβ with the TRβ L266S mutation. This novel mutation is located in the thyroid hormone-binding area of the TRβ gene, suggesting that reduced hormone binding may cause thyroid hormone resistance.

# Thyroid

## THYROID DISORDERS CASE REPORTS II

### *Progression of Graves Disease to Hashimoto's Thyroiditis Following Alemtuzumab Therapy for Multiple Sclerosis*

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**SAT-518**

**Introduction:** Alemtuzumab, an anti-CD52 monoclonal antibody used in the treatment of relapsing-remitting multiple sclerosis is most commonly associated with Graves disease, but autoimmune hypothyroidism may also be seen. We present an unusual case where both were present in the same patient and progression from hyperthyroidism to hypothyroidism was seen within only a few months.
**Clinical Case:** A 33-year-old female referred to Endocrinology clinic for evaluation of hyperthyroidism. She was complaining of palpitations, tremors, increased sweating, heat intolerance, and unintentional weight loss for 3 months. She received 2 cycles of alemtuzumab treatments over the last 21 months for her multiple sclerosis. Last treatment was 8 months before she developed hyperthyroid symptoms. Patient had no prior history of thyroid disorder. Thyroid stimulating hormone (TSH) level was within normal range before alemtuzumab was administered. TSH was monitored periodically and was normal till 8 months after receiving alemtuzumab therapy. Physical exam was remarkable for diffuse enlarged thyroid, not tender, without palpated thyroid nodules but with thyroid bruit. No proptosis was present.
Thyroid function tests obtained by her primary care physician were consistent with hyperthyroidism. Patient found to have suppressed TSH <0.015 IU/mL [0.465 - 4.680IU/mL], elevated total T3 372ng/dL [97-169ng/dL], and elevated total T4 >24.9 ug/dL [5.5 - 11.0 ug/dL].
Further workup revealed elevated Free T3, 10.90 [2.77 - 5.27 pg/mL] and elevated free T4 > 6.99 ng/dL [0.78 - 2.19 ng/dL]. Thyrotropin receptor antibody (TR Ab) was elevated as well at 3.43 IU/L [<1.75 IU/L]. Pregnancy test was negative. Thyroid ultrasound demonstrated goiter with no focal thyroid nodules seen. She was started on methimazole 10 mg daily.
One month later, TSH was elevated at 31.58 though she only took methimazole for one week and then discontinued due to rash and pruritus. At that time, she reported severe fatigue and 25 lbs weight gain. Repeated labs one month later showed elevated TSH, 60.978 IU/ML, low free T4 0.08 pg/mL and low free T3 0.72 ng/dL. Thyroid peroxidase Antibody (TPO Ab) was obtained and was 5308.8 IU/mL [0.0 - 5.5 IU/mL]. She was started on levothyroxine 100 mcg daily. Two months later, levothyroxine dose was increased to 112 mcg daily due persistent TSH elevated. At subsequent visit, patient was euthyroid with normal TSH 3.191IU/mL and normal free T4 1.48 ug/dL.
**Conclusion:** This case was unique in that the patient developed both TR Ab and TPO Ab after alemtuzumab therapy which resulted in Grave's disease followed by Hashimoto's thyroiditis. The case highlights the importance of continuous monitoring of thyroid function in patients treated with alemtuzumab given the unpredictable autoimmune phenomena which may occur.

# Pediatric Endocrinology

## PEDIATRIC OBESITY, THYROID, AND CANCER

### *The Clinical and Endocrinologic Manifestations of Germinoma in Taiwanese Pediatric Population: One Medical Center Experience*

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**MON-085**

**Background**:Intracranial germ cell tumors are rare extragonadal neoplasms. These patients may present with headache, visual impairment and endocrine disorder, depending on the size and location of the tumor. The aim of this study is to assess the clinical features of patients with germinomas in our hospital. **Methods**:We performed a retrospective chart review of 58 children diagnosed with intracranial germ cell tumors from January, 1990 to December, 2018. The initial clinical presentation, tumor markers (beta-hCG and alpha-fetoprotein, etc.), pituitary function, and brain images were reviewed and further analyzed. **Results**:Total 58 patients (45 boys and 13 girls) were included in the study. The mean age at diagnosis was 13.44 ± 2.64 years, ranging from 6.51 to 17.92 years. The initial complaints were weakness (n= 30, 51.7%), eye manifestation (n=27, 46.6%), polyuria (n=27, 46.6%), headache (n= 22, 27.9%), nausea or vomiting (n=16, 27.6%), dizziness or vertigo (n=16, 27.6%), and short stature (n= 8, 15.7%), respectively. Laboratory data showed central hypothyroidism (n = 14, 42.4%), central diabetes insipidus (n=14, 66.7%), hypogonadotropic hypogonadism (n= 4, 40%), and growth hormone deficiency (n=14, 73.7%). **Conclusions**:Germinomas may present with neurologic signs such as weakness, visual impairment, headache, nausea or vomiting. Some patiens presented short stature or polyuria due to central hypothyroidism, diabetes insipidus and growth hormone deficiency. Some atypical