

Pancreatic Neuroendocrine Tumor Presenting as a Cushing's Syndrome Associated with Hypertension

Chinedu Ivonye*, Ebere Okeke, Rohan Mankikar and Jolene Lowery

Department of Medicine, Morehouse School of Medicine, Atlanta, USA

Abstract

A young female was evaluated in the emergency department (ED) for persistent headache and fatigue one week after being started on antihypertensive therapy with poor response. Her medications were Amlodipine 10 mg daily, Hydrochlorothiazide 25 mg daily, Atenolol 100 mg daily and Hydralazine 50 mg three times daily. Further evaluation revealed cushingoid appearance, her blood pressure was 171/100 mmHg despite compliance with multiple antihypertensive therapy. Her clinical manifestation prompted the evaluation for secondary causes of hypertension with laboratory evidence of hypokalemia, hyperglycemia, hypercortisolism with high ACTH that did not respond to low and high dose dexamethasone suppression. A splice mutation in MEN 1 gene was found with the eventual diagnosis of metastatic pancreatic neuroendocrine tumor. Her turbulent course unravels how complex medical problems continue to masquerade as general medical ailments.

Abbreviations: ROS: Review of Systems; ACTH: Adrenocorticotropic Hormone; MEN: Multiple Endocrine Neoplasia; DHEA: Dehydroepiandrosterone; CA 19-9: Carbohydrate Antigen 19-9; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; FNA: Fine Needle Aspiration

Case Presentation

A 41 year old female with hypertension was evaluated in the ED for persistent headache and fatigue one week after initiating antihypertensives. She endorsed polydipsia, polyuria, nocturia, unintentional weight loss, blurry vision and hirsutism. ROS was not contributory. Family history was positive for hypertension and diabetes mellitus type 2 in her sisters, no malignancy.

Physical examination revealed BP of 171/107 mmHg, moon facies, central obesity, facial acne, hirsutism and pallor. She was anicteric with no oral ulcers or thyromegaly. Abdominal exam revealed striae and hepatomegaly. Both hands had acral muscle wasting and dorsal hyperpigmentation.

Significant laboratory findings included potassium of 3.0 MEQ/L, glucose 238 MG/DL, cortisol 50 MCG/DL. ACTH was 547 PG/ML and non-responsive to low and high dose dexamethasone suppression; elevated DHEA sulfate 555 MCG/DL and CA 19-9 of 44 U/ML. CT imaging revealed diffuse hepatic lesions, a pancreatic tail mass, splenic hypodensity, gastric mucosa irregularity, bilateral adrenal hyperplasia without focal nodularity, and a right lower lobe 3 mm soft tissue nodule. MRI brain showed no pituitary enlargement. FNA of the liver lesion revealed poorly differentiated carcinoma with neuroendocrine features (Figures 1 and 2). MEN 1 gene sequencing showed one copy of a splice mutation in MEN 1 gene. She was diagnosed with metastatic pancreatic neuroendocrine tumor. Chemotherapy was initiated and Cushing syndrome treatment was planned.

Clinical course was complicated by hypertension, hyperglycemia, hypokalemia, non-adherence, chemotherapy, and eventual spinal metastasis.

Case Discussion

Pancreatic neuroendocrine tumor (NET) is a rare neoplasm arising from pancreatic endocrine tissues with incidence of 1 in 100,000 per year, constituting 1-2% of pancreatic tumors. Risk factors include ages

40 to 60 and genetic syndromes (as in the case presentation) although most cases are sporadic. Functioning pancreatic NET are classified based on the predominant hormone they secrete. For example, our patient had an ACTHoma, in which the tumor secretes ACTH. The other types of pancreatic neuro endocrine tumors include glucagon

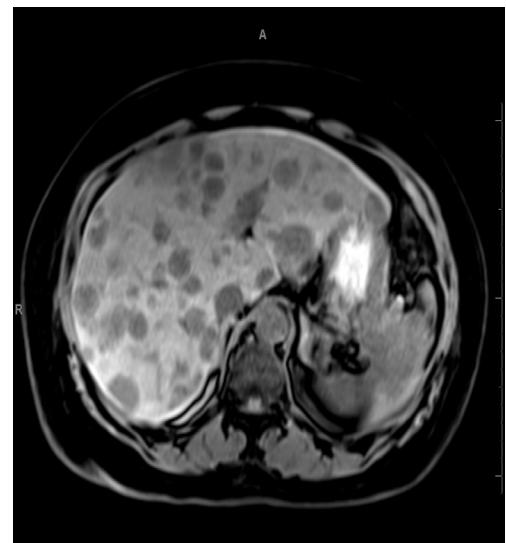


Figure 1: MRI abdomen at diagnosis showing pancreatic tail mass invading the spleen with multiple hepatic metastatic lesions.

*Corresponding author: Chinedu Ivonye, Associate Professor of Medicine, Morehouse School of Medicine, 720 Westview drive SW Atlanta, GA 30310, USA, Tel: 01 404 510 9919; Fax: 01 404 616 6201; E-mail: civonye@msm.edu

Received November 28, 2013; Accepted January 20, 2014; Published January 22, 2014

Citation: Ivonye C, Okeke E, Mankikar R, Lowery J (2014) Pancreatic Neuroendocrine Tumor Presenting as a Cushing's Syndrome Associated with Hypertension. J Hypertens 3: 132. doi:10.4172/2167-1095.1000132

Copyright: © 2014 Ivonye C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

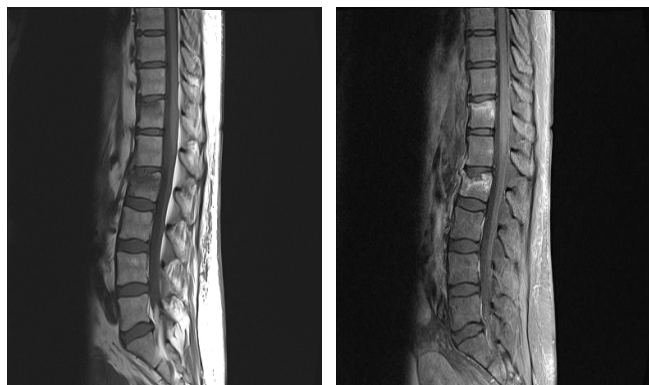


Figure 2: Spinal MRI before and after contrast obtained 22 months following diagnosis showing fracture in T 12 and L 2.

secreting Glucagonomas, Somatostatinomas, Insulinomas secreting insulin, gastrin producing Gastrinomas, vasoactive intestinal peptide secreting VIPomas and growth hormone secreting GRFomas [1].

The other manifestations of ACTHomas include weight gain, depression, skin pigmentations and recurrent infections due to ACTH mediated increase in steroids production. The importance was to emphasize a detailed history, physical examination and work up of common medical diseases. The diagnosis of Cushing's syndrome or disease should be considered when there is a constellation of symptoms and signs complex suggestive of diabetes existing with hypertension and hypokalemia [2]. The pancreas should be imaged to search for tumors when diabetes is associated with symptoms of muscle weakness, diarrhea and back or abdominal pain. It is important to note that

patients with rapid onset of Cushing's syndrome and weight loss in the setting of an elevated ACTH levels may have an ectopic source of ACTH production usually from small cell lung cancer [3].

The MEN type 1 mutation a risk factor for NET of the pancreas, the manifestations of MEN type 1 include tumors of the pancreas, parathyroid glands and the pituitary. The diagnosis of NET of the pancreas should lead to a high index of suspicion for tumors in the pituitary and parathyroid glands [4].

We present this case of rare pancreatic neuroendocrine tumor masquerading as Cushing Syndrome along with the primary presentation of hypertension and diabetes mellitus. This case emphasize the need to screen for secondary hypertension in those presenting with a diagnosis of hypertension early and late in life, also those with difficult to control hypertension as well as symptoms and signs of disease associated with hypertension should warrant screening for secondary hypertension.

References

1. Klöppel G, Perren A, Heitz PU (2004) The gastroenteropancreatic neuroendocrine cell system and its tumors: the WHO classification. *Ann N Y AcadSci* 1014: 13-27.
2. Reimondo G, Pia A, Allasino B, Tassone F, Bovio S, et al. (2007) Screening for Cushing's syndrome in adult patients with newly diagnosed diabetes mellitus. *Clin Endocrinol* 67: 225-229.
3. Nieman LK, Biller BM, Findling JW, Newell-Price J, Savage MO, et al. (2008) The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrine Metab* 93: 1526-1540.
4. Brandi ML, Gagel RF, Angeli A, Bilezikian JP, Beck-Peccoz P, et al. (2001) Guidelines for diagnosis and therapy of MEN type 1 and type 2. *J Clin Endocrinol Metab* 86: 5685-5671.