Adrenal

ADRENAL CASE REPORTS

Synchronous Malignant Pheochromocytoma With Renal Cell Carcinoma: A Case Report

Charles Ma, MD, Noah Bloomgarden, MD, Simona Stefan, MD.
Montefiore/Albert Einstein School of Medicine, New York, NY, USA.

Introduction: In the US, Pheochromocytoma/paraganglioma incidence is estimated to be 2–8 per 1 million people each year with around 100–200 of these cases being malignant. Malignant pheochromocytoma is defined by documented presence of metastases or evidence of extensive local invasion. There are certain genetic syndromes which are also associated with renal cell carcinoma, including SDHB mutations type 4, VHL disease and familial pheochromocytoma. These syndromes are important to recognize as they may signify a worse prognosis. Here, we describe a case of co-occurrence of malignant PC with renal cell carcinoma.

Case Report: A 53-year-old Hispanic male with history of HTN and recently diagnosed metastatic pheochromocytoma was admitted for surgical debulking of the left retroperitoneal/adrenal and renal masses. Symptoms began five months prior after he presented with an ischemic stroke in the setting of labile hypertension. He was diagnosed with a 6.3 x 4.6 x 6.8 cm incidental left retroperitoneal mass and suspicious left renal mass on CT imaging but also noted several lytic bony lesions concerning for bone metastasis. A spinal biopsy was obtained which was consistent with a well-differentiated metastatic neuroendocrine tumor. Laboratory evaluation was notable for Chromogranin A level of 6959ng/mL (25–140). He was started on Lanreotide. Given persistently difficult to control HTN he underwent work up for secondary hypertension. Hormonal evaluation was notable for plasma free metanephrine of 534pg/mL (<57pg/mL), normetanephrine 6155pg/mL(<148pg/mL), and total metanephrine of 6689pg/mL (205pg/mL) consistent with metastatic Pheochromocytoma. After appropriate alpha blockade he underwent left adrenalectomy, nephrectomy and liver tumor microwave ablation. Pathology was consistent with an 8.7cm pheochromocytoma with extensive retroperitoneal soft tissue invasion and PASS score of 9 as well as a 3.6 cm renal cell (clear cell-papillary type) carcinoma. On follow up, Plasma metanephrine decreased significantly postoperatively to a free metanephrine of 28pg/ml, normetanephrine 1153pg/ml, and total metanephrine of 1181pg/mL. He was referred for genetic testing but unfortunately, he was readmitted one month later with cerebral hemorrhage and expired.

Conclusion: Advancements in genetics have led to improved understanding of the molecular etiologies of pheochromocytomas. A number of genetic defects are associated with PC and RCC, including SDHB mutations type 4, VHL and familial pheochromocytoma. Our case underscores the high morbidity and mortality in patients with metastatic PC with RCC and perhaps the catastrophic outcomes in such patients. Assessing patient's genetics in these cases is now the standard of care, however further research studies are warranted to better understand the significance of tumor genetics on prognosis and management.

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Taking it with a Grain of Salt: A Woman with 'PCOS' and Infertility Diagnosed with Nonclassic Congenital Adrenal Hyperplasia and a Large Renal Mass

Marcos D. Villarreal, MD, MPH, Viraj Desai, DO, MBA, Pratima V. Kumar, MD.
University of Texas at Austin Dell Medical School, Austin, TX, USA.

Background: Clinical manifestations of Nonclassic CAH (NCCAH) in women may range from asymptomatic to hirsutism, oligo-menorrhea, or infertility. Testicular adrenal rest tumors are common in men with classic CAH though uncommon in NCCAH. In women with classic CAH, ovarian adrenal rest tumors are even rarer. 11–58% of patients with classic CAH will have at least one adrenal nodule but the prevalence is unknown in NCCAH (1).

Clinical Case: A 34-year-old Hispanic woman was seen by reproductive endocrinology for evaluation of infertility. She had been unable to conceive for the past 7 years. She was diagnosed with PCOS by her PCP. She was referred to our clinic for further workup. The patient denied galactorrhea. Laboratory evaluation revealed prolactin 49.3 (< 20.0 ng/ml), TSH 2.290 (0.5–5.0 µU/mL), fT4 1.14 (0.9–2.3 ng/dL), total testosterone 92 (15 -70 ng/dL for women), DHEAS 361 (45 -270 µg/dL), 8 AM cortisol 20.0 (5–23 µg/dL), ACTH 59.0 (6–76 pg/ml), 17-hydroxyprogesterone (17OHP) >2000 ng/dL, and A1c 5%. 24-hour urinary free cortisol was 26.4 (3.5–45 mcg/day). MRI of the pituitary did not show any adenoma. Pelvic ultrasound did not reveal any ovarian cysts.

Cosyntropin stimulation test showed baseline 17OHP 1076 ng/dL, 30 minutes 8812 ng/dL, and 60 minutes 9452 ng/dL. She was begun on hydrocortisone and cabergoline. CT of the abdomen did not reveal any adrenal masses but showed mildly thickened adrenal limbs suggesting adrenal hyperplasia. A 4.5 cm exophytic enhancing mass on the left kidney was noted representing an adrenal rest tumor versus angiomyolipoma.

Given the exophytic nature of the mass and increased risk of hemorrhage with angiomyolipomas greater than 4 cm, the patient was referred to urology and interventional radiology for radioembolization and possible biopsy of the mass. We are unsure if this renal mass is an angiomyolipoma or an adrenal rest tumor, which are uncommon in the kidneys. The patient was also referred for genetic counseling. Patients with CAH typically have *CYP21A2* gene mutations, and the chance that a patient with NCCAH will have a child with classic CAH is reported to be 1 to 2% in two large cohort studies (2).

Conclusion: This case is a reminder that evaluation of infertility/subfertility includes less common diagnoses, such as NCCAH. This genetic disorder is seen more frequently in certain ethnic groups, including Hispanics; and after diagnosis, patients should be referred to a genetic specialist. Additional abdominopelvic imaging should be considered in both men and women with a new diagnosis of NCCAH to evaluate for rare but clinically significant tumors.

Reference: 1. Nordenström, A., Falhammar H. Diagnosis and management of the patient with non-classic CAH due to 21-hydroxylase deficiency Eur J Endocrinol. 2019 Mar;180(3):R127-R145.2. Merke, D, Auchus, R Congenital