Atypical Carcinoid Tumor with Ectopic ACTH Production used as a Biochemical Marker of Recurrence

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ABSTRACT

Bronchopulmonary carcinoids, including typical and atypical histologies, are uncommon neuroendocrine tumors that have a wide range of clinical phenotypes. In addition to the carcinoid syndrome, other paraneoplastic syndromes are well-described, including ectopic adrenocorticotropic hormone (ACTH) production. The authors describe a case presentation of a 23 year-old man with ectopic ACTH production from a bronchopulmonary atypical carcinoid. The use of ACTH as biochemical marker is described here, as its use predicted disease recurrence and helped to guide management.

ABBREVIATIONS

ACTH: Adrenocorticotropic Hormone; ACE-I: Angiotensin Converting Enzyme Inhibitor; CCB: Calcium Channel Blocker

CASE PRESENTATION

A 23 year-old active duty United States Navy service member was found to have new-onset hypertension as part of a routine deployment physical. He was placed on antihypertensive therapy, but this was unable to be controlled with three-drug therapy including an ACE-I and CCB. He also complained of weight gain of 30 pounds despite participation in daily physical therapy and having swelling in his legs. The patient had no prior medical or surgical history. He smoked a half-pack of cigarettes daily and occasionally consumed alcoholic beverages. Family medical history was significant for diabetes mellitus and hypertension in his parents; there were no known malignancies in the family history. Vital signs at initial consultation with endocrinology: blood pressure 190/105 mmHg, heart rate 95, and respiratory rate of 20. On physical examination he was found to be obese with purple striae covering the abdomen as well as upper and lower extremities; enlarged supravacular fat pads and buffalo hump were identified. Cardiopulmonary examination was normal. Laboratory work-up (morning labs) were as follows: renin 23.6 ng/ml/hr, aldosterone 6.7 units, cortisol 34.8 mcg/dL, creatinine 0.9 mg/dL, sodium 138 mmol/L, and potassium 2.9 mmol/L. Further evaluation for this elevated morning cortisol level revealed an ACTH level of 252 pg/mL and his cortisol level did not suppress with overnight dexamethasone suppression test, suggesting an ectopic ACTH-dependent process. Computed topography of the chest, abdomen, and pelvis showed a 3 by 6 cm left lower lobe mass with ipsilateral hilar adenopathy; octreotide analogue scintigraphy revealed somatostatin receptor disease that correlated with the CT findings (Figure 1).

The patient was subsequently taken for left lower lobectomy and lymph node dissection revealing a histopathologic diagnosis of neuroendocrine tumor, 5 cm in largest dimension, with 10 of 10 lymph nodes sampled being positive for metastatic involvement. There was 1 mitotic figure per 10 high-powered fields and the Ki-67 proliferative index was 5%, making this an intermediate grade neuroendocrine tumor (atypical carcinoid). There was extensive...
lymphovascular invasion present with extracapsular extension. His pre and post thoracotomy ACTH values were 290 and 24 pg/mL, respectively. Other biochemical markers for neuroendocrine tumors were not elevated. He was sent to Walter Reed National Military Medical Center for further management of his condition.

At this institution, the patient was in good spirits and had recovered from his surgery well. He reported a 20 pound weight loss and no neurologic symptoms. Laboratory examination showed an up trending ACTH level of 98 pg/mL, suggestive of persistent disease. Octreoscan confirmed that there was localized somatostatin receptor disease in the left hilar and precarinal spaces (Figure 2). Given his good performance status and young age, he elected to pursue aggressive chemoradiation therapy. He will undergo chemotherapy with cisplatin and etoposide every 21 days with concurrent radiation therapy during cycle two. He will be followed with serial octreotide analogue scintigraphy and ACTH levels to monitor for recurrence thereafter.

**DISCUSSION**

Bronchopulmonary neuroendocrine tumors are diverse clinical entities confronted in the oncologic practice, which often require multimodality therapy. They exist within a spectrum of diseases ranging from often-benign, low-grade typical carcinoid tumors to aggressive small cell lung cancer. Though bronchopulmonary carcinoid tumors (including typical and atypical histologies) account for only 1% of all invasive lung cancers [1], they account for 10-21% of cases of ectopic ACTH-dependent Cushing’s syndrome [1,2]. The use of somatostatin analogue scintigraphy can be a useful imaging modality and is able to be correlated with the presence of carcinoid tumors in up to 80% of cases [3]. Increasing the detection of recurrence and completing our early detection of recurrence is measuring serum ACTH. This case illustrates the use of both ACTH secretion as a clinical biomarker to predict disease recurrence followed by imaging to allow early detection and the potential to offer our patient a curative plan.

There are few randomized clinically controlled trials to determine how to best manage bronchopulmonary carcinoid tumors in the metastatic setting. Current guidelines for the management of intermediate grade neuroendocrine Stage II tumors are with definitive surgery, followed by monitoring for disease recurrence. Because of the lack of large randomized trials, the use of chemotherapy agents in the adjuvant setting is lacking. Most neuroendocrine tumors appear to be sensitive to both cisplatin and etoposide [4], which is referred, based secondary to the frequent use in small cell lung cancer. For patients with the carcinoid syndrome, the use of long-acting formulations of somatostatin analogues appears to be quite effective at reducing symptoms but only has as modest effect on disease control [5]. The world is lacking large randomized trials, which could position modern chemotherapy against agents that are 30 years in use.

**REFERENCES**


