

Ectopic ACTH secreting pheochromocytoma, a case study.

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Abstract

Ectopic ACTH syndrome is rarely caused by pheochromocytoma. We report a case of a 44-year-old woman with Cushing's syndrome due to ACTH-producing adrenal pheochromocytoma. The patient initially presented with diabetes mellitus, hypertension, muscular weakness and hirsutism. Laboratory examination revealed high ACTH 849 pg/ml and high cortisol 463 ng/ml (7-30). Abdomen CT revealed adrenal macro nodular hyperplasia. A high dose Dexamethasone test was performed; basal ACTH (16:00) 849 pg/ml, basal cortisol (16:00) 436 ng/ml, and after the suppression ACTH (8:00) 1330 pg/ml cortisol 557 ng/ml, Aldosterone 55.9 (42-201), Renin 7.5 ng/ml (3.6-20.1). The results suggested for Cushing disease. Ketoconazole was started 200 mg 2x2 and cortisol dropped to 223 ng/ml. Even though an ectopic ACTH production was suspected the head MRI revealed a microadenoma of 2.5 x 2.5 mm and a lesion of 3.3 x 3 mm in the hypophysis. In order to better understand the ACTH production site a CRH stimulation test was suggested. CRH stimulation inferior petrosal sinus sampling in the minute suggested for an ectopic ACTH production. Chest MRI revealed no tumors. PET CT revealed a metabolic activity in the hypophysis, an hypodense lesion measuring 46 x 20 mm on the right adrenal and high metabolic rate in the left adrenal. Near the left adrenal a soft tissue lesion measuring 60 x 20 mm with a high metabolic rate is observed. Inferiorly a lymphonodule measuring 13 x 12 mm with focal metabolic activity. The patient underwent left adrenalectomy with asportation of the inferior lobe of the left kidney. Mixed pheochromocytoma and adrenal cortical adenoma (corticomedullary adenoma) were disclosed by immunohistochemical stains. After surgery diabetes and hypertension treatment was no longer needed, ACTH levels dropped to 25.9 pg/ml (8-65) but hydrocortisone treatment was necessary.

Keywords: pheochromocytoma, ACTH, ectopic, Cushing

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INTRODUCTION

Ectopic ACTH syndrome represents a tumor-induced amplification of a property [proopiomelanocortin (POMC) peptides production] normally present in the cells from which the tumor originated but with aberrant posttranslational processing of POMC resulting in a greatly elevated secretion of ACTH precursors (1). Localizing the tumor is not always an easy task. With the advance of science, imaging technics have advanced. They initially started with X-rays to evolve in computed tomography and magnetic resonance of the chest and abdomen. Finally, somatostatin receptor scintigraphy permitted demonstration of unrecognized tumors and/or metastases, even when the tumors were occult. Of great relevance was the immunostaining in the ectopic tumors and/or metastases. Cushing syndrome caused by pheochromocytoma is a rare condition. Only a few cases are reported in the literature (2-4). In most cases the ectopic ACTH is associated with lung carcinomas. Symptoms and signs in pheochromocytoma and Cushing are not always specific and typical clinical features may be absent in some cases.

CASE REPORT

A 44-year-old woman initially presented with diabetes mellitus, hypertension, muscular weakness and hirsutism. Cushing syndrome was suspected. Laboratory examination revealed high ACTH 849 pg/ml (normal range 8-16 pg/ml) and high cortisol 463 ng/ml (normal range 55-130 ng/ml). Abdomen CT revealed adrenal macro nodular hyperplasia. A high dose Dexamethasone test was performed; basal ACTH (16:00) 849 pg/ml and basal Cortisol (16:00) were 436 ng/ml (normal range 7-30 ng/ml), after dexamethasone suppression ACTH (8:00) 1330 pg/ml (normal range 8-65 pg/ml) and cortisol 557 ng/ml, Aldosterone 55.9 (normal range 42-201), Renin 7.5 ng/ml (normal range 3.6-20.1) resulting positive for Cushing disease. Treatment with ketoconazole was started, 200 mg 2x2. After the treatment cortisol dropped to 223 ng/ml. Even though an ectopic ACTH production was suspected the head MRI revealed a microadenoma of 2.5 x 2.5 mm and a lesion of 3.3 x 3 mm in the hypophysis. In order to better understand the ACTH production site a CRH stimulation test was suggested. CRH stimulation inferior petrosal sinus sampling suggested for an ectopic ACTH production. Chest MRI revealed no tumors. PET CT revealed a metabolic activity in the hypophysis, an hypodense lesion measuring 46 x 20 mm on the right adrenal and high metabolic rate in the left adrenal. Near the left adrenal a soft tissue lesion measuring 60 x 20 mm with a high metabolic rate is observed. Inferiorly a lymphonodule measuring 13 x 12 mm with focal metabolic activity. The patient underwent left adrenalectomy with asportation of the inferior lobe of the left kidney and of the lymphonodules. Mixed pheochromocytoma and adrenal cortical adenoma (corticomedullary adenoma) were disclosed by immunohistochemical stains. After surgery diabetes and hypertension treatment was no longer needed, ACTH levels dropped to 25.9 pg/ml (8-65) but hydrocortisone treatment was necessary.

CASE DISCUSSION

Pheochromocytomas originates from chromaffin cells in the adrenal medulla and extra-adrenal paraganglial regions. Several cases have reported their association with ectopic production of a wide variety of hormones or cytokines, including ACTH, adrenomedullin, and IL-6 (5). We presented a case of Cushing syndrome caused by an ATCH secreting pheochromocitoma. Step by step protocols were followed until a diagnosis was set. After

surgery and the exportation signs and symptoms improved and only hydrocortisone replacement treatment is necessary. To our opinion an ACTH-secreting pheochromocytoma should be checked for in patients with an adrenal mass and elevated ACTH levels.

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