Thyroid Storm Followed by ATD Induced Agranulocytosis in Late Pregnancy: A Management Dilemma

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Background: Management of Graves’ disease (GD) in pregnancy presents challenges. Thionamide Antithyroid drugs are the treatment for GD hyperthyroidism with goal of achieving mild but persistent hyperthyroidism and avoiding over-treatment in pregnancy. ATD Induced Agranulocytosis is a rare but serious side effect and presents management dilemmas.

Clinical Case: A 37-year-old woman with history of Graves’ disease was admitted to our hospital at gestational age of 34 weeks with fever, palpitations and diarrhea. Burch-Wartofsky Point Scale was 35 concerning for impending thyroid storm. She had been diagnosed with hyperthyroidism 6 weeks into her pregnancy, initially treated with PTU which was then changed to methimazole in 2nd trimester. A work up for infection and PE was negative. Non-compliance was suspected, methimazole was resumed, and hydrocortisone and propranolol were added. After 2 days, her vital signs and free hormone levels normalized. Her methimazole dose was decreased and she was discharged home in a stable condition.

Five days after her discharge, she presented with sore throat, fever and chills. She had an absolute neutrophil count (ANC) of 0 and a positive rapid strep test. ATD Induced Agranulocytosis was suspected. Her labs showed elevated fT3 of 4.5 (nl 1.7–3.7), normal fT4 and suppressed TSH with <0.01 (nl 0.3–4.9). A CT scan of the neck showed no evidence of retropharyngeal or thyroid abscess. Methimazole was decreased and she was started on glucocorticoids (initially betamethasone for fetal lung maturity, then switched to dexamethasone) for fetal lung maturity, then switched to prednisone) and cholestyramine. She was also started on Cefepime and G-CSF for her neutropenia. A thyroid ultrasound showed enlarged and hypervascular gland. TSI was 157% (nl <122%), and thyroglobulin 155 ng/ml (nl <33 ng/ml). After 4 days, her ANC started to recover. Simultaneously, she started to show worsening thyrotoxicosis but remained hemodynamically stable. A decision to induce labor was then made and was successfully done on the 6th day of her admission. Post-delivery, PTU was started at low dose along with SSKI to prepare her for total thyroidectomy which was done on day 3 post-delivery. Post-thyroidectomy, she had an uncomplicated course and was discharged on levothyroxine. Her child did well with no evidence of thyroid disease.

Conclusion: We present a unique case of thyrotoxicosis in late pregnancy complicated by ATD Induced Agranulocytosis. Given the high risk of thyroid surgery during pregnancy, our multi-disciplinary team approach opted for labor induction, followed by preparation for thyroidectomy and subsequent surgery. Individualization of management approach using a multi-disciplinary team with emphasis on maternal and fetal well-being is of paramount importance with such challenging presentations.

Neuroendocrinology and Pituitary
Case Reports in Secretory Pituitary Pathologies, Their Treatments and Outcomes
A Fierce Presentation of Cushing Disease
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Introduction: Cushing disease refers to the endogenous overproduction of glucocorticoid due to an ACTH-producing pituitary adenoma. It is important to recognize and treat due to the adverse health outcomes associated with it. We describe an unusual case of Cushing disease which presented very rapidly and progressively with extremely high cortisol levels mimicking those seen in ectopic production of ACTH. Case Presentation: A 43 year old Caucasian man, with no past medical history, presented with hypertensive crisis. He was discharged home with anti-hypertensive medications. Over the next 4 months, he gained 20 pounds, mainly around his abdomen, developed fatigue, and blood pressure continued to be high despite six anti-hypertensive medications, developed diabetes and hypokalemia, requiring 120 meq/day of potassium chloride. On exam, he had plethora, central obesity and wide, purple striae over his abdomen. Work-up for secondary causes of hypertension showed normal renal Doppler US, normal aldosterone and renin activity, normal plasma metanephrines, however, his 24 hour urinary free cortisol was dramatically elevated at 4022ug/day with a urine volume of 4 L, 1 mg dexamethasone suppression test showed unsuppressed serum cortisol of 55ug/dl. Morning ACTH of 125 pg/ml with concurrent serum cortisol level of 53.8 mcg/dl, indicated ACTH-dependent hypercortisolism. Inferior petrosal sinus sampling indicated a pituitary source of ACTH. Sellar MRI initially did not show a pituitary adenoma, however, repeat MRI with a 3-Tesla magnet showed a 4 mm pituitary adenoma. He was treated with ketoconazole and was started on atovacuone for PCP prophylaxis while awaiting trans-sphenoidal resection, which he had a month later. Pathology showed a 4 mm adenoma which stained strongly for ACTH. On postoperative day 1, serum cortisol dropped to 2.1 from 52.3 mcg/dl, and patient was discharged on hydrocortisone replacement. Three weeks later, he had lost 12 pounds, hyperglycemia improved with discontinuation of insulin, hypokalemia resolved and hypertension was well controlled on two anti-hypertensives. Discussion: ACTH-dependent Cushing syndrome is either caused by Cushing disease, or from ectopic ACTH production from a tumor.

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Cushing disease is characterized by a gradual onset and subtle manifestations of hypercortisolism. Acute, severe presentation favors an ectopic ACTH producing tumor, and is associated with much higher cortisol levels. In our patient, clinical data suggested ectopic ACTH production, yet he was found to have Cushing disease, and was treated successfully with trans-sphenoidal resection of the pituitary adenoma. It is imperative to consider all possibilities, and do the full work up so as not to miss an atypical presentation of Cushing disease, and direct treatment accordingly.

**Cardiovascular Endocrinology**

**HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS II**

**Effect of Testosterone Replacement Therapy Added to Intensive Lifestyle Intervention in Frail, Older Male Veterans with Hypogonadism and Obesity: A Randomized Clinical Trial**

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**SUN-541**

**Background**

Both hypogonadism and obesity are common in older men which additively exacerbate their age-related decline in physical function resulting in frailty. However, the appropriate treatment approach for frail, older men with hypogonadism and obesity is still controversial.

**Methods**

In this randomized, comparative efficacy, double-blinded, placebo-controlled (for testosterone) trial, we examined the effect of 6-months: 1) lifestyle therapy (diet-induced weight loss and supervised aerobic and resistance exercise training) + testosterone replacement therapy (LT+Test) vs. 2) lifestyle therapy + placebo (LT+Pbo) in 83 older (age≥65 years) male veterans with obesity (BMI≥30 kg/m²) and evidence of persistently low AM serum testosterone (<300 ng/dl) associated with physical frailty. The primary outcome was change in score in the modified Physical Performance Test (PPT).

Secondary outcomes included other frailty measures, body composition, bone mineral density, and physical functions.

**Results**

In the intention-to-treat analysis, the score in the PPT increased similarly in the LT+Test group and LT+Pbo (increase from baseline of 17% vs. 17%, respectively; P=0.78 for between-group comparison). Peak oxygen consumption ($VO_2_{peak}$) increased more in the LT+Test group than in the LT+Pbo group (increase of 23% vs. 16%, respectively; P=0.04). Moreover, despite equivalent weight loss between groups (both groups lost 9% of body weight from baseline), lean body mass decreased less in the LT+Test group than in LT+Pbo group (-1.8% vs. -3.5%, respectively; P=0.02). Likewise, bone mineral density at the total hip was relatively preserved in the LT+Test group compared to the LT+Pbo group (+0.5% vs. -1.1%; respectively; P<0.01). Knee extension and flexion strength assessed by isokinetic dynamometry increased similarly in the LT+Test group and LT+Pbo group (increase of 17 and 25% vs. 18 and 27%, respectively; P=0.89 to 0.99). Both hematocrit and PSA increased more in the LT+Test group than in the LT+Pbo group (increases of 5% vs. 1% and 45% vs. 0.1%, respectively while HDLc decreased less (increase of 0.5% vs. 13%, respectively) (P<0.001 to 0.01 for all comparisons). Total testosterone levels measured by LC-MS increased more in the LT+Test group than in the LT+Pbo group (125% increase [from 222 ng/dl to 546 ng/dl] vs. 19% increase [from 247 ng/dl to 335 ng/dl], respectively; P<0.001).

**Conclusions**

In older men with hypogonadism and obesity associated with frailty, testosterone replacement therapy significantly augments the increase in endurance capacity in response to lifestyle intervention with diet and regular exercise and helps to preserve muscle and bone mass during weight loss. However, testosterone replacement therapy does not lead to greater amelioration of frailty than in response to intensive lifestyle intervention alone in this population.

**Pediatric Endocrinology**

**PEDIATRIC OBESITY, THYROID, AND CANCER**

**The Neonatal Screen That Cried Wolff**

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**MON-082**

**Introduction:**

Hypothyroidism is one of the major causes of preventable mental retardation. Neonatal screening aids in the prompt diagnosis of newborns with congenital hypothyroidism. There are other clinical conditions that can alter thyroid function during the newborn period, including exposure of high iodine concentrations.

**Case Presentation:**

One day old female born at 37 3/7 weeks of gestational age by C-section with imperforated anus and congenital heart disease was transferred to our children’s hospital within the first day of life for a hybrid cardiac procedure of bilateral pulmonary artery banding and PDA stenting. She had an Illinois Neonatal screen done at 36 hours of life that was normal. Her cardiac surgery was performed at 10 days of life, where she was exposed to iodine products transdermally. At 14 days of age, she had a repeat Illinois Neonatal screen that was positive for congenital hypothyroidism with a TSH of 78 mU/mL (normal < 20 mU/mL) and reflex total T4 of 5.4ug/dL (normal > 8ug/dL). No family history of thyroid disease; mother was healthy during pregnancy and was not on medications that could affect baby’s thyroid function. Subsequent serum laboratory testing confirmed a TSH of 74.3mU/mL and Free T4 of 0.6ng/dL. Patient was diagnosed with Wolff-Chaikoff effect, which is the phenomenon of transient hypothyroidism caused by exposure to high doses of iodine (iodine containing contrast agents or topical antiseptics). Pediatric