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CASE REPORT

AN ECTOPIC ACTH PRODUCING LUNG CARCINOID

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ABSTRACT

We present a case of a 45 years old woman who presented with a complaint of progressive obesity, hirsutism, easy bruisability, muscle weakness, episodes of hot flashes and diaphoresis and was diagnosed with ectopic Cushing syndrome secondary to neuroendocrine tumor (lung carcinoid). We summarized diagnostic methods and the difference between Cushing and ectopic Cushing. We also discussed a very rare case of PTH (parathyroid hormone) secretion from this tumor (lung carcinoid).

INTRODUCTION

Cushing syndrome often represents a diagnostic challenge especially at early stages. Some of the early clues of Cushing such as hypertension (HTN), glucose intolerance and obesity are unfortunately common in our society and thus not very useful in diagnosis. Neuroendocrine tumors (NETs) which include carcinoids are a rare cause of ectopic Cushing syndrome and have been well discussed in the literature.

Case presentation

A 45-year-old woman came to the Endocrinology clinic with a complaint of progressive obesity gaining 15kgs centered in the abdomen during the last year, changing facial features three years ago, hirsutism (increased hair especially on the upper lip, under the chin, lower abdomen and upper back),easy bruisability even due to minor trauma, episodes of hot flashes and diaphoresis(excessive sweating) and muscle weakness characterized with difficulty in walking upstairs and when standing up from sitting position. She also suffered from skeletal pains without fractures, fever or lymphadenopathy. Our patient is a married woman, working as a clerk in the opera, smoker (1pack/year) and not alcohol dependent.

She has HTN discovered 2 years ago, no diabetes mellitus nor ischemic heart disease. She has no history of drugs usage except for analgesics. She had three caesareans and a hysterectomy with left ovary removal due to a 9cm leiomyoma.

Her vital signs were as follows: Blood pressure: 180/70 mmHg in both sides, pulse rate: 80/min, respiratory rate: 16/min, O2 sat: 98%. Her weight was 79 kg and her BMI was 32.8 kg/m2.

The physical examination showed purple cheeks, moon face, acanthosis nigricans, hyperpigmentation in the hand knuckles (Figure 1) , painless reddened skin under breasts, caesarean section scar and purple striae 1 cm wide on the abdomen, and proximal muscle weakness in both legs on neurological exam.

Potassium	3.01	3.5-5 mmol/l
Calcium	8.04	8.6-10 mg/dl
Phosphorus	1.9	2.6-4.5 mg/dl

Table - 1

Cortisol11 P.M	20.18 mcg/dl(< 7.5)[1]
Cortisol 8 A.M post 1mg DEXA	24.36 mcg/dl(< 1.8)[1]

Table - 2

25-OH vitamin D	**8.1** ng/ml NL (> 20)
PTH	**232**pg/ml NL(15-65)

Table - 3

DISCUSSION

Our patient's abnormal initial tests included those in table 1. (Normal tests were not included). According to the clinical examination, we suspected that our patient had hypercortisolism therefore; specific tests were done as shown in table 2. After Initial evaluation, we suspected for vitamin D deficiency and tests shown in table 3 confirmed it.

CS diagnosis is made by one of the following tests: 24h urine free cortisol, an overnight 1mg dexamethasone suppression test (ODST) or (two or more) late night salivary cortisol tests. [1] Any of the previous tests should be done after exclusion of exogenous cortisol exposure.

Plasma ACTH levels differentiate ACTH dependent (pituitary, ectopic ACTH and CRH producing tumors) from ACTH independent causes (adrenal gland tumors or hyperplasia) [2]. Our patient ACTH value was 139.3 pg/ml

A plasma ACTH level less than 5mg/dl with high serum cortisol level indicate an independent cause, while an ACTH level >10 pg/dl indicates a dependent cause regardless of cortisol level. [2] An 8mg ODST is used to differentiate pituitary from Ectopic Cushing. [1] Persistently high cortisol levels after 8mg ODST are suggestive of an ectopic tumor because ACTH secretion from most adenomas is suppressed by high glucocorticoids doses (8mg ODST). [1] Our patient cortisol level after the test was 33.46 mcg/dl. Ectopic Cushing is a disorder characterized by excessive secretion of cortisol due to a tumor producing high levels of ACTH outside the pituitary gland. [3]

Ectopic ACTH secreting tumors are rare and represent 8-18% of all CS causes.[11].The small cell lung carcinoma (SCLC) along with other NETs such as bronchia, thymic and pancreatic represent the commonest ACTH producing tumors.(doctor study) Ectopic Cushing usually has less symptoms than the classic Cushing does. [3]

Carcinoid tumors are slow growing NETs tumor. They arise from the small intestine, the rectum, bronchial system of the lung, appendix, stomach, pancreas, liver in 39%, 15%, 10%, 7%, 2-4%, 2-3%, 1% cases, respectively and rarely in the ovaries, testicles and other organs. [4]

These tumors produce hormone like substances and grow slowly for many years without any symptoms. Gastrointestinal tumors do this more commonly than lung tumors. [4] Lung carcinoid tumors are divided into Typical (TC) and Atypical (AC). [4]

Radiological tests included a chest X-ray was performed for the patient as shown in (figure A- figure 2) then a multi slice computerized tomography (MSCT) as shown in figure 2 revealed a solitary pulmonary nodule measuring 1.3cm in the base of the left lung and hyperplasia in both adrenal gland (compatible with suspected Cushing).

One of the most important markers of carcinoid tumors is the Chromogranin A test [5].In our patient its value was 4.1 nmol/L (normal range up to 3 nmol/L)

TREATMENT

The lung tumor was surgically removed under general anesthesia by posterior lateral intercostal entrance. A drainage tube was placed in the left side after surgery and was removed in the day after without any complications. Our patient was put on hydrocortisone after surgery and the serum cortisol level at 8am after surgery by 3 days and 24 hours hydrocortisone cessation was 0.9 mcg/dl. There is no consensus on the criteria for remission after resecting an ACTH-producing tumor.

In two pediatric series using a strict criterion for remission post-TSS serum cortisol of <1 mcg/dL[6] or <1.8 mcg/dL[7], remission rates were 100 and 69%, respectively. The pathological report confirmed the diagnosis of carcinoid tumor by strongly chromogranin staining and ectopic Cushing was confirmed by positive ACTH staining as shown in figure 3.

Ki-67 is a nuclear protein strictly associated with cell proliferation. The Ki-67 is divided into three grades used for NETs classification: low<3%, and intermediate 3-20% and high>20 %. [8] Figure 4 our patient Ki-67 value (5%) revealed that the tumor is of an intermediate grade.

After confirming remmision we tested parathyroid hormone(PTH) in the 5th day after surgery because of suspesion of ectopic PTH secretion (vitamin D replacement was made just before one week) we surpreised that PTH declined to 37 pg/ml in such a time Secondary hyperparathyroidism usually resolves after 2-4weeks after vitamin dreplacement [9] and may continue for weeks to months.[10] We couldn't confirm our

suspision by performing PTH staining because it is unavailable at our lab, such cases for ectopic PTH secretion are extremely rare and some of them reported the same case such as[12]

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCES

1. Nieman LK, Biller BM, Findling JW, 2008. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab; 93:1526–1540.

2. Coe SG, Tan WW, Fox TP, 2008. Cushing's syndrome Due to Ectopic Adrenocorticotropic Hormone Production Secondary to Hepatic Carcinoid: Diagnosis, Treatment, and Improved Quality of Life. Journal of General Internal Medicine.;23(6):875-878

3. Gut P, Czarnywojtek A, Fischbach J, 2016. Chromogranin A – unspecific neuroendocrine marker. Clinical utility and potential diagnostic pitfalls. Archives of Medical Science : AMS. 12(1):1-9.

4. Magiakou MA, Mastorakos G, Oldfield EH, 1994**.** Cushing's syndrome in children and adolescents. Presentation, diagnosis, and therapy. N Engl J Med. 331:629–636.

5. Storr HL, Alexandraki KI, Martin L, 2011. Comparisons in the epidemiology, diagnostic features and cure rate by transsphenoidal surgery between paediatric and adult-onset Cushing's disease. Eur J Endocrinol.; 164:667–674.

6. Bosnen F, Carneiro F, Hruban RM, 2010. WHO-Classification of Tumors of the Digestive System. Lyon, France: IARC Press.

7. F. Richard Bringhurst, Marie B. Demay, Henry M, Kronenberg, 2016. Hormones and Disorders of Mineral Metabolism. Williams Textbook of Endocrinology. 13th Ed. Philadelphia, Pa: Elsevier Saunders; Chap 28. 1315-131710-

8. Haden ST, Stoll AL, McCormick S, 1997. Alterations in parathyroid

dynamics in lithium treated subjects. J Clin Endocrinol Metab ; 82:2844.)

9. Thomas Dacruz, Atul Kalhan, Majid Rashid, Kofi Obuobie, 2015. An Ectopic ACTH Secreting Metastatic Parotid Tumour. Jmpas - V04-I10, 404-414.

10. Kandil J, Emad M, 2011. A Case Report Ectopic secretion of parathyroid hormone in a neuroendocrine tumor : a case report and review of the literature; 4(3):234–40.