Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Anti-thyroid Drug Response in Graves’ Disease: Predictors of Biochemically Persistent Disease

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SAT-423
Introduction: Anti-thyroid Drugs (ATD) have become the most frequently used treatment for Graves’ disease (GD) in the United States. However, the response to this therapy is variable. Factors that predict biochemically responsive vs. biochemically persistent disease remain unknown. Identifying predictors of disease poorly responsive to ATD can help guide treatment decision making, follow up planning and prognosis.

Methods: From a database of patients with GD treated with ATD and receiving care at an academic medical center between 2009–2019, we selected adults with incident GD treated with ≥14 days of ATD.

Results: 172 patients (from a database of 730 patients with GD on ATD) were sampled for the purpose of this pilot and 97 of these met inclusion criteria. Patients had a median age of 50 (18–90); female, 70.1%; never smokers, 64.9%; median goiter size of 40 g (15–100); and median TRab on presentation of 8.1 mIU/L (1.0–60). Graves’ orbitopathy (GO) was present in 13.4% at baseline. Patients (100%) were started on methimazole at a median dose of 20 mg (2.5–60). The median time from presentation until biochemical improvement (defined as the first instance of FT4 ≤1.7 ng/dL) was 120.9 days (18–1525), and to biochemical euthyroidism (normal TSH & FT4) was 251 days (41–1259) including a median of 3 (0–17) dose adjustments. In a univariate analysis, response to ATD was divided into two groups; biochemically responsive and biochemically persistent disease (based on reaching biochemical improvement in ≤6 months, or >6 months respectively). Biochemically persistent disease was more common in those with GO at presentation (38.5% vs.11.1%) (p .024). There was a trend towards greater prevalence of biochemically persistent disease in those with TRAb ≥ 8.0 mIU/L (46.2% vs. 27.8%) (p .204), and goiter estimated 30 grams or above by physical examination (30.8% vs. 19.4%) (p .460). Biochemically responsive disease was associated with higher frequency of hypothyroidism during treatment (p .047).

Conclusion: Our preliminary results illustrate the spectrum of response to ATD and predictors of biochemically persistent disease. We aim to expand this analysis utilizing a large database. As use of ATD increases, clinicians and patients can apply this data to estimate response to therapy, and identify patients that may require more aggressive therapy, thereby tailoring management plans.

Thyroid

THYROID DISORDERS CASE REPORTS I

A Case of Thyroid Storm with Systemic Thromboembolism

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SUN-498
Background
Thyroid storm is a rare but potentially life-threatening complication of hyperthyroidism. Whilst a thyroid storm is known to be a hypercoagulable state, it remains unclear if routine anticoagulation should be initiated, especially in the absence of atrial fibrillation.

Case presentation
A 22-year-old seaman presented to Accident and Emergency Department with a history of severe generalized abdominal pain and vomiting for 9 days. He was previously well with no significant past medical history. On examination, he appeared very anxious and agitated. He had sinus tachycardia (170 beats/min), was normotensive (Blood pressure 116/90 mmHg). He had exophthalmos, lid lag, a diffusely enlarged goiter with bruit and fine tremors on outstretched hands. There was generalized abdominal tenderness with guarding and sluggish bowel sounds. Electrocardiogram confirmed sinus tachycardia. Laboratory results showed primary hyperthyroidism [Free T4 66.2 (0.8–14.4 pmol/L), TSH <0.010 (0.65–3.70 MU/L)]. TSH Receptor Antibody was elevated at 6.23 IU/L (<1.76 IU/L), consistent with Graves’ Disease. He had acute renal impairment [urea 10.8 (2.7–6.9 mmol/l), creatinine 221 (54–101 umol/l)]. Burch & Wartofsky score was 60. Treatment with rectal propylthiouracil (PTU), i.v sodium iodide and i.v hydrocortisone were initiated.

An initial CT Abdomen on Day 1 of admission demonstrated a long segment of jejunitis and marked distension of the duodenum, stomach and oesophagus. 4 days later, fT3 and fT4 levels had improved as did tachycardia and his confusion state, yet he remained febrile. Blood and urine cultures did not reveal any causative organisms. A contrast-enhanced CT revealed extensive thrombosises of the portal, superior mesenteric, right external iliac, common femoral veins with left lower lobe pulmonary embolism. Thombohilia screen was normal. He was given low-molecular-weight heparin and required total parenteral nutrition in view of prolonged bowel ileus from mesenteric ischaemia. Rectal PTU was continued to treat thyrotoxicosis. He made sufficient progress with improvement of the bowel ileus with s.c enoxaparin and was discharged 6 weeks later on oral carbimazole (on discharge: fT4 10pmol/L, TSH<0.010). However, due to extensive thrombosises within the mesenteric venous system and consequent ischaemic jejunitis, he required a jejunectomy eventually 2 weeks later. Radioiodine ablation was subsequently given and he is currently hypothyroid requiring thyroxine replacement.

Conclusion
Extensive systemic thromboembolism may occur in the setting of a thyroid storm. Routine prophylactic
anticoagulation should be considered, even in the absence of atrial fibrillation.

References
1. Lin HC et al. Journal of Thrombosis and Haemostasis 2010, 8: 2176–2181
2. Koitte et al. Thromb Haemost 2012; 107: 417–422
3. Franchini et al. Clinical and Applied Thrombosis 2010, 17(4) 387–392

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORTS I
A Bone to Pick with FGF23
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SAT-362
A 48 yo M with a past medical history of bilateral femoral neck stress fractures at age 44 status post closed reduction percutaneous pinning (CRPP) presented to the emergency room with bilateral lower extremity pain after a ground level fall. Plain films were notable for a right intertrochanteric fracture and left hip nonunion. The patient underwent removal of right CRPP hardware and revision fixation with a short TFN-Advanced Femoral Nailing System (TFNA) and fixation of the left femoral neck nonunion. Given his injuries following a ground level fall, endocrinology was consulted for recommendations for his hospital course. Labs during his hospital course were notable for hypophosphatemia as well as normal levels of alkaline phosphatase, serum calcium, and PTH. Serum protein electrophoresis and urine protein electrophoresis were within normal limits. A 24-hour urine calcium and phosphorous were done and the patient was found to have a low calculated renal phosphate threshold (TmP04/GFR), concerning for hypophosphatemic osteomalacia. An FGF23 level was drawn and was elevated, suggestive of an FGF23-induced hypophosphatemic osteomalacia. A low vitamin D 1,25-OH was also found consistent with this process, given interference of alpha-hydroxylation of vitamin D 25-OH from FGF23. The patient therefore underwent a PET scan to rule out a mesenchymal tumor-induced osteomalacia but his PET scan was largely unremarkable. Given that there were no issues with bone development or fractures during childhood, the suspicion for X-linked hypophosphatemia or autosomal recessive hypophosphatemia was low. The patient was believed to have either a small mesenchymal tumor not seen on PET scan or an autosomal dominant hypophosphatemia, which can manifest clinically during adulthood, and so was treated with daily Calcitriol and phosphate with subsequent correction of his serum phosphorous. Such a delayed presentation of hereditary hypophosphatemic osteomalacia, however, has been reported only in women either soon after puberty, during pregnancy, or after delivery (1). This case thus represents a possible autosomal dominant hypophosphatemia in a male patient or a rare case of tumor-induced hypophosphatemic osteomalacia.

Reference: (1) Drezner MK, Whyte MP. Heritable renal phosphate wasting disorders. Genetics of bone biology and skeletal disease, 2nd ed. 2018; 761–782.

Diabetes Mellitus and Glucose Metabolism
DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS
Body Weight and Body Composition in Patients with Chronic Pancreatitis Are Associated with Islet Function After Total Pancreatectomy and Islet Cell Transplantation
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SUN-621
Background: Total pancreatectomy with islet autotransplant (TPIAT) is done in patients with chronic pancreatitis to treat intractable pain. In TPIAT, islets are isolated after pancreatectomy and infused into the liver via the portal vein to mitigate post-operative diabetes. Outcomes vary, with ≥60% needing exogenous insulin supplementation to maintain normoglycemia. The current study’s aim was to determine if pre-surgical body composition is associated with islet function and insulin sensitivity after TPIAT.
Methods: We characterized body weight and composition as related to insulin sensitivity and dependence and diabetes outcome in 88 adults who underwent TPIAT for chronic pancreatitis at the University of Minnesota. At baseline, 12 and 18 months after TPIAT, insulin independence was assessed; metabolic testing used mixed meal tolerance testing and frequent sample intravenous glucose tolerance testing. Body composition was measured by Dual X-ray absorptiometry (DXA). Statistical analyses used linear and logistic regression.
Results: At baseline, mean age was 39.9 (SD 11.1) years. 9.1% were underweight (BMI<18.5 kg/m²), 45.5% normal weight (BMI=18.5–24.9), 22.7% overweight (BMI=25–29.9) and 22.7% obese (BMI≥30). Islet equivalent per kg did not differ between body weight categories (p=0.17). Overweight/obese patients had higher peak and AUC c-peptide and lower insulin sensitivity index, as expected. Compared to baseline, android to gynoid fat ratio was lower at 12 (0.80 vs 0.88; p=0.012) and 18 months (0.81 vs 0.88; p=0.041), and lean mass was lower at 18 months (38848 vs 42338 kg; p=0.029).
Baseline body weight was positively associated with acute insulin response to glucose (AIRg) at 12 months (effect size 38.5, SE 17.1 mU/L/min; p=0.029) and 18 months (38.3, SE 18.5 mU/L/min; p=0.045), while baseline lean mass was inversely associated with AIRg at 12 (p=0.01) and 18 months (p=0.033). Baseline body weight was positively associated, and fat mass inversely associated with disposition index (Di; islets’ ability to secrete insulin normalized to insulin resistance) at 18 months (p=0.019 for both).
Percent body fat and percent gynoid fat predicted Sg (glucose effectiveness index, i.e., ability of glucose to promote its own disposal and inhibit hepatic glucose production absent an incremental insulin effect) at 18 months (p=0.042 and p=0.019, respectively). Insulin independence at 12 and 18 months was not significantly associated with baseline body weight or body composition.
Conclusions: Overweight/obesity is common in patients with chronic pancreatitis. After TPIAT, patients had lower muscle mass and A/G ratio. Preoperative body weight and