Sudden Clinical Development Of Ectopic Cushing’s Syndrome Due To A Non-Catecholamine Producing Pheochromocytoma

Shannon Comley Sood, DO; Matthew Leinung, MD; Ming-Tseh Lin, MD; Timothy Jennings, MD; and Daniel W. Lee, MD

Department of Medicine, Division of Endocrinology and Division of Pathology and Laboratory Medicine
Albany Medical College, Albany, New York

Abstract

To our knowledge, there is only one previous report of a patient with Cushing’s syndrome caused by a non-secreting adrenal pheochromocytoma. We now present a 54-year-old female who developed sudden ectopic Cushing’s syndrome in a previously diagnosed but apparently non-functioning adrenal incidentaloma. The incidentaloma was noted one year prior to her presentation with Cushing’s syndrome. Identification was also evaluated by the authors in endocrine clinic four months after discovery of this lesion. Despite a search for signs and symptoms of Cushing’s syndrome, none were identified. Seven months later the patient presented to an endocrinology clinic with rapid onset and worsening of swelling in her face, neck, and abdomen accompanied by a syncope-like episode. Hypokalemia, hypertension, hyperglycemia, and Cushingoid habitus were noted. Her cortisol was 119 mcg/dl; her ACTH was 518 pg/dl (normal 9-52 pg/ml). A 24-hour urine free cortisol was elevated at 8479 ug/24 hr (normal 0-50 ug/24 hr). MRI of pituitary was negative and inferior petrosal sinus sampling did not reveal an elevated central to peripheral ratio after CRH stimulation. The ACTH appeared ectopic in origin. A CT scan chest/adrenals/pelvis was repeated and the mass had increased in size to 3.7 cm and the opposite adrenal was now noted to be hypertrophic. Urinary metanephrines and catecholamines were collected and levels were all within normal limits. During testing her clinical condition deteriorated rapidly with refractory hypertension and the development of psychosis. The patient underwent left adrenalectomy and a 3.5 cm tumor was removed. Pathologic examination was consistent with a pheochromocytoma. Immunohistochemical markers for pheochromocytoma.

Introduction

Ectopic ACTH production is responsible for approximately 15% of ACTH-dependent Cushing’s syndrome (1). Ectopic ACTH production can occur from a variety of sources; one of the most rare being pheochromocytomas, which are believed to cause only 3% of cases of ectopic ACTH production (1). In those that have been reported, approximately 90% of pheochromocytomas have catecholamine-secreting tumors of the adrenal are rare, it is possible that they can present without the usual biochemical markers for pheochromocytoma.

Presentation

CASE HISTORY: A 54-year-old female was evaluated in endocrinology clinic for an incidental finding of an adrenal adenoma. Despite a search for signs and symptoms of Cushing’s syndrome, none were identified. Urinary metanephrines and catecholamines were ordered at the initial visit, but the patient did not complete the urinary collection. The patient was to be followed for any change in size of the adenoma. She was a chronic smoker and had recently been diagnosed with lymphocytic inflammatory colitis, depression, and fibromyalgia. She was a former smoker but denied alcohol use and was on Synthroid, Wellbutrin, spironolactone, Toprol XL, and diuretics. She was noted at time of presentation to our office, after hospitalization. Spironolactone, metoprolol, and potassium had been started at the outpatient hospital for refractory hypertension and hypokalemia. Upon initial physical examination, her blood pressure was 160/110 and her pulse was 110-120 and regular. Cushing habitus with facial and posterior cervical swelling was noted. Lungs were clear. Abdomen was slightly distended. No violaceous striae were noted. Lower extremities showed +1 pitting edema and multiple ecchymoses. Proximal muscle weakness was also appreciated. There were no neurologic deficits appreciated. Skin showed mild acne and facial hirsutism.

Lab Data

Her white blood cell count was 12.6 thousand/ml, and her Hemoglobin/Hematocrit was 11.7/33%. Her potassium was 2.2 (normal 3.5-5.3), her bicarbonate was 40.1 (normal 21-32), and her glucose was 186 (normal 60-110). A random cortisol was sent and found to be greater than 60 ug/dl (normal 8-72-24). A repeated cortisol value of 119 ug/dl was obtained. ACTH was also obtained and found to be 518 pg/dl (normal 9-52). A 24-hour urine cortisol was elevated at 8479 mcg/24 hr (normal 0-50 mcg/24 hr). Urinary metanephrines and catecholamines were collected. These levels were all within normal limits; metanephrines 178 ug/24 hrs (normal 35-460), normetanephrines 138 ug/24 hr (normal 10-1050), epinephrine 6 ug/24 hr (normal 0.24), norepinephrine 21 ug/24 hr (normal 0-140), and dopamine 105 ug/24 hr (normal 65-610). Other tests included thyroid function, complete blood count and liver function. Results were all normal except for 2.7 cm in size less than one year prior was now 3.7 cm in size and the right adrenal was now also noted to be hypertrophic. A chest CT was also done, but no mass was noted. Inferior petrosal sinus sampling did not reveal an elevated central to peripheral ratio after CRH stimulation.

Diagnostic Imaging

MRI of the pituitary was completely normal and inferior petrosal sinus sampling was planned. A CT of the adrenals/pelvis was performed. The adrenal adenoma previously 2.7 cm in size less than one year prior was now 3.7 cm in size and the right adrenal was now also noted to be hypertrophic. A chest CT was also done, but no mass was noted. Inferior petrosal sinus sampling did not reveal an elevated central to peripheral ratio after CRH stimulation.

Summary

We present a case of Cushing’s syndrome due to a noncatecholamine secreting, ACTH producing pheochromocytoma. Her rapid clinical presentation implies that the biologic behavior of the tumor had changed from what it was first discovered and 2.5 cm in size. The explanation for this apparent transformation is unclear. One should be aware that while ACTH producing pheochromocytomas may present without classic biochemical markers and yet be a source of ectopic ACTH, change in symptoms occurs. We believe we have illustrated that it is possible for pheochromocytomas to present without classic biochemical markers and yet be a source of ectopic ACTH.

Medical Course

The patient’s clinical condition continued to deteriorate over the next several weeks. She remained hypertensive despite anti-hypertensive therapy, she was unable to ambulate or lift herself from a sitting position without assistance, and she became acutely psychotic requiring medication. She was started on ketoconazole, and for lack of another potential source of ACTH, a left adrenalectomy was planned.

Case History

Our past medical history was significant for autoimmune hepatitis, Hashimoto’s thyroiditis, lymphocytic inflammatory colitis, depression, and fibromyalgia. She was a former smoker but denied alcohol use and was on Synthroid, Wellbutrin, spironolactone, Toprol XL, and diuretics. She was noted at time of presentation to our office, after hospitalization. Spironolactone, metoprolol, and potassium had been started at the outpatient hospital for refractory hypertension and hypokalemia.

Pathology

Upon initial physical examination, her blood pressure was 160/110 and her pulse was 110-120 and regular. Cushing habitus with facial and posterior cervical swelling was noted. Lungs were clear. Abdomen was slightly distended. No violaceous striae were noted. Lower extremities showed +1 pitting edema and multiple ecchymoses. Proximal muscle weakness was also appreciated. There were no neurologic deficits appreciated. Skin showed mild acne and facial hirsutism.

Clinical Outcome

Serum ACTH was undetectable on postoperative day one. Her hypokalemia, hyperglycemia, hypertension, edema, and psychosis all resolved within one week. Muscle strength slowly improved over the next month. She remained on hydrocortisone replacement for six months post operatively and recently discontinued hydrocortisone.

References