

cessation. Psychiatry determined that the patient's psychosis was not consistent with lamotrigine overdose. Given these recommendations, alternative causes of psychosis were considered. The patient's husband stated she had not taken levothyroxine for over one year. Thyroid function tests revealed a thyroid stimulating hormone (TSH) of 299 mcIU/ml (0.35-5.50 mcIU/ml) with a free thyroxine (T4) level of 0.27 ng/dl (0.89-1.76 ng/gl). The patient was started on levothyroxine intravenously. After five doses of intravenous levothyroxine, her mental status improved to baseline and she was transitioned to oral levothyroxine. She denied that the lamotrigine ingestion was a suicide attempt. Based on the patient's presentation and clinical course, we concluded that her overdose was due to severe hypothyroidism leading to myxedema madness.

Conclusion

Severe hypothyroidism with myxedema coma often presents with depressed mental status, which can manifest as progressive confusion, lethargy, and eventually coma. However, in the case of our patient, severe hypothyroidism presented as psychosis, a rare manifestation. Remarkably, the patient had no other obvious physical manifestations of severe hypothyroidism. Psychosis, though rare, has been seen in cases typically after thyroidectomy or in patients with previously undiagnosed Hashimoto's thyroiditis. In this patient's case, it is likely that her myxedema madness was precipitated by long-term nonadherence with her thyroid replacement therapy, as the patient had no prior psychiatric history. Additionally, her rapid reversal of symptoms after the administration of levothyroxine supports the diagnosis of hypothyroid-induced myxedema madness.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Indiscriminate Thyroid Function Testing on Acute Hospital Admissions Reveals a High Abnormality Rate Requiring Follow Up

Robert P. McEvoy, MB, B Eng, PhD, Anthony O'Riordan, MB, Mark J. Hannon, MB, MSc, MD, FRCPI.

Bantry General Hospital, Cork, Ireland.

SUN-425

The population attending the Medical Assessment Unit at our hospital comprises patients attending electively for investigation and acutely unwell patients presenting for unscheduled care. The standard panel of blood tests taken on arrival includes thyroid function tests (TFTs, i.e. TSH and free-T4), despite a recent review questioning the clinical utility of this practice [1]. We performed a retrospective audit to determine what proportion of our patients had abnormal thyroid function on presentation, and whether these abnormal test results were being followed up.

Using the iSoft Clinical Manager software, a list was generated of all patients who attended the hospital between January 2018 and June 2018 inclusive. For each attendance, we recorded the date, medical record number, patient age, gender, and TFT result. Abnormal TFT results were classified as overt or subclinical hyper- or hypothyroid, or non-thyroid illness syndrome (NTIS), based on their

admission TSH and free-T4. We then examined the hospital and primary care records of patients with abnormal TFTs to determine if they had ongoing thyroid follow up post discharge.

In total, 2,298 patients attended over the 6-month study period. The mean patient age was 67.2 years, and 49% were female. Thyroid function tests were ordered on the day of attendance for 1,688 patients (73%). Of these, 181 results (11%) were abnormal: 20 overt hyperthyroid (11%), 72 subclinical hyperthyroid (40%), 12 overt hypothyroid (7%), 35 subclinical hypothyroid (19%), and 42 NTIS (23%). Twenty of these patients died within 3 months of the abnormal TFT result (4 overt hyperthyroid, 3 subclinical hyperthyroid, 3 overt hypothyroid, 6 subclinical hypothyroid, and 4 NTIS). Of the remaining 161 patients, 74 (46%) had not been followed up within 3 months (4 overt hyperthyroid, 34 subclinical hyperthyroid, 3 overt hypothyroid, 15 subclinical hypothyroid, and 18 NTIS).

The low percentage of abnormal TFTs (11%) in this audit is in keeping with similar studies where thyroid function testing was performed on unselected hospital populations [1]. Subclinical hyperthyroidism was by far the most common abnormality found. A high percentage of abnormal tests (46%) were not followed up, with poor compliance with thyroid management guidelines [2]. Future work will investigate adoption of an 'opt-in' order system [3] and electronic alerts to flag abnormal results for follow-up.

[1] Premawardhana LD. Thyroid testing in acutely ill patients may be an expensive distraction. *Biochemia medica*. 2017; 27(2): 300-307.

[2] Ross DS *et al*. 2016 American Thyroid Association Guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016 Oct; 26(10):1343-1421.

[3] Leis B *et al*. Altering standard admission order sets to promote clinical laboratory stewardship: a cohort quality improvement study. *BMJ Qual Saf*. 2019; 28(10): 846-52.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

A Tale of Two Mutations: Familial Hypocalciuric Hypercalcemia Caused by a Novel CaSR Start Codon Mutation Found in the Setting of a CaSR Hypercalciuric Variant

Sindhura Bandaru, MD, Elaine Michelle Pelley, MD.

University of Wisconsin Hospital and Clinics, Madison, WI, USA.

SAT-350

Background: The calcium-sensing receptor (CaSR) mediates PTH production and renal calcium excretion by sensing circulating calcium levels. Activating mutations in the CaSR can cause a spectrum of phenotypes from overt hypoparathyroidism to isolated hypercalciuria. Inactivating mutations of the CaSR lead to the syndrome of familial hypocalciuric hypercalcemia (FHH) where the protein produced is less sensitive to calcium. A mutation in the start codon of the CaSR leading to FHH has not previously been reported. **Case:** 60-year-old female was seen for evaluation of osteoporosis with lowest T- score of -2.9 at spine. She had no family history of calcium disorders. Biochemical evaluation for secondary etiologies of bone loss

showed persistent PTH-dependent hypercalcemia (with albumin-corrected serum calcium of 10.4-10.8 mg/dl, and PTH 64-78 pg/ml), initially raising suspicion for primary hyperparathyroidism. Subsequent testing showed a low 24-hour urine calcium (82 mg/day) despite adequate daily calcium intake, robust 25-hydroxy vitamin D levels (47 ng/ml), and normal renal function. Calcium/creatinine clearance ratio was low at 0.0064 and FHH was suspected. CaSR gene sequencing revealed two heterozygous abnormalities: (1) a likely pathogenic mutation in the start codon of the CaSR (c.3G>A (p.M1?)) that has not been previously reported (p.M1? indicates that it is not known whether the mutation leads to no CaSR being produced from that allele or if an abnormal protein is produced using an alternate methionine start codon) and (2) a low-prevalence activation mutation variant of the CaSR (p.R990G), which is associated with hypercalciuria and increased risk of kidney stones but generally does not cause hypocalcemia. Genetic testing was unable to determine if these two mutations were on the same (cis) or opposite (trans) alleles. If they are on opposite alleles, the phenotype represents the heterozygous loss-of-function CaSR abnormality with compensation by an activating mutation in the opposite allele. If they are on the same allele, the activating variant is either not expressed at all due to nontranslation or is located on an abnormal/shortened protein. CaSR sequencing of the patient's daughter was normal. In the absence of recombination occurring between the two loci, this strongly suggests the two were on the same allele in this case. **Discussion:** Thus far, > 100 mutations in the CaSR gene causing FHH have been described; but to our knowledge, this case is the first report of a start codon mutation causing FHH. This happened to be identified in the setting of a low-prevalence hypercalciuric variant. Familial testing strongly suggested the two mutations were on the same allele. The activating mutation, therefore, was likely functionally silenced in this case.

Thyroid

THYROID DISORDERS CASE REPORTS II

Conversion of Hashimoto's Thyroiditis to Grave's Disease: A Case Report

Tayba S. Wahedi, MD¹, NAJAH YOUNES DOUBA, MRCP².

¹KING SAUD MEDICAL CITY, RIYADH, Saudi Arabia,

²MINISTRY OF HEALTH, RIYADH, Saudi Arabia.

SAT-497

Conversion of Hashimoto's Thyroiditis to Grave's Disease: A case report

Introduction: Hashimoto's thyroiditis and Grave's disease are common causes for autoimmune thyroid disease. Conversion from Grave's disease to hypothyroidism have been previously reported in literature. But development of Grave's disease after a long standing hypothyroidism rarely occurs. **Case report:** a 22 -year-old Saudi pregnant female patient, was diagnosed with subclinical hypothyroidism with positive anti -thyroid peroxidase antibodies (Anti-TPO) in 2009. She was started on thyroxin and eventually became euthyroid with normal TSH levels till 2016. During subsequent follow-ups, patient was increasingly complaining of palpitations, weight loss and fine tremors.

Thyroid function revealed increasingly suppressed TSH levels and over-replacement was suspected. Thyroxin dose was then gradually reduced and finally stopped for few months. Yet her symptoms persisted. Repeated thyroid function showed suppressed TSH level and elevated T4, T3 levels in keeping with overt hyperthyroidism. Thyroid scan further confirmed the diagnosis with diffuse thyroid uptake suggestive of Grave's disease. Patient was started on medical treatment initially, then successfully treated with radioactive ablation. **Conclusion:** Although it rarely occurs, possibility of conversion from hypothyroidism to hyperthyroidism should always be kept in mind while treating hypothyroid patients with persistent clinical or biochemical evidence of hyperthyroidism despite dose reduction. **References:** [1] McLachlan SM, Rapoport B. Thyrotropin-blocking autoantibodies and thyroid-stimulating autoantibodies: Potential mechanisms involved in the pendulum swinging from hypothyroidism to hyperthyroidism or vice versa. *Thyroid*. 2013;23(1):14-24. [2] Ohye H, Nishihara E, Sasaki I, et al. Four cases of Graves' disease which developed after painful Hashimoto's thyroiditis. *Intern Med*. 2006;45(6):385-9.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Loss of DHEA-Targeting SULT2b1b Sulfotransferase Exacerbates Aggressive Traits of Prostate Cancer

Chung Seog Song, PHD¹, Sulgi Park, MS², Shoulei Jiang, PhD³, Pawel Osmulski, PhD², Brett T. Marck, BS⁴, Alvin M. Matsumoto, MD⁵, Colm Morrissey, PhD⁶, Maria E. Gaczynska, PhD², Elahe A. Mostaghel, MD, PhD⁴, Bandana Chatterjee, BSC,MS,PHD².

¹Univ of Texas Hlth Science Ctr, San Antonio, TX, USA, ²Univ of TX Hlth Sci Ctr, San Antonio, TX, USA, ³University of Texas Health Science Center at San Antonio, San Antonio, TX, USA, ⁴VA Puget Sound Health Care System, Seattle, WA, USA, ⁵VA Puget Sound Hlth Care System, Seattle, WA, USA, ⁶University of Washington, Seattle, WA, USA.

SAT-114

The prostate-expressed sulfotransferase SULT2B1b (SULT2B) regulates intracrine androgen homeostasis by mediating 3β-sulfation of DHEA, thus reducing the precursor pool in the androgen biosynthesis pathway. We explored how loss of SULT2B might influence prostate cancer progression. Results show that SULT2B ablation in castration-resistant prostate cancer (CRPC) cells, generated by stable RNA interference or gene knockout, led to robust activation of the ERK1/2 Map kinase survival signal and induction of epithelial to mesenchymal transition (EMT). EMT activation was concluded on the basis of increased levels of vimentin (a mesenchymal protein) and the EMT-activating transcription factors SNAI1 (Snail) and TWIST1, shown by Western blotting, mass spectrometry and single-cell mass cytometry. Loss of SULT2B was associated with enhanced motility and invasive activity of CRPC cells *in vitro* and their growth escalation *in vivo* as xenografts. Higher invasion and metastasis potential of SULT2B-ablated CRPC cells was further indicated by results that these cells are less adhesive (i.e. easily