

**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 vena cava (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 x 11 x 13 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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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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**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