response. Reevaluation of surgical pathology was consistent with metastatic neuroendocrine cancer, the likely source of ectopic ACTH.
Our case highlights the importance of maintaining a broad differential when considering cases of cyclical cortisol elevation, including consideration of concurrent chemotherapy for seemingly unrelated malignancies.

Adrenal

ADRENAL CASE REPORTS

Severe Hyponatremia With Partial Hypoadrenalism in Acute Porphyria

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Background: Hyponatremia is the most common electrolyte-abnormality in hospitalized-patients, it increases likelihood of hospital death up-to 50% when serum Na<120mEq/L. Syndrome of inappropriate ADH secretion (SIADH) is the most common cause of hyponatremia in hospital inpatients. **Clinical Case:** 29 years-old woman, hospitalized several times due to severe hyponatremia of 103mEq/L; Admissions were accompanied by severe abdominal-pain and vomiting. She complained of severe premenstrual syndrome with severe abdominal pain and was hospitalized twice after intra-uterine insemination. She was euvolemic and due to high urinary-sodium was diagnosed with SIADH. Brain MRI, chest x-ray, thyroid-function test, and 1-mcg ACTH-test were normal. Insulin Tolerance Test for hypoadrenalism was abnormal with cortisol levels of 14.2mcg/dl and 40mg/dl glucose. She was instructed to take strong analgesics and prednisone during attacks, this did not prevent hyponatremia. Finally, due to recurrent abdominal pain, porphyria workup was done and was positive. There are 30 case-reports of porphyria and SIADH. Porphyrias are a group of 8 inherited metabolic-disorders of heme biosynthesis, often classified as hepatic or erythropoietic according to the organ in which heme precursors accumulate. Acute intermitted porphyria is estimated in ~1/75000 people of European descend, yet clinical disease is seen in ~10% of carriers. Attacks present with severe abdominal-pain, nausea, vomiting, constipation, occasionally excretion of red colored urine and signs of increased sympathetic activity. Hyponatremia due to SIADH develops in 40% of patients and can lead to convulsions. Porphyria can exacerbate by several drugs, infectious processes, alcohol, and menstruation-induced hormonal-changes. Diagnosis is made by excess of urine porphobilinogen and 5-aminolaevulinic-acid. Treatment should include avoidance of precipitating factors and hemein infusions. **Conclusions:** SIADH is considered responsible for the hyponatremia seen in porphyria patients. Our patient showed an abnormal cortisol response to Insulin induced hypoglycemia, in accordance to (1) that demonstrated decreased output of cortisol and metabolites in porphyria patients secondary to decreased hemoproteins, as p450 cytochromes. Importantly, levels of endogenous hormones, particularly progesterone, can trigger an attack especially in luteal phase and in clomiphene citrate administration.1. Pozo et al Orphanet Journal of Rare Diseases 2014

Adrenal

ADRENAL CASE REPORTS

Severe Virilization in a Girl With the Homozygous G200SNicotinamide Nucleotide Transhydrogenase Mutation Is Surprisingly Caused by Rare Bilateral Para-Overian Adrenal Rest Tumors

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Background: Patients with NNT (Nicotinamide Nucleotide Transhydrogenase) gene mutations, a rare cause of glucocorticoid and mineralocorticoid deficiency require hormone replacement therapy. Adrenal Rest Tumor (ART) in females is very rare (<20 cases world-wide) and was reported only in noncompliant patients with congenital adrenal hyperplasia having extremely elevated ACTH levels. This study characterizes the clinical characteristics, the pathophysiology and the molecular ontogeny of a unique ART in a female with adrenal failure due to the G200S mutation in NNT.
Clinical presentation and Method: A 15-year-old girl, with homozygous G200S NNT-mutation that caused adrenal insufficiency reappeared to follow-up after several years with severe virilization and elevated serum testosterone (28.3 nmol/l) and ACTH (> 1500 pmol/l) levels. Pelvic MRI and Ultrasound demonstrated one sided para-ovarian round tumor with pathological vascularization. Laparoscopic exploration revealed bilateral para-ovarian mesosalpinx masses involving the serosa of the Fallopian tube (3 and 1 cm in diameter); the testosterone level normalized within one day after removal of those masses (0.2 nmol/l).
Results: Histopathology demonstrated a pattern of adrenal rest tissue with strong intracellular positive staining for adrenal markers such as SF-1, calretinin, MART1, inhibin and the pituitary corticotroph marker-ACTH. The staining for ovarian characteristic markers such as PAX 8 was negative. Studying mRNA extracted from the tissue by RT-PCR revealed the presence of CYP17A1, CYP21A2 and MC2R (ACTH receptor) cDNA confirming typical adrenocortical transcriptional pattern in the tissue. cDNA of POMC was not detected suggesting that in spite of dense ACTH staining the tissue is not classically originated from pituitary corticotrophs. Methylome studies to further characterise the tissue are underway.
Conclusion: This study exemplifies severe virilization that resulted from a unique and rare type of ART in ovarian related tissue that was caused by incompliance to treatment in a patient with NNT gene mutation. Given the ubiquitous expression of NNT and its reported pathophysiology as free radicals scavenger in all adrenocortical layers, it is surprising to have high ACTH induced severe virilization in spite of severe NNT dysfunction and adrenal insufficiency. This study may indicate timely testosterone screening in females with NNT mutation and when increased they should probably be laparoscopically surveyed for ART even when not detected by imaging. How NNT mutation damages mineralo and glucocorticoid secreting cells while androgen secreting cells are rescued is a theme for further studies.