SAT-499

Background

Myxedema coma is a life-threatening decompensated form of hypothyroidism. Current treatment recommendation is intravenous levothyroxine. However, in areas where parenteral form of levothyroxine is unavailable, levothyroxine tablet is the only option.

Clinical Case

A 48-year old male known to have chronic glomerulonephritis and hypertension, came in due to lacerated scalp wound sustained after falling asleep. Pertinent laboratory exams showed mild anemia, hemoglobin 10.6 g/dL (reference range 13–17) and hyponatremia 128 mmol/L (reference range 136–145). His estimated creatinine clearance was 60 mL/min. Cranial CT scan showed no signs of acute hemorrhage or fracture. There was scalp swelling and laceration with subgaleal hematoma over the frontal region.

Electrocardiogram showed low voltage complexes. Chest radiograph showed an enlarged cardiac silhouette suggesting pericardial effusion. Transthoracic echocardiography was requested revealing a massive pericardial effusion with tamponade physiology. Patient underwent emergency pericardial window with pericardiostomy tube placement, debridement and suturing of scalp laceration under general anesthesia. He was able to tolerate the procedure well but noted to have decreased sensorium post-operatively. ABG revealed respiratory acidosis with pH 6.9 and incaulcable pCO2. He was subsequently intubated. Further laboratory investigations showed undetected FT4 0.0ng/dL (reference range 0.58–1.64) and elevated TSH 23.87 µIU/mL (reference range 0.38–5.33). Anti-TPO was elevated 333 µIU/ml (reference range 0.58–1.64) and elevated TSH 23.87 µIU/mL (reference range 0.38–5.33). His estimated creatinine clearance was 60 mL/min. Cranial CT scan showed no signs of acute hemorrhage or fracture. There was scalp swelling and laceration with subgaleal hematoma over the frontal region.

Diabetes Mellitus and Glucose Metabolism

ISLETS, LIVERS, PLACENTA, AND VASCULARITY — THE MULTITISSUE IMPACT OF DIABETES

Hepatocyte Peroxisome Proliferator-Activated Receptor Gamma (PPARG) Offsets the Antisteatogenic Effects of Thiazolidinediones in Obese Male Mice

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OR14-05

Pparg is a nuclear receptor that regulates glucose and lipid metabolism. Thiazolidinediones (TZD) are PPARG agonists that may reduce hepatic steatosis through their effects in adipose tissue. However, some studies suggest that expression and activation of hepatocyte Pparg may exacerbate steatosis. In this study, we have assessed the relevance of hepatocyte Pparg, and its TZD-mediated activation in the development and/or reduction of steatosis, with adult-onset hepatocyte-specific Pparg knockout (PpargΔHep) mice. We reported that a single iv injection of AAV8-TBG-Cre in Pparg-floxed mice, knocked out hepatocyte Pparg expression (PpargΔHep mice), and that prevented diet-induced steatosis. In this study, a group of 5 wk-old Pparg-floxed mice were fed a low fat (LF) or a high fat (HF) diet for 7 weeks before generating control and PpargΔHep mice. Then, half of the HF-fed mice in each group were switched to a HF diet supplemented with the TZD Rosiglitazone maleate, for 5 weeks. HF diet induced mild obesity (36.8 +/- 1.4 g of body weight [BW]), while TZD slightly increased BW (41.3 +/- 1.3 g) and insulin sensitivity. Liver weight was not altered in HF-fed mice with or without TZD, and we did not observe any effect induced by PpargΔHep. Due to the mild phenotype observed in this cohort, we generated a 2nd cohort adjusting for age and length of diet. Briefly, 10 wk-old Pparg-floxed mice were fed a LF or HF diet for 16 weeks before generating control and PpargΔHep mice. Then, half of the HF-fed mice in each group were switched to a HF diet supplemented with Rosiglitazone maleate for 7 weeks. In this group of mice, HF diet induced obesity (50.1 +/- 1.05 g BW), and increased liver weight independent of hepatic Pparg expression. TZD treatment exacerbated obesity (62.4 +/- 1.2 g BW) and adiposity, but increased insulin sensitivity as compared to mice fed a HF diet without TZD. Interestingly, PpargΔHep mice fed a HF diet with TZD showed enlarged subcutaneous white and brown adipose tissue weight, and a dramatic reduction in liver weight and steatosis as compared to obese control mice treated with TZD. The expression of hepatic Cd36, Cidea, Cidec, and Fabp4 was increased by TZD in a Pparg-dependent manner in HF-fed mice. Altogether, this data suggest that hepatocyte Pparg expression may offset the antisteatogenic actions of TZD in mice with severe obesity. In obese and insulin resistant individuals, TZD-mediated activation of hepatocyte Pparg may exacerbate steatosis.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Bone Health Outcomes in a Large, Diverse Pediatric Cohort Undergoing Hematopoietic Stem Cell Transplant

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SUN-065

Background: Impaired bone mineral density (BMD) is a known complication of hematopoietic stem cell transplantation (HSCT)
in adults and may lead to increased fracture risk. Little is known in pediatrics about the risks for impaired BMD and fragility (low trauma) fractures after HSCT. Factors that may influence the risk of bone disease include underlying diagnosis, glucocorticoid exposure, and HSCT complications (e.g. graft versus host disease (GVHD)). Our study aims to describe the incidence of fragility fractures in a large diverse pediatric HSCT population and to identify risk factors of both fracture and impaired BMD.

Methods:
We reviewed the records of 237 patients (age ≤ 21 years at time of transplant) who underwent HSCT at our institution between January 2015 and March 2018. The primary endpoint was incidence of fragility fractures and the secondary endpoint was assessment of BMD on dual-energy X-ray absorptiometry (DXA). We analyzed DXA results at one-year post-HSCT in 72 out of 206 patients alive at 1 year.

Results:
There were 25/237 (10.5%) patients with evidence of fragility fracture on x-ray. Of those, 18/25 (72%) were spine fractures. For patients who had fractures, median time to fracture was 5.9 months after BMT. Mortality at one-year was proportionally higher, though not significant (p=0.11) in patients who had at least one fragility fracture (24%; 6/25) compared to patients without fragility fracture (12%; 25/212). Vitamin D status at one-year post transplant was sufficient (>20ng/mL) in 94% (160/171) of patients measured. There was no difference in incidence of fracture between vitamin D sufficient and insufficient patients. The median height-for-age adjusted Z-score (HAZ) for spine BMD at one-year post transplant was 0.13 in all patients. The median HAZ spine BMD Z-score in patients with fragility fracture was -1.64, though data was available for only 5 patients.

Conclusions:
The incidence of fragility fractures, especially vertebral compression fractures, after pediatric HSCT is striking and is higher than in adult populations. Furthermore, there are likely additional asymptomatic patients with occult fractures not detected in out cohort. Additional analysis will assess the associations between underlying medical diagnosis, GVHD, and chronic glucocorticoid exposure on fragility fracture risk. The high incidence of fragility fractures seen in this study advocates for establishing bone health screening protocols with attention toward spinal imaging in pediatric patients undergoing HSCT.

Thyroid
THYROID NEOPLASIA AND CANCER

ATA and ACR TIRADS Classification Systems as Additional Predictors of Malignancy in Afirma GSC Suspicious Thyroid Nodules

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MON-525
Objective: Evaluation and management of thyroid nodules with cytologically indeterminate results remain challenging in clinical practice. Despite the implementation of molecular testing in an attempt to avoid surgical intervention, diagnostic thyroidectomy still occurs due to the relatively low positive predictive value of these molecular testing. We conducted a study to analyze whether combining US characteristics and results of molecular testing would better elucidate predicting true positive results.

Methods: We retrospectively reviewed thyroid ultrasound images of 172 nodules in 162 patients (mean age, 55 years +/- 14) with indeterminate cytology results (Bethesda III and IV) that underwent Afirma Gene Sequencing Classifier (GSC) testing at a single academic medical center between 2017–2019. All nodules were classified according to 2015 American Thyroid Association (ATA) and 2017 American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS).

Results: A total of 172 with subsequent Afirma GSC molecular testing were included in the study. There were 127 nodules with Bethesda III (AUS/FLUS) (73.8%), and 45 nodules with Bethesda IV (SFN/HCN) (26.2%) results. The mean nodule volume was 5.4 +/- 10 cm³. Afirma GSC identified 129 nodules (75%) as benign and 43 nodules (25%) as suspicious. Per ATA classification, 10.4% (19) of nodules were classified as very low risk, 36.5% (62) as intermediate and 12.8% (22) as high risk for malignancy. There was a significant association between ATA classification and Afirma benign nodules (P=0.002). All nodules were also classified per TIRADS system with the following distribution: 5 (1.16%) TIRADS 1, 7 (4%) TIRADS 2, 54 (31%) TIRADS 3, 90 (52%) TIRADS 4, and 16 (9.3%) TIRADS 5. We did not observe the similar association between TIRADS system and benign nodules as we did with ATA classification (P=0.4).

35 patients (79.5%) with Afirma suspicious results underwent surgery, of which 18 (51.4%) surgical pathology were malignant. 8 patients with Afirma suspicious results decided to proceed with ultrasound surveillance. The malignancy rates of nodules with low, intermediate and high suspicion for malignancy classified by the ATA guidelines were 44% (9 of 18), 33% (56 of 18) and 22% (4 of 18). The malignancy rates of TIRADS category 3, 4 and 5 nodules were 44% (8 of 18 nodules), 44% (8 of 18 nodules) and 11% (2 of 18 nodules). Subset analysis of surgical pathology benign and cancerous nodules did not show significant association between ATA (P=0.5) or TIRADS (P=0.4) classification systems.

Conclusion: Our study showed that Afirma benign nodules were associated with a lower risk of malignancy per ATA classification but not with TIRADS system. We did not find a significant association between pathology proven cancer cases and high-risk ATA or TIRADS ultrasound classification systems.

Steroid Hormones and Receptors
STEROID BIOLOGY AND ACTION

Common Genetic Variants Associated with SERPINA6 Expression in Liver Influence Cortisol-Responsive Transcriptional Networks in Human Adipose Tissue

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