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Background: Endocrine hypertension accounts for 5–10% of hypertensive population, with primary hyperaldosteronism being the most frequently encountered diagnosis. Biochemical tests are subject to interference with many drugs that may lead to false positive or negative results.
We present a case of aldosterone producing adenoma associated with false negative screening test due to Levetiracetam use.
Clinical Case: A 30 year-old Middle Eastern woman was referred to endocrinology clinic for evaluation of secondary hypertension and persistent hypokalemia. Six years ago, she presented to emergency room during the 3rd trimester of her second pregnancy with severe preeclampsia and seizure. Postpartum, she was discharged on Levetiracetam (Keppra) 500 mg orally BID. Upon follow up visits, she continued to have persistent elevation of blood pressure readings with spontaneous hypokalemia ranging 2.5–3.2 mEq/L. She was started on Perindopril 10 mg daily and potassium supplement. Amlodipine 5 mg daily was added shortly later on. Clinically, she had regular menstrual cycle. She did not have plethora, central obesity, easy bruising, or proximal muscle weakness. Her review of systems including thyroid-related symptoms were normal. There was no family history of hypertension or adrenal tumors. On examination, BP 180/110, pulse rate 78, weight 58 kg and BMI 25. Her physical examination was otherwise unremarkable. After holding Perindopril for 4 weeks, biochemical tests showed creatinine 0.52 mg/dL (0.49–1.1), urea 16.8 mg/dL, potassium 2.9 mEq/L (3.5–5.2), direct renin concentration (DRC) 100.6 pg/mL, aldosterone 54.25 ng/dL. Plasma fractionated metanephrines were normal and morning cortisol level after 1 mg overnight dexamethasone suppression test was 0.72 mcg/dL. Renal arterial doppler showed normal renal blood flow without any significant stenosis. Despite increasing potassium supplement she continued to have hypokalemia. As levetiracetam was reported by literature review to cause severe hypokalemia, it was stopped after discussion with neurology. Four weeks later, repeated DRC was suppressed 4.0 pg/mL with elevated aldosterone 62.73 ng/dL. Furthermore, primary hyperaldosternism was confirmed after normal saline suppression test revealed unsuppressed aldosterone 15 ng/dL. An Adrenal CT scan showed a small hypodense right adrenal lesion measuring 11x9 mm with a pre-contrast density of 7 HU and post contrast absolute washout more than 60%. Patient elected to undergo right adrenalectomy. 24 hours post surgery, aldosterone level dropped to 4.0 ng/dL and potassium increased to 5 mEq/L. Fortunately, hypertension and hypokalemia have both resolved after surgery. **Conclusion:** We are first to report that Levetiracetam can cause unsuppressed direct plasma rennin concentration (DRC) and potentially could result in a false negative screening test for primary hyperaldosteronism.

Adrenal

ADRENAL CASE REPORTS

Limited Efficacy of Mifepristone Due to Poor Tolerance: A Clinical Challenge in Managing Cortisol Excess

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A 53-year male with incidental bilateral adrenal masses along with symptoms of proximal muscle weakness, anxiety, and depression. Past medical history of uric acid nephrolithiasis, hypertension, hyperlipidemia, type 2 diabetes mellitus, anxiety, and depression. A right adrenal mass of 2.8cm and a left adrenal mass of 1.5cm both of <10 HU on non-enhancing CT. Hormonal activity workup was ordered which showed cortisol levels of 4.7mcg/dL on 1mg ONDST suggestive of autonomous cortisol excess and workup for primary hyperaldosteronism was negative. On follow up CT adrenal masses remained stable, but the patient underwent the annual hormonal workup for incidentaloma with 1mg ONDST and found with cortisol 4.5mcg/dL, eventually repeated with 2-day LDDST which showed no suppression of cortisol with levels at 4.5 mcg/dL confirming the diagnosis of autonomous cortisol excess. ACTH found to be suppressed at 3.1pg/dL (7.2–63.3 pg/dL) which helped confirm the diagnosis of non-ACTH dependent autonomous cortisol excess. Referred to surgery evaluation due to complications associated with cortisol excess as osteoporosis and uncontrolled hyperglycemia however surgical intervention was deferred until the source of cortisol excess could be identified within the bilateral adrenal masses and it was recommended to continue with medical therapy.
As the cortisol excess source cannot be identified by localizing procedures and despite adequate medical therapy and stable adrenal masses on imaging, patient persisted with uncontrolled DM/hypertension and worsening BMD in the spine and hip with surgery not being an option. The patient was started on glucocorticoid receptor antagonist mifepristone in which upon reevaluation weakness and fatigue were noticeable along with hypokalemia of 3.1mmol/L after 2 weeks of therapy that was eventually replaced but 2 weeks later the patient discontinued therapy as he could not tolerate side effects related to adrenal insufficiency associated with mifepristone, such as weakness, fatigue, and dependence of potassium supplementation due to hypokalemia.
This effect is physiologically important, because cortisol binds as avidly as aldosterone to the mineralocorticoid receptor, and the plasma cortisol concentration is approximately 100-fold higher than the plasma aldosterone concentration and it can lead to hypokalemia by the mechanism of apparent mineralocorticoid excess. Also, as mifepristone blocks cortisol action, the levels of ACTH and cortisol increase so high that hormonal measurement cannot be used to judge either therapeutic efficacy or adrenal insufficiency, we must go based on signs and symptoms.

Adrenal

ADRENAL CASE REPORTS

Looking Beyond Diabetes: A Case of Worsening Hyperglycemia as a Manifestation of Ectopic Cushing's Syndrome Secondary to an Adrenocorticotropic Hormone-Producing Pheochromocytoma

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A 76-year-old woman presented with worsening fasting hyperglycemia on routine blood sugar measurement, previously well-controlled on Metformin, requiring initiation of insulin. Her medical history included type 2 diabetes mellitus, hypertension, and aortic stenosis. Over the next few weeks, she developed bilateral upper and lower extremity proximal muscle weakness, episodes of confusion, rapid weight loss and increasing lower extremity edema. She did not have typical Cushingoid features of moon facies, easy bruising, centripetal obesity, abdominal striae, dorsocervical fat padding, or hyperpigmentation. Laboratory data revealed severe hypokalemia, elevated cortisol of 138 (3.7–19.4 ug/dL) and ACTH of 368 (6–50 pg/mL) consistent with ACTH-dependent Cushing's syndrome. She was hospitalized for emergent therapy with etomidate infusion, potassium supplementation, and started on spironolactone. 24-hour urinary analysis demonstrated elevated catecholamines and metanephrines: epinephrine 552 (2–16 mcg/g cr), norepinephrine 1881 (7-5 mcg/g cr), metanephrine 4095 (21–153 mcg/g cr), normetanephrine 3920 (108–524 mcg/g cr).
CT abdomen showed 3.8 cm mass in the left adrenal gland with enhancing walls and central hypoattenuation and a normal contralateral adrenal gland. MR brain showed a partial empty sella without any mass. ^{123}I-metaiodobenzylguanidine scintigraphy showed uptake in the left adrenal mass. Once cortisol was reduced to <25 ug/dL, she was transitioned from etomidate to metyrapone; alpha-methyltyrosine and prazosin was also begun. Following left laparoscopic adrenalectomy, ACTH decreased to <5 pg/mL confirming that the pheochromocytoma was the source of ectopic Cushing's. Gross examination of the mass was notable for a spongy, tan, roughly spherical medullary neoplasm (3 cm in diameter) with a rim of brown and focally yellow adrenal cortex up to 4 mm thick. Marked diffuse adrenal cortical hyperplasia was noted. The tumor showed varied growth patterns, including solid areas and spongy, angioma-like areas with prominent small blood vessels. Immunohistochemical staining was positive for somatostatin receptor 2A, tyrosine hydroxylase and ACTH in tumor cells and negative for T-PIT. She was discharged on replacement hydrocortisone therapy, minimal insulin for diabetes and has shown substantial clinical improvement.
Cushing's syndrome due to ectopic ACTH-producing pheochromocytoma is rare. Worsening hyperglycemia in the presence of hypertension, even without typical clinical findings of Cushing's, should prompt further hormonal work up. The absence of the transcription factor TPIT, which is a lineage determinant for pituitary corticotrophs, suggests that novel pathways are involved in differentiation of cells that produce ectopic ACTH.

Adrenal

ADRENAL CASE REPORTS

Malignant Testicular Paraganglioma: The Importance of Adequate Clinical Follow-Up

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Background: Paragangliomas (PGL) are rare neuroendocrine tumors derived from neural crest cells. The presence of metastases is the only absolute criterion of malignancy. **Clinical Case:** A 59 y.o. male patient reports the appearance of a tumor in the right inguinal region operated in 2014 with tumor removal and right orchiectomy, with anatomopathological (AP) outcome spermatic cord adenomathoid tumor and immunohistochemistry (IHC) compatible with PGL: Ki-67 1% (S 100 diffusely positive protein), diffusely positive chromogranin A, weak positive CD99. However, no new tests were performed in the follow-up. After 5 years, the patient started to present sporadic episodes of sweating, palpitations and increased tension levels after doxazosin suspension. Investigation for reoccurrence with Urinary Catecholamines: Noradrenaline (VR< 97 mcg/24h) 112/179, Adrenaline (VR< 27 mcg/24h) 4/4, Dopamine (< 500 mcg/24h) 184/ 342, Plasma Metanephrines: Normetanephrines (VR< 196 pg/ml) 880.7/ 2402 Metanephrines (VR< 65 pg/ml) 44.6/ 53.1. Tests was performed: chest CT Multiple bilateral non-calcified pulmonary nodules with contrast enhancement, measuring 1.2 cm. Abdominal CT: Two retroperitoneal solid lesions located anteriorly to the inferior vena cava and aorta, in a discretely paramedian position on the right, intense arterial enhancement, with a hypoattenuating center. The largest lesion is located just below the emergence of the renal arteries and after the head of the pancreas and third portion of the duodenal. It measures 4.4 x 3.2 x 4.4 cm (LL x AP x CC). The smallest lesion is immediately inferior to the largest and measures 3.1 x 2.6 x 3.6 cm (LL x AP x CC). The lesions have contact with retroperitoneal vascular structures, notably with the inferior vena cava and with the vascular pedicle of the right kidney. Scintigraphy with MIBG: Radiopharmaceutical hyperconcentration in focal areas in the projections of lung fields, in greater number on the left, with intensity of uptake varying from mild to moderate; two contiguous focal areas in the median projection of mesogastrics, in moderate/acentuated degree. Patient was reoperated and removed abdominal lesions with new conclusive AP for PGL whit PASS 3, currently performing therapeutic MIBG for thoracic injury control. Clinical Lesson: Patients with lesions suggestive of PGL but without confirmatory AP should request IHC and clinical follow-up will be according to the findings in it.

Adrenal

ADRENAL CASE REPORTS

Management of Pheochromocytoma in a Patient With Severe Aortic Stenosis Undergoing Transcatheter Aortic Valve Replacement

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Background: There are few guidelines for the management of patients with both significant cardiac valvular disease and pheochromocytoma. Resection of pheochromocytoma is challenging for surgeons and anesthesiologists