missense substitutions resulting in truncated proteins: (i) the previously reported p.S138* and (ii) p.C170*, in two patients with retinal dystrophy, EPP and IGHD respectively, and (iii) the novel p.E79* in a patient with microphthalmia, EPP and CPHD. A novel insertion-deletion resulting in a truncated protein p.S167* in a patient with microphthalmia, GHD, ONH, EPP and an enlarged abnormal pituitary, and a novel deletion resulting in a frameshift p.Val139Aspfs*39 in a patient with microcephaly, microphthalmia, ONH and an EPP were also identified. The human OTX2 variants caused a significant reduction in transactivation compared to wild type. Our gene expression data identified human OTX2 transcripts in the posterior pituitary, retina, ear, thalamus, choroid plexus, and in the hypothalamus during embryogenesis, but not in RP. To conclude, we identified OTX2 variants in 7 unrelated CH patients with eye abnormalities including 3 with retinal dystrophy and one with a cerebellar abnormality. As OTX2 is involved at multiple levels during HP development, these patients should be monitored for evolving endocrinopathies. Human OTX2 is expressed in the posterior pituitary, the retina and the ear at CS19 and 20 (between 6-7 weeks gestation), and in areas of the hind-brain at CS23, but not in RP at any stage analyzed in this study. The endocrine phenotypes in patients with OTX2 mutations are most likely of hypothalamic origin.

Adrenal

ADRENAL CASE REPORTS I

Retropertioneal Paraganglioma: Case Report

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SAT-216

Introduction: Paraganglioma (PGL) is a rare type of neuroendocrine neoplasm able to secrete neuropeptide and catecholamines. It can occur in any location between the neck and the pelvis. Most of the PGLs are diagnosed in the third to fifth decades and clinical presentation is variable and depends upon catecholamine secretion and tumor location. PGLs occur in the abdomen in 85% of cases. There are no unique imaging characteristics specific for PGLs, consequently, these tumors can be mistaken with other primary abdominal tumors.

Clinical-Case: We present the case of a 65-year-old woman with history of hypertension (diagnosis at 40 years) and dyslipidemia. She denied family history of hypertension. In the context of a recent diagnosis of type 2 Diabetes Mellitus, she underwent abdominal ultrasound which revealed a large, heterogeneous nodular formation with partial liquid content, measuring 12x15 cm, adjacent to the left hepatic border. Abdominal CT scan revealed an intra-abdominal mass, with 14cm (largest diameter), showing intimate contact, with no cleavage plan with the posterior wall of the gastric fundus, suggesting Gastrointestinal Stromal Tumor. A left adrenal nodule with 3.3 cm was also present, rounded, hypoechogenic, with regular margins and homogeneous. Echoendoscopy with biopsy of the retrogastric mass showed a neuroendocrine neoplasia.

At this point she was sent to an endocrinologist. When questioned she referred headache, diaphoresis and anxiety complaints for 3 years. At examination, a painless abdominal mass in the epigastrium and left hypochondrium was found. Laboratory evaluation revealed urinary metanephrines 11738 (64-302) ug/day, urinary normetanephrines 5832 (162-527) ug/day, renin 15.5 (1-8.2) pg/mL, aldosterone 28.6 (10-160) ng/dL, cortisol after 1 mg dexamethason 1.18 µg/dl (less than 1.8ug/dl) and chromogranin A 36.6 nmol / L (less than 3nmol/l). MIBG scintigraphy revealed fixation only in the large known retroperitoneal mass. The patient underwent excision of the retroperitoneal mass and of the left adrenal gland without complications. The histological diagnosis revealed, respectively, paraganglioma and adrenal cortical adenoma. Four weeks after surgery laboratory results were normal (urinary metanephrines 202 ug/24h and normetanephrines 382.0 ug /day; Chromogranin A 2.60 nmol/l). The results of the genetic tests including SDHB, SDHD, SDHC, VHL and MAX were negative.

Conclusion: This report emphasizes the necessity to include paraganglioma in the differential diagnosis and management of retroperitoneal tumors avoiding the risk of the biopsy in this kind of tumors.

Adrenal

ADRENAL CASE REPORTS II

A Silent Bomb: A Case of Severe Primary Adrenal Insufficiency in the Context of Adrenal Metastatic Disease

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SUN-177

Background: Adrenals glands are the most commonly involved endocrine organ in cancer metastasis due to its abundant lymphatic communication and blood supply. Up to 4% of non-small-cell lung cancers and 71% of lymphomas have bilateral adrenal metastasis. Early detection with hormone replacement can be life-saving.

Clinical Case: A 58 year old male was admitted for hyperkalemia (potassium 6.4 mmol/L, range: 3.5-5.1) with prolonged PR interval on EKG, hypernatremia (sodium 131 mmol/L, range: 136-145), hypoglycemia (glucose 48mg/dl), and renal function impairment (creatinine level elevation of 1.38 mg/dl from a baseline of 0.94 mg/dl). He had been diagnosed with Stage IVb non-small-cell lung cancer about 20 months prior, and had a known history of chemotherapy, adrenal
metastasis and left adrenal gland radiation (20 G in 5 daily fractions) about 10 months ago. For the past 10 months, the patient had reported no weight loss, nausea, vomiting, or other symptoms or signs of adrenal insufficiency, apart from intermittent fatigue, which he had attributed to his lung cancer diagnosis. On review, a previous PET/CT scan showed intense FDG uptake in the bilaterally enlarged adrenal glands, measuring 3.3 x 2.8 cm on the left, and 3.1 x 1.8 cm on the right. His ACTH level was found to be elevated to 1,023 pg/ml (range: 6-63) with borderline low free cortisol level 0.06 mcg/dl (range 0.04-0.35). Aldosterone level was found to be 3.4 ng/dl (range: 4-31), with a renin level of 36.2 ng/ml/hr (range: 0.5-4). Primary adrenal insufficiency was diagnosed, and the patient was started on hormone replacement therapy, which was titrated as outpatient. Now he is continued on a regimen of hydrocortisone 15 mg and 5 mg, at 8 am and 3 pm respectively, and fludrocortisone 0.1 mg daily. In two months, his ATCH level fell from 1,023 to 89 pg/ml with normalization of kidney functions, sodium level (now 137 mmol/L) and potassium level (now 4.8 mmol/L). He gained 4 kg, and has been feeling more energetic and functional on his follow up visits.

Conclusion: Patients with adrenal metastatic cancer may have atypical symptoms and signs despite having severe primary adrenal insufficiency. High risk patients should be monitored, even in the absence of symptoms, for the development of adrenal insufficiency.

Reference:
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Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Severe Hypophosphatemia Induced by Intravenous Ferric Carboxymaltose Therapy for Iron Deficiency Anemia
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MON-338
Severe hypophosphatemia induced by intravenous ferric carboxymaltose therapy for iron deficiency anemia

Background: Ferric carboxymaltose (Injectafer), a newer intravenous iron agent permits larger iron concentrations to be delivered in fewer doses compared to traditional preparations of intravenous iron. However, ferric carboxymaltose has been shown to up-regulate fibroblast growth factor 23 (FGF23) which can result in severe hypophosphatemia. We present a case illustrating this phenomenon.

Clinical Case: A 48 year-old Caucasian female was admitted to the emergency department with complaints of gradual onset muscle weakness and severe exhaustion. Over the course of several months she noticed significant muscle weakness in all extremities. Her co-morbidities included morbid obesity (status-post Roux-en-y bypass surgery), asthma, and hereditary angioedema. Due to her history of gastric bypass surgery, the patient required monthly iron sucrose infusions over the previous two years. Her regimen was changed to ferric carboxymaltose (Injectafer) about five months prior to the admission, receiving 750mg treatments twice monthly. On admission, she was found to have severe hypophosphatemia of 1.5 mg/dL (2.1 – 4.7 mg/dL) with 25-OH vitamin D 21 ng/mL and PTH of 155 pg/mL. A random urinary phosphate was 72 mg/dL with a urine creatinine of 45 mg/dL, with calculated fractional excretion of phosphorus of 74%. Further diagnostic tests including EMG / nerve conduction studies, inflammatory markers, autoimmune workup, and creatine kinase were negative. She was found to have a ferritin of 2159 ng/mL (11 – 306 ng/mL) from previous baseline of 12.8 ng/mL with normal ESR and CRP. This was elucidated to be due to iron overload from IV iron infusions out of proportion to her needs. Therefore, ferric carboxymaltose was discontinued. Her symptoms gradually improved with phosphorus and vitamin D supplementation. Two months later, when seen by Endocrinology, her ferritin was 1220 ng/mL, PTH 44 pg/mL, and phosphorus normalized to 2.6 mg/dL.

Conclusion: Ferric carboxymaltose can cause profound phosphaturia and hypophosphatemia by inhibiting the cleavage of intact FGF23 to the inactive form, a mechanism similar to autosomal dominant hypophosphatemic rickets. Previous clinical trials show the incidence of hypophosphatemia to be as high as 41-70%. We conclude that baseline phosphorus and vitamin D levels should be obtained prior to therapy and monitored closely during treatment.

Reference: Adkinson NP et al. Comparative safety of intravenous ferumoxytol versus ferric carboxymaltose in iron deficiency anemia: A randomized trial. Am J Hematol. 2018;93(5):683.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Novel Estrogenic Gene Regulation Induced by OTC Medications Containing Paraben Preservatives Is Dependent on Concentration that Varies Between Products and Batches
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SAT-713
Methylparaben, ethylparaben, and propylparaben are widely used as preservatives in food products, cosmetics, and pharmaceuticals. Parabens have been shown to be weak estrogens and this laboratory has described that extracts of some over the counter (OTC) medications with paraben preservatives can induce estrogen activity in tissue culture-based bioassays. At the same time, this laboratory determined that extracts from OTC medications containing the laxative bisacodyl induce estrogen activity regardless of parabens present and that bisacodyl