Ectopic production of ACTH in the adrenal medulla (case report)

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Introduction

Ectopic Cushing Syndrome (ECS) is a rare neuroendocrine disorder, representing about 5-20% of all cases of Cushing's syndrome. ACTH-secreting neuroendocrine neoplasms are usually localized in the thymus, lungs, or gastrointestinal tract, but are rare in the adrenal glands.

We would like to present a clinical case of ECS with possible localization in the adrenal medulla.

Clinical case

Female patient M., 64 years old, noted a prompt progression in muscle weakness, leg cramps, edema of the lower extremities, confusion, and an increase in blood pressure up to 220/110 mm Hg for two months, no other signs of hypercortisolism. Therapist and cardiologist did not found explanation of the clinical symptoms and redirected a patient to an endocrinologist.

Established diagnosis

- laboratory diagnosis (Tab.1)
- MRI of the brain and CT of the adrenal glands, no lesions were identified
- CT scan of the neck, chest, abdominal and pelvic organs was performed, a focal lesion 9x6mm was found in left lung

COVID-19

- Bilateral pneumonia affected <25%(CT)
- Without fever and catarrhal symptoms

Surgery treatment

- Bilateral adrenalectomy according to vital indications

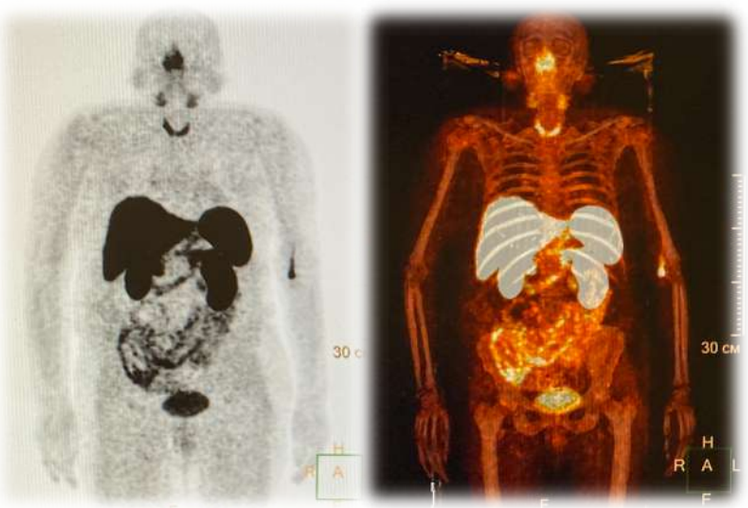
Search for ACTH ectopia

- PET-CT with 68Ga-DOTA-TATE was performed aimed to find the primary focus of ACTH ectopic secretion.

	Before surgery	After surgery	Reference range
K+ (mmol/l)	<1,9	4,4	4,0-5,2
Urine cortisol excretion (nmol/l)	7364		57,7-806,8
Cortisol 8.00 (nmol/l)	3533,16	<11,8	101-536
ACTH 8.00 (pmol/l)	124	35	1,6-13,9
ACTH 23.00 (pmol/l)	95,7	18,2	1,6-13,9

Table 1. Laboratory parameters

Figure 1,2. PET-CT with 68Ga-DOTA-TATE, 6 months after bilateral adrenalectomy



Pathologic histology *examination, diffuse hyperplasia of the fascicular zone of the cortical layer of both adrenal glands was revealed.*

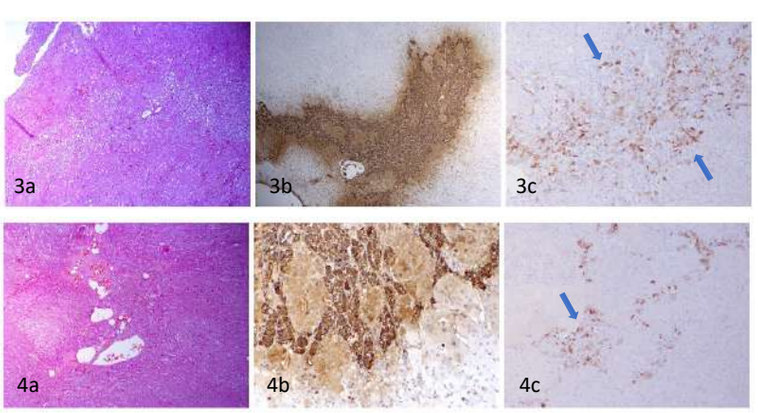


Figure 3 (a,b,c) *Medulla of right adrenal gland;* ***Figure 4 (a,b,c)*** *Medulla of left adrenal gland; a - hematoxylin* ***b -*** *Expression of chromogranin A;* ***c -*** *ACTH-producing cells*

Six months after bilateral adrenalectomy, the blood ACTH level decreased significantly, which indicated a possible focus of ACTH ectopia in removed adrenals. ***An immunohistochemical (IHC)*** *study demonstrated diffusely distributed ACTH-producing cells in the medulla of both adrenal glands (see Fig. 3-4b,c). Thus, we suggested that the adrenal glands were the source of ACTH-ectopic secretion.* We continue the patient's follow up.

Conclusion. In this case, severity of clinical symptoms and the COVID-19 infection could not allow to carry out all diagnostic procedures before treatment and bilateral adrenalectomy was performed. However, significant drop of ACTH concentrations after surgery as well as postoperative PET-CT results allow to hypothesize that the ectopic source of ACTH secretion was in adrenals. ACTH concentrations slightly above upper normal level can be explained as a physiological reaction to primary adrenal insufficiency.

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