Review Article

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Cushing syndrome in a 55-year-old case of small-cell lung cancer

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ABSTRACT

Lung cancer is one of the most fatal types of cancer and paraneoplastic syndromes are commonly associated with lung cancer. Paraneoplastic Cushing can be associated with different types of tumors, especially small cell lung cancer (SCLC). The aim of this report was to describe the status of a patient presenting with progressive weakness, who did not have a previous medical history. Clinical examination revealed bilateral edema of the lower limbs. Lab results exhibited severe hypokalemia and metabolic alkalosis. physical examination showed elevated blood pressure. Imaging revealed a large mass with necrosis. Bronchoscopy was done and biopsy pathology showed SCLC. The patient underwent chemotherapy with cisplatin and etoposide. Following SCLC, the patient developed a type of paraneoplastic syndrome called Cushing syndrome. He experienced a severe decrease in saturation in the second session of chemotherapy and eventually died. With respect to the fact that most paraneoplastic syndromes are associated with poor response to treatment, high clinical suspicion is essential for the rapid diagnosis of these syndromes to improve outcomes.

Keywords: Small Cell Lung Cancer; Paraneoplastic; Cushing Syndrome

INTRODUCTION:

Lung cancer is the most common type of cancer with an unfavorable prognosis. SCLC, which accounts for 12-19% of lung cancers, is a deadly tumor that is on the rise [1]. Among different types of lung cancer, SCLC is distinct because of its rapid rate of cell proliferation, short doubling time, and tendency to metastasize early. Most patients are in a condition that indicates disease progression [2]. According to estimates, 1-7.4% of patients with cancer will develop paraneoplastic syndrome. Paraneoplastic syndromes are a heterogeneous group of clinical syndromes characterized by a recognizable set of signs and symptoms in a patient in association with neoplastic disease [2].

It is estimated that 4.5% of SCLC patients develop ectopic Cushing syndrome. Chronic exposure to excess glucocorticoids leads to Cushing syndrome [3], which is associated with systemic manifestations such as abnormalities in glucose and lipid metabolism, hypertension, and the classic appearance of cushingoid. Cushing syndrome is also known as a rare cause of dilated or hypertrophic cardiomyopathy and heart failure with reduced ejection fraction [4]. It can be associated with a variety of tumors, a significant proportion of which are SCLC and bronchial carcinoid tumors [3]. We report a patient presenting with progressive weakness, bilateral edema of the lower limbs, and severe hypokalemia, who was found to have Cushing syndrome followed by SCLC.

Case presentation:

The case was a 55-year-old male smoker patient, without a past medical history complaining of fever and chills, diarrhea, and occasional cough who recovered after an outpatient visit to the doctor and treatment with oral metronidazole. After a few days, the patient went to the hospital emergency department because he was suffering from severe generalized weakness and dyspnea, so that he was not able to easily perform daily activities. Blood test showed that the potassium level was 1.5 mg/dl (normal range: 3.5-5 mg/dl) [3]. Despite medical' advice to pursue treatment, the patient had left the hospital after receiving a dose of potassium with personal consent. Due to the persistent progressive weakness, the patient referred to our medical center. Preliminary examinations at the beginning of the visit showed that the patient suffers from bilateral edema of the lower extremities. Accumulation of supraclavicular fat was also evident. On physical examination he had a high blood pressure of 170/110 mmHg and the skin (NL) and muscle force of the upper and lower limbs (NL). Laboratory results were shown in Table 1. Laboratory data revealed hypokalemia of 1.4 mg/dl and metabolic alkalosis with a bicarbonate of 50 mEq/L (normal range: 22-28 mEq/L) [3].

Due to severe hypokalemia, the patient was injected first through a peripheral vein and then through a central venous catheter. The amount of potassium eventually reached 3.3 mg/dl. Complete abdominal and pelvic ultrasounds showed mild bilateral hydronephrosis. Due to high blood pressure and hypokalemia, the patient was evaluated for hyperaldosteronism and Cushing syndrome. With respect to the high value of low dose overnight dexamethasone suppression test (46.2), a brain MRI, and a high dose overnight dexamethasone suppression test were requested after consultation with endocrinologists. Brain MRI showed partial empty Sella.

Table 1. Laboratory results of Cushing syndrome that show hypokalemia and metabolic alkalosis

Test	Ca	P	Mg	CPK	LDH	ALB
Level	8.3 mg/dl	2.5 mg/dl	1.7 mg/dl	2.5 mmol/L	894 U/L	3.3 g/dl
Test	K	Na	Cr	pH	PCO2	HCO3
Level	1.4 meq/l	142 meq/l	1 mg/dl	7.6	52.7 mm Hg	50 mmol/L

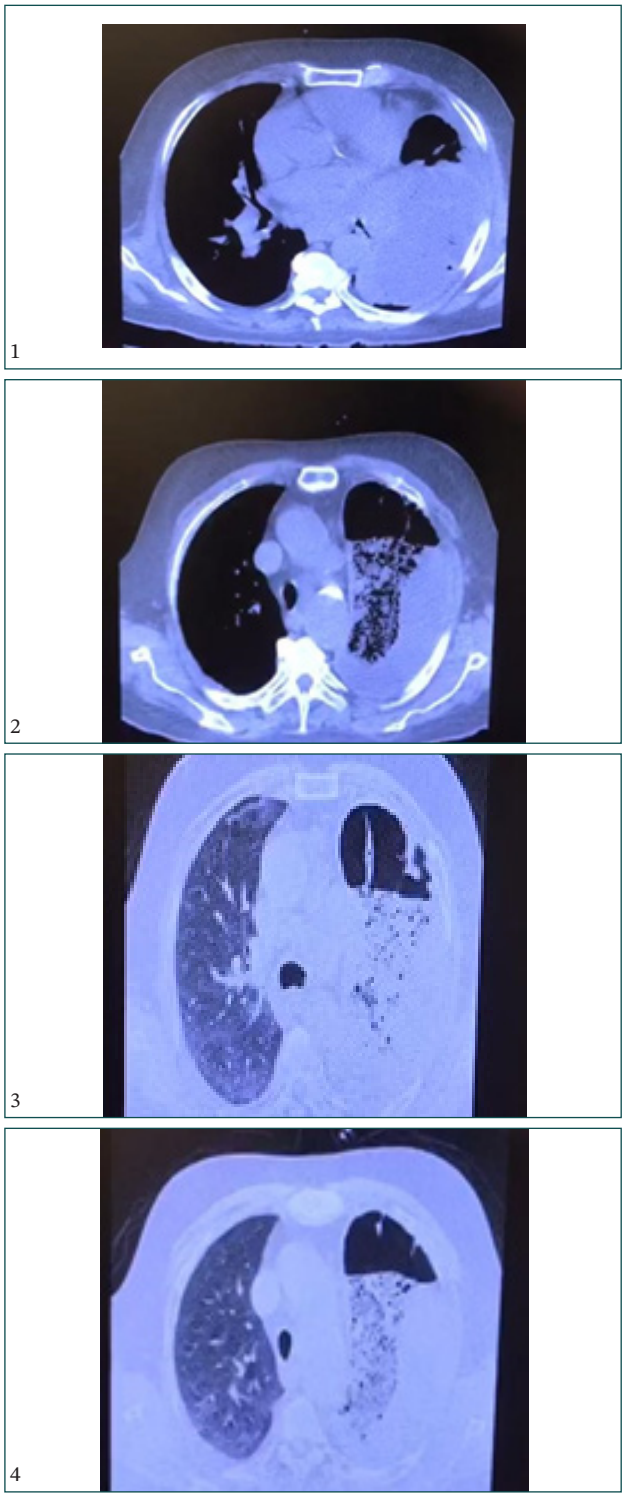

Figure 1. Mediastinal view (1&2) and Parenchymal view (3&4) in Lung CT Scan which show Necrotic mass in the upper lobe of the left lung with endobronchial involvement

Due to the disturbed status of high dose overnight dexamethasone suppression test, Lung CT and abdominal and pelvic CT were performed with contrast (Figure 1). The image of the hypodense foci in the left adrenal gland with enhancement after contrast, reported to be 58 * 38 * 33, which led to the recommendation for CT with adrenal protocol. Several small hypodense foci with a maximum diameter of 5 mm were seen in the left lobe of the liver. Lung CT also showed a necrotic mass in the upper lobe of the left lung with endobronchial involvement and the patient was candidate for bronchoscopy. Mucosal thickening and narrowing in LMB and vegetative mass in LUL were seen on bronchoscopy. Then, a biopsy was taken from the mass and sent for pathology. The pathology response of the bronchial biopsy specimen revealed SCLC. According to hematology and oncology consultation, chemotherapy with cisplatin and autoposide was started for the patient. After the second session of chemotherapy, the patient experienced a severe drop in saturation. As a result, the patient was intubated and connected to a ventilator. The next day, the patient died after two CPR cycles following cardiac and respiratory arrest.

Discussion:

According to the results of this study, the patient developed Cushing syndrome and did not respond to treatment. Ectopic Cushing syndrome has the worst prognosis for SCLC because it occurs in the advanced stages of the disease and responds poorly to chemotherapy. Paraneoplastic syndrome also increases susceptibility to opportunistic infections and sepsis by suppressing the immune system, and increases thromboembolic events due to hypercoagulable state [5]. In a case-series study [3], three cases of paraneoplastic syndrome were reported, including a 46-year-old woman and two men aged 51 and 41, all of whom were smokers and died several months after diagnosis. The first case had hypertension, hypokalemia, hyponatremia, metabolic alkalosis, and right lung mass with locoregional lymphatics. The second case suffered from mild leukocytosis, hypokalemia and metabolic alkalosis while Positron emission tomography (PET) scan showed 2 enlarged anterior medias-

tinal lymph nodes. The third case showed hypochloremic metabolic alkalosis and severe hypokalemia that was persisted despite potassium replacement. Imaging revealed bilateral pleural effusion, and multiple mediastinal lymph nodes. Another case report study [1] described two smoker patients with diabetes mellitus while there were no classical symptoms of lung cancer. The diagnosis in both cases was SCLC with Ectopic adrenocorticotropic hormone (ACTH) syndrome (EAS). The mentioned study suggested that SCLC may begin with diabetes and increased cortisol and hypokalemia or other EAS symptoms. A study in Japan [6] on a 53-year-old man showed that ectopic Cushing syndrome can develop during effective chemotherapy for SCLC. Although the patient's symptoms were controlled, his early cancer progressed and he died 5 months after starting chemotherapy. In a study about a 67-year-old male patient with hypertension, diabetes mellitus and long history of smoking, severe hypokalemia and hyperglycemia, along with tumor lesions of the right lung, liver and bilateral adrenal glands were revealed. Liver biopsy confirmed SCLC. This case suggested that severe hypokalemia with excessive cortisol in combination with short-term illness should be suspected for ectopic Cushing syndrome [7]. Some paraneoplastic syndromes can appear both as a unique primary disease and as paraneoplastic syndrome due to a malignant disease process [8]. By recognizing paraneoplastic syndromes related to different types of cancers, we can provide an opportunity for early diagnosis and intervention. The challenge, however, is that the clinical manifestations of patients can be very wide [9,10].

Conclusion:

Regardless of whether the tumor was detected at the time of diagnosis or not, it is better to consider the possibility of Cushing syndrome in the condition of hypertension, hypokalemia and electrolyte disturbance especially in smokers to assist in early detection and rapid management to improve outcomes.

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