**SAT-LB85**

**Use of Weekly Levothyroxine Regimen for Rapid Normalization of Thyroid Hormone Levels: A Case Report**

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**Background:** Hypothyroidism affects around 4.6% of the U.S. population. Non-adherence with thyroid hormone replacement is one of the biggest challenges in treating hypothyroidism. The half-life of T4 and T3 in hypothyroidism is about 7.5 and 1.4 days respectively. A large dose once-weekly administration of levothyroxine (LT4) is possible. Recent publications suggest that once-weekly LT4 does not increase the risk of cardiovascular events and is well tolerated by most of patients. Once weekly LT4 produces similar results as daily LT4 as evidenced by thyroid function tests, and potentially improves patient compliance and satisfaction with the treatment.

**Clinical Course:** A 29-year-old female with a history of Hashimoto’s hypothyroidism, polycystic ovarian syndrome, depression, presented with irregular menses. Her symptoms included depression, fatigue, increased appetite. Her TSH was grossly elevated at 217 uIU/mL (0.27-4.20 uIU/mL). However upon re-visit, after increasing LT4 to 100 mcg daily her TSH increased to 280 uIU/mL. She admitted to non-adherence with her daily LT4 prescription. Physical exam was notable for sinus bradycardia and slow mentation, otherwise unremarkable. Blood count, basic metabolic panel and hemoglobin A1C were within normal limits. Liver function tests showed mild transaminitis, ALT 46 U/L (10-45 U/L). LT4 was started at 875 mcg per week. After five weeks, her TSH was 6.31 uIU/mL and at seven weeks, the patient was euthyroid with a TSH of 2.53 uIU/mL. Her periods have since normalized.

**Conclusion:** The current discourse on weekly dosing mainly focuses on its use for non-adherent patients. This case provides a clear time course also demonstrating rapid normalization of TSH using weekly dosing. Weekly LT4 dosing as first-line therapy in noncompliant depressed patients with severe hypothyroidism should be considered. Hepp, Z., Wyne, K., Manthena, S., Wang, S. and Gossain, V. (2018). Adherence to thyroid hormone replacement therapy: a retrospective, claims database analysis. *Current Medical Research and Opinion*, 34(9), pp.1673-1678.2.Colucci, P., Yue, C., Ducharme, M. and Benvenega, S. (2010). A Review of the Pharmacokinetics of Levothyroxine for the Treatment of Hypothyroidism. *European Endocrinology*, 9(1), p.40.3.Jayakumari, C., Nair, A., Puthiyaveettil Khadar, J., Das, D., Prasad, N., Jessy, S., Gopi, A. and Guruprasad, P. (2019). Efficacy and Safety of Once-Weekly Thyroxine for Thyroxine-Resistant Hypothyroidism. *Journal of the Endocrine Society*, 3(12), pp.2184-2193.4.Rajput, R. and Pathak, V. (2017). The Effect of Daily versus Weekly Levothyroxine Replacement on Thyroid Function Test in Hypothyroid Patients at a Tertiary Care Centre in Haryana. *European Thyroid Journal*, 6(5), pp.250-254.

**SAT-LB87**

**Thyroid DISORDERS CASE REPORTS II**

**Golimumab Induced Thyroiditis**

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**Background:** Subacute thyroiditis is caused by an inflammation and a destruction of the thyroid cells, leading to hyperthyroidism due to leakage of thyroid hormones, followed by possible hypothyroidism and/or full recovery of thyroid function. This is a case report describing a rare occurrence of drug-induced thyroiditis secondary to golimumab.

**Clinical Case:** A 79-year-old female with HTN, hyperlipidemia, dementia and rheumatoid arthritis was brought to the ER for abnormal behavior including visual hallucinating and insomnia.Initial ER evaluation showed UTI for which antibiotic therapy was initiated. Dementia workup was performed including a negative head CT, nonreactive RPR, and borderline low vitamin B12 level. TPT obtained showed low TSH of 0.2mIU/L, elevated serum FT4 of 1.72ng/ml (n=0.58-1.64ng/ml) and elevated serum FT3 4.38pg/ml (n=2.5-3.9pg/ml), suggestive of hyperthyroidism. The patient reported no heat intolerance, hyperdefecation, or weight changes, but had intermittent palpitations. She denied any history of thyroid problem and did not take thyroid medication, amiodarone, biotin, or any new drug. She reported no fever or URI symptoms within the few weeks prior to admission. In addition to prednisone and methotrexate, she was taking golimumab 50mg every 30 days for the last 22 months for RA. The patient had a family history of hypothyroidism of two daughters and sister. She denied smoking, alcohol, or any other recreational drug use. Her home medications included prednisone 5mg daily, methotrexate, folic acid, lisinopril, simvastatin, and golimumab. On physical examination, she did not appear thyrotoxic and had no exophthalmos, thyroid tenderness, thyroid enlargement or thyroid nodules. Her HR range was 80bpm. Further analysis revealed normal TSI, TPO, and TgAb levels. The thyroglobulin level was very high at 2505ng/ml (n=1.6-59.9ng/ml). Her thyroid sonogram revealed bilateral thyroid nodules, largest at 1.9cm in the right mid pole. A 24-hr RAIU scan showed very low uptake (1.8%) consistent with hypothyroidism. The patient reported no heat intolerance, hyperdefecation, or weight changes, but had intermittent palpitations. She denied any history of thyroid problem and did not take thyroid medication, amiodarone, biotin, or any new drug. She reported no fever or URI symptoms within the few weeks prior to admission. In addition to prednisone and methotrexate, she was taking golimumab 50mg every 30 days for the last 22 months for RA. The patient had a family history of hypothyroidism of two daughters and sister. She denied smoking, alcohol, or any other recreational drug use. Her home medications included prednisone 5mg daily, methotrexate, folic acid, lisinopril, simvastatin, and golimumab. On physical examination, she did not appear thyrotoxic and had no exophthalmos, thyroid tenderness, thyroid enlargement or thyroid nodules. Her HR range was 80bpm. Further analysis revealed normal TSI, TPO, and TgAb levels. The thyroglobulin level was very high at 2505ng/ml (n=1.6-59.9ng/ml). Her thyroid sonogram revealed bilateral thyroid nodules, largest at 1.9cm in the right mid pole. A 24-hr RAIU scan showed very low uptake (1.8%) consistent with thyroiditis (hyperthyroid phase). Endocrinology team did not recommend any antithyroid medications. In addition, she did not warrant NSAIDs or beta blockers as she was not symptomatic or tachycardic. In the absence of an autoimmune or an obvious viral process, her subacute thyroiditis was thought to be induced by golimumab.

**Conclusion:** TNFα inhibitors used to treat chronic inflammatory diseases, have been rarely associated with subacute thyroiditis as described in case reports with adalimumab and....

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etanercept use. We report the first subacute thyroiditis associated with golimumab use. We suggest that drug-induced subacute thyroiditis should be one of the differential diagnoses of thyroid dysfunction in patients treated with golimumab.

Bone and Mineral Metabolism
BONE DISEASE FROM BENCH TO BEDSIDE
Optic Disc Edema in Patients With Craniofacial Fibrous Dysplasia /McCune-Albright
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SUN-LB63
Background: Fibrous Dysplasia (FD) is a mosaic disorder that involves fibro-osseous lesions in bone. In the presence of coexisting extra-skeletal features, it is termed McCune-Albright Syndrome (MAS). Optic disc edema (ODE) is a potentially serious finding that may progress to optic disc ischemia and nerve atrophy. We sought to determine the prevalence and identify risk factors for the development of ODE in the NIH FD/MAS cohort. Methods: A retrospective review was conducted and identified 7 patients with craniofacial FD/MAS with a diagnosis of ODE. Controls were patients with a normal eye examination and without potentially confounding ophthalmologic conditions. The cohort consisted of 73 patients with craniofacial FD, 7 (10%) of whom were diagnosed with ODE. Results: Radiographic and statistical analysis identified Chiari I malformation (CM1) and mass lesions, including aneurismal bone cysts (ABCs) and arachnoid cysts, as significant risks for developing ODE (odds ratio [OR] 48.8; 95% confidence interval [CI], 5.3 to 633.1; p < 0.01) and (OR 16.3; 95% CI, 2.8 to 81.9; p <0.01) respectively. There was no significant association of ODE with endocrinopathies, medications, optic canal diameter or intracranial volume. Conclusion: ODE can be found in association with craniofacial FD and may be the initial presenting symptom of intracranial mass lesions or CM1, which has previously been shown to be at an increased prevalence in the FD/MAS cohort. Patient with craniofacial FD/MAS and intracranial mass lesions or CM1 are at an increased risk of developing ODE and require close monitoring.

Adrenal
ADRENAL PHYSIOLOGY AND DISEASE
ATAC-Seq Reveals Dynamic Changes in Chromatin Accessibility Following PKA Activation in NCI-H295R Adrenocortical Cells
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SUN-LB39
The adrenal cortex is comprised of distinct concentric zones that produce hormones essential for life - the outermost zona glomerulosa (zG) produces aldosterone, and the innermost zona fasciculata (zF) produces cortisol. Adrenal zonation is maintained by a balance between paracrine (Wnt/β-catenin) and endocrine (ACTH/PKA) signaling. Wnt/β-catenin signaling is maintained in the outer cortex (zG, upper zF) by a gradient of Wnt ligands that diminish centripetally, and PKA signaling is maintained in the inner cortex (zF) by ACTH. Recent studies in vivo suggest that sustained PKA signaling promotes zF proliferation, enabling lineage conversion towards zF by inhibiting Wnt/β-catenin transcriptional programming. While these studies were crucial in elucidating mechanisms supporting adrenal zonation, it remains unclear if PKA-mediated repression of Wnt/β-catenin is carried out at the chromatin level or if it is secondary to ligand-dependent modulation of paracrine signaling as may happen in vivo. To address this question, we utilized the adrenocortical cell line (NCI-H295R), which harbors a mutation in CTNNB1 rendering Wnt/β-catenin signaling constitutively active. We stimulated PKA in NCI-H295R using forskolin, and assessed genome-wide chromatin accessibility by ATAC-seq and transcriptome changes by RNA-seq. Motif analysis of ATAC-seq from baseline NCI-H295R revealed that chromatin accessibility is dominated by transcription factors SF1 (master regulator of the adrenal cortex and steroidogenesis), AP1 (effector of PKA) and LEF1 (effector of Wnt/β-catenin). Following forskolin administration, we observed decreased accessibility in chromatin containing LEF1 binding motifs, and increased accessibility in chromatin bearing AP1 and SF1 motifs, suggesting that PKA activation drives AP1/SF1-dependent transcription and inhibits Wnt/β-catenin-dependent transcription at the chromatin level. Indeed, RNA-seq revealed that forskolin administration decreased the expression of zG and Wnt/β-catenin target genes, while simultaneously increasing expression of AP1/SF1 target genes. Collectively, these data demonstrate that PKA activation leads to profound chromatin remodeling that enables zF identity even in the setting of constitutive Wnt/β-catenin signaling. Ongoing studies are aimed at elucidating how chromatin modifiers and transcriptional machinery coordinate the dynamic regulation of differentiation programs required for adrenocortical homeostasis and zonation.

Genetics and Development (including Gene Regulation)
GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I
Frequency and Impact of Mutations in Tumor Suppressor Gene CDC73 in General Population and Malignant Tumors
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SUN-LB132
Background: CDC73 gene is a putative tumor suppressor gene, and somatic and germline mutations of this gene have been linked with parathyroid tumors. There are also some reports suggesting that germline CDC73 mutations may increase risk of jaw, kidney and uterine tumors. However, the