CLINICAL VIGNETTE

Metastatic Mucoepidermoid Carcinoma Causing Ectopic Cushing's Syndrome

Dina R. Block, M.D., and Nancy Mora Becerra, M.D.

A 52-year-old male with a history of mucoepidermoid carcinoma presented to endocrine in 2015 for elevated cortisol levels and high ACTH. He was originally diagnosed with mucoepidermoid carcinoma of the larynx in 2004 and treated with partial laryngectomy. He received radiation therapy and was doing well until 2008 when he was found to have multiple pulmonary nodules and a local recurrence in the neck. He was treated with surgery, radiation therapy, and chemotherapy. A tracheostomy was placed in 2013 due to worsening dyspnea. Biopsies taken at the time of tracheostomy were positive for carcinoma, and he subsequently underwent total laryngectomy. He continued treatment with chemotherapy and radiation therapy. At the end of 2014, he began to complain of leg cramping, puffy cheeks, and worsening vision. He was referred to endocrinology for evaluation of Cushing's syndrome.

At presentation, his exam was remarkable for hyperpigmented and proximal muscle weakness. He had Cushingoid facies and facial plethora as well. Blood pressure was normal.

Laboratory results were remarkable for potassium levels on the lower end 3-3.4 mmol/L (normal 3.6-5.3 mmol/L). His A1c was slightly elevated at 5.8%.

Initial lab workup included 24 hr urine cortisol 880.77 ug/g crt (normal <24 ug/g crt). Initial cortisol levels were 25 mcg/dL with ACTH of 38 pg/mL. Cortisol did not suppress with 48-hour dexamethasone suppression test (cortisol 11 mcg/dL, ACTH 51 pg/mL). Pituitary MRI did not show any abnormal signal in the pituitary gland to suggest a microadenoma. Based on these results, he was diagnosed with ectopic Cushing's syndrome.

He was started on potassium supplementation along with ketoconazole 200 mg daily with improvement in urine cortisol levels to 31.30 ug/g crt. Intermittently cortisol levels would rise requiring further titrations of ketoconazole, achieving a maximum dose of 400 mg TID. He was found to have multiple new pulmonary nodules which coincided with a rise in his urine cortisol to 563.64 ug/g crt.

At this point, he was started on metyrapone 250 mg TID and referred for bilateral adrenalectomy. Because urine cortisol improved to 15.17 ug/g crt, the patient decided to defer surgery. While cortisol levels were improved, the patient's condition ultimately deteriorated, and he died 5 months after starting metyrapone.

Discussion

Mucoepidermoid carcinoma (MEC) was first described in 1924, and today is well recognized as a common salivary gland neoplasm. This carcinoma accounts for approximately 30% of all malignancies of the major and minor salivary glands. Women are more commonly affected than men (3:2), and the mean age of onset is in the 5th decade of life. Of note, MEC is also the most common salivary malignancy in children.[1]

Contrary to MEC of the salivary glands, MEC of the larynx is an extremely rare neoplasm with only 83 cases documented in a recent review of the literature. These tumors are believed to develop from ductal elements of the submucosal glands.[2]

Our patient initially presented with MEC of the larynx and later had a recurrence in the lungs. MEC tumors of the lungs are extremely rare, accounting for only 0.1-0.2% of all lung cancers. There have been very few case reports of MEC causing ectopic Cushing syndrome (ECS). ECS is described as having high ACTH levels (>20ng/L) and cortisol levels that are not suppressible with high doses of dexamethasone (8mg/day).[3] Untreated ECS is associated with a risk of life-threatening cardiovascular, infectious, and metabolic complications. The risk of death increases with the rate of cortisol secretion. Successful surgery of ACTH-secreting tumors can normalize cortisol secretion and lower the mortality to that of the general population.[4] When surgical removal of the primary tumor is not possible, bilateral adrenalectomy has been shown to achieve biochemical resolution and at least partial clinical resolution of the signs and symptoms associated with hypercortisolism.[5]

In our patient, medical treatment of the hypercortisolism was necessary as surgical removal of the lung lesions was not possible, and he had opted not to proceed with bilateral adrenalectomy. Unfortunately, due to rapid progression of his pulmonary disease, we were not able to determine long-term effectiveness of medical therapy alone.

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