SUN-182

Introduction: Adrenocortical carcinoma is a rare and highly aggressive malignancy with an incidence rate of 1-2 per million population per year. It is an aggressive tumor with early metastasis to lungs, liver, bone and lymph nodes. Venous tumor thrombosis to inferior venacava (IVC), atrium or ventricle is rare and is considered as a tumor extension instead of metastatic disease, but with a poor prognostic outcome.

Clinical Case: We present a rare case of adrenocortical carcinoma with tumor extension into the IVC, right atrium and right ventricle. A 62-year-old female with history of breast cancer on anastrozole presented to the clinic for a routine screening colonoscopy. Patient was noted to have uncontrolled hypertension before the procedure, so was sent to the ER. Upon further interviewing she complained of increasing abdominal distension, hirsutism, and bilateral lower extremity swelling over the past six months. CT abdomen revealed a large 10 x11 x13 cm heterogeneously enhancing mass arising above the right kidney, with extensive tumor extension into the IVC, right atrium and right ventricle. MRI too characterized a large mass in the right adrenal gland with tumor thrombus extension into the IVC, right atrium, and right ventricle. Hormonal studies demonstrated elevated cortisol, dehydroepiandrosterone-sulfate and testosterone levels. A 1 mg dexamethasone suppression test inadequately suppressed cortisol levels, consistent with Cushing's syndrome due to endogenous over secretion of cortisol. Free plasma and urine metanephrine levels were normal. Plasma renin and aldosterone concentration were within normal limits. With the cooperation of a multidisciplinary team, patient underwent right adrenalectomy with removal of tumor thrombus from right atrium and right ventricle under cardiopulmonary bypass. Surgical pathology confirmed adrenocortical carcinoma. She was started on mitotane as adjuvant therapy. Patient was also noted to have a lung nodule with biopsy showing oncocytic neoplasm favoring metastasis from adrenal cortex. She did receive chemotherapy for the lung metastasis with decrease in the size of the nodule.

Conclusion: Adrenal cortical carcinoma is a rare disease and the venous tumor thrombus to IVC, atrium and ventricle is even rarer and has a poor prognostic outcome. Complete tumor resection is the only curative approach with adjuvant therapies aiming to decrease the risk of recurrence only. Due to the aggressive nature of the tumor and quick development of metastasis, early diagnosis gives the best chance of resection and hence the greatest chances of survival.

Diabetes Mellitus and Glucose Metabolism

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

The Transcriptional Coactivation Function of EHMT2 Restricts Chronic Glucocorticoid Exposure Induced Insulin Resistance

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OR14-03

Glucocorticoids are required for metabolic adaptations during times of stress. However, chronic glucocorticoid exposure is associated with metabolic disorders such as insulin resistance. Glucocorticoids mainly convey their signals through an intracellular glucocorticoid receptor (GR). GR is a transcription factor that requires interactions with transcriptional coregulators to modulate the transcription of GR primary target genes, which in turn regulate specific aspects of physiology. Euchromatic Histone Methyltransferase 2 (Ehmt2) is a transcriptional coregulator for GR that can act as a corepressor or a coactivator. We found that glucocorticoid-induced insulin resistance was exacerbated when Ehmt2 levels were reduced in the liver. Intriguingly, this phenotype resulted from the transactivation function of Ehmt2. This is because a mutation at the lysine 182 automethylation site, which is required for the coactivation but not the corepression function of Ehmt2, results in similar exacerbated GC-induced insulin resistance. These results suggest that Ehmt2 coactivation dependent GR primary target genes restrict the extent of glucocorticoid-induced insulin resistance. Gene expression analysis identified *Dusp4* (a.k.a. *Mkp-2*) as an Ehmt2 coactivation dependent GR-activated gene, which when overexpressed in liver, attenuated glucocorticoid-induced insulin resistance. Thus, we have identified a novel GR-Ehmt2-Dusp4 axis that plays a key role in controlling the extent of the development of insulin resistance. Notably, the classical view of how GC induce hepatic insulin resistance is that GR activates genes that inhibit insulin signaling and enhance hepatic gluconeogenesis. Our study, however, provides a revolutionary concept in which the extent of GC-induced insulin resistance is controlled by the balance of GR-activated genes that promote insulin sensitivity or insulin resistance.

Neuroendocrinology and Pituitary

NEUROENDOCRINE & PITUITARY PATHOLOGIES

The Effects of Traumatic Brain Injury on Pituitary Function: A Systematic Review and Meta-Analysis

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SUN-294

Background: The impact of traumatic brain injury (TBI) on pituitary function remains unclear. Yet, applying appropriate diagnostic and treatment strategies for affected patients is crucial for mitigating morbidity related to hypopituitarism and improving patient outcomes. Currently, data regarding the prevalence of post-TBI hypopituitarism and its predisposing factors are inconsistent. The goals of this systematic review and meta-analysis were to evaluate the prevalence of acute and chronic post-TBI hypopituitarism and assess for predictors of pituitary dysfunction.

Methods: Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid

Cochrane Database of Systematic Reviews, Scopus, Web of Science, and references of key articles were searched from inception to 2019. Studies enrolling ≥20 adult patients with TBI and reporting on pituitary dysfunction were included. A total of 992 studies were generated by the initial search. Titles and abstracts were screened in duplicate by two independent reviewers for inclusion criteria. Of these, 265 full text manuscripts were subsequently reviewed for eligibility. Predefined data were extracted from 14 representative studies for the preliminary analysis (7 cross-sectional studies, 6 prospective studies, and 1 retrospective study).

Results: There was a total of 813 (78% male) patients with TBI. Of those with available data, 124/248 (50.0%) had mild TBI, 112/476 (23.5%) had moderate TBI, and 308/569 (54.1%) had severe TBI. Mean age at TBI diagnosis was 34.2±4.6 years, with time to evaluation of pituitary function following TBI ranging from 0 days to 120 months (mean, 27.1±35.1 months). Acute and chronic hypopituitarism was reported in 10.7% and 19.6% of patients, respectively. TBI was associated with increased risk for hypopituitarism compared to the general population (RR=765.8, 95% CI 538.8-1088.5). Secondary hypogonadism was noted in 15.7% of patients, growth hormone deficiency in 15.7%, secondary adrenal insufficiency in 11.6%, secondary hypothyroidism in 8.7%, and diabetes insipidus in 0.2%. Older age (40.4±5.5 vs 36.7±1.0 years, P<0.0001) and higher BMI (25.0±0.7 vs 23.9±0.2 kg/m^2, P<0.0001) were associated with increased risk of post-TBI hypopituitarism.

Conclusion: Available moderate- to low-quality evidence suggests that post-TBI hypopituitarism is common and correlates with older age and higher BMI. Secondary hypogonadism and growth hormone deficiency are the most predominant pituitary deficiencies. Further investigations are warranted to

determine the most effective strategies for identifying patients at risk for post-TBI hypopituitarism in order to implement prompt assessment and management.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS I

Autosomal Dominant Hypophosphatemic Rickets in Premature Twins Resolved with Iron Supplementation

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SAT-056

Introduction

Autosomal dominant hypophosphatemic rickets (ADHR) is a condition with variable phenotype in terms of age of presentation, severity, and possible resolution. ADHR is caused by mutations of *FGF23*, preventing its cleavage, producing high levels of FGF23, which leads to renal phosphate wasting. Studies in mice and adult humans, have shown a correlation between low iron levels and increased FGF23 levels. To our knowledge, three pediatric patients with ADHR resolved with iron supplementation have been reported in the literature.

Clinical case

We report on identical twins born at 28 weeks and 5 days by cesarean section due to premature rupture of membranes with complicated pregnancy due to twin-to-twin transfusion syndrome. Birth weights were 780 grams (2nd percentile) for twin A, 1,200 grams (50th percentile) for twin B. Hypophosphatemia was documented starting at 2 weeks of life and during the first 6 of months of life, with phosphorus levels between 2.9-3.9 mg/dL for twin A and between 2.4-5.1 mg/dL for twin B.

During their NICU admission phosphorus had a positive relationship with the hemoglobin level, which was more severe on twin A. Both were treated with calcitriol and a low dose of phosphorus starting on their 2nd month of life.

At 6 months of age, both had persistent hypophosphatemia, more prominently in twin A (2.7mg/dL) with high alkaline phosphatase (1,209 IU/L) and high FGF23 (343 RU/dL). At that time his hemoglobin was 9.8 g/dL and his hematocrit was 29.5%. Both were started on Polyvisol with iron.

At 14 months of life phosphorus and calcium were within normal limits, therefore calcitriol and phosphate were discontinued. At 15 months of age their hemoglobin, hematocrit, iron level, and TIBC levels were normal for both twins. Phosphorus was 4.6 and 4.3 mg/dL, alkaline phosphatase reduced significantly to 819 and 413IU/L, and FGF23 normalized to 100 RU/dL and 32 RU/dL on twin A and B respectively.

Upon physical examination at 15 months of age, twin A was at the 0.02% for length and weight/length at the 31%; twin B was at the 5% for length and weight/length at the 50%. Both twins had high arched palates. Twin A had craniosynostosis, left renal agenesis, bilateral epicanthal folds, overlapping 2nd toes, and clinodactyly of the fifth digits. Note the donor kid (twin A) had a more severe presentation.

Genetic testing showed heterozygous mutation c536G>a (p.Arg179GLN) in the *FGF23* gene. This is the same mutation previously reported to be related with ADHR resolved with iron supplementation

Conclusion

The study of patients with hypophosphatemia and hypophosphaturia should include evaluation of iron status (ferritin, TIBC). Treating iron deficiency on these patients might normalize phosphate levels. This would avoid cumbersome treatment with phosphate and calcitriol.

Laboratory values

Phosphorus:4-8 mg/dL

Alkaline Phosphatase: 130-317 IU/L

FGF23: 44-215 RU/dL

Thyroid

THYROID DISORDERS CASE REPORTS III

Rapidly Expanding Thyroid Goiter as the First Manifestation of Systemic Amyloidosis

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MON-469

INTRODUCTION

Amyloidosis is a condition manifesting with extracellular tissue deposition of fibrils of low molecular weight proteins.