Uncommon Presentation of An Uncommon Malignancy

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ABSTRACT

Introduction: Ectopic ACTH syndrome is a rare cause of cushings syndrome accounting for about 15% of all cases of cushings syndrome. Small cell lung carcinoma and bronchial carcinoid are the common cause of Ectopic ACTH syndrome. Surgery is the treatment of choice for Ectopic ACTH syndrome.

Case report: A 40 year old hypertensive male presented to the hospital with chief complaint of pain in both lower limbs and inability to get up from squatting position since 3 months. On evaluation the patient is found to have Cushing's syndrome with a mass in the lower lobe of left lung as source of ACTH. Biopsy of the mass revealed it to be bronchial carcinoid.

Conclusion: The case is reported in view of very low incidence of bronchial carcinoid and its rarity to present with features of cushings syndrome without any respiratory manifestations.

Keywords: Pain in lower limbs, ACTH, lung mass, Cushing's syndrome, Bronchial carcinoid.

INTRODUCTION

Cushing's syndrome refers to symptom complex resulting from excess steroid harmone production by adrenal gland.[1] The causes for excess steroid production can be in pituitary gland, adrenal gland or an ectopic site. Ectopic ACTH syndrome results from autonomous ACTH production from extrapitutary malignancies accounting for about 15% of all causes of cushings syndrome. Small cell carcinoma of lung and carcinoids account for majority of causes of Ectopic cushings syndrome.

The common clinical features of cushings syndrome are Moon facies, Buffalo hump, Central obesity, Diabetes mellitus, Hypertension, Purplish striae, Proximal myopathy and Electrolyte imbalances.[2] Chronic excess of cortisol in the body is associated with life threatening infections.

Localisation of the Ectopic site of ACTH is a diagnostic challenge. It has been reported that about 50% of Ectopic ACTH syndrome are undetectable by CT and MRI.[7] FDG PET scan offers higher spatial resolution for detection of small lesions but its results are dependent on the tumor metabolism.[8]

CASE REPORT:

A 40 years old male known Hypertensive since 1 year on Tab Telmisartan 40 mg OD presented to internal medicine OPD with chief complaint of Pain in both calf muscles and inability to get up from squatting position since 3 months. He is a non smoker, occasional alcoholic (weekly twice). For the above complaints he was admitted in another hospital found to have hypokalemia, symptomatic treatment was given and discharged.

O/E: The patient was obese (BMI: 27), with acanthosis nigricans and proximal myopathy. Blood pressure: 150/ 90 mm hg. Other systemic examination was in normal limits.

During the hospital stay, routine laboratory tests revealed severe hypokalemia (k+ 2.7), Hb: 14.5 gm /dl TC: 12000, ESR: 16mm/ hr, AST: 35, ALT: 37, HbA1C: 7.2%, Creatinine: 0.8, ECG, 2DECHO and CXR were in normal limits.

As the patient had refractory hypokalemia with urinary spot potassium (35.18) , HTN, type 2 DM and proximal myopathy cushings syndrome was considered as one of the differentials and serum cortisol (6 am) was sent. Serum cortisol 6 AM: 43.38 that persisted to be high even after low dose of dexamethasone (1mg) the prior night. So a diagnosis of cushings syndrome was made and Serum ACTH levels were sent. ACTH was high (131) which favoured the diagnosis of ACTH dependent cushings syndrome.

To identify the source of ACTH production (Pituitary or Ectopic) an MRI brain (Figure-1) and high dose dexamethasone suppression test were done, which were in favour of Ectopic ACTH production. An FDG PET scan is done to localise the site of ectopic ACTH production that revealed a 6X5X4 cm (Figure-2) lobulated heterogeneously enhancing mass in the lower lobe of left lung parenchyma. Endoscopic ultrasound guided biopsy of the lesion (Figure-3) revealed it to be malignancy, with the aid of immunohistochemistry (Figure-4) it was proven to be Carcinoid.

	Serum cortisol
Initial	43.38
Low dose dexamethasone supression	58.95
High dose dexamethasone supression	76

DISCUSSION

The syndrome of Ectopic ACTH Secretion which relates to source other than pituitary or adrenals is rare. WH Brown first described it in 1928 as Diabetes of Bearded Women in a patient suffering from oat cell lung carcinoma.[3] The definition of the syndrome was established by Meadar and Liddie in 1962 who were the first to demonstrate biologically active ACTH in a lung carcinoid tumor.

The case repoted here is to emphasise the need of complete evaluation of patient presenting with hypertension and hypokalemia with Cushing's syndrome as one of the differential diagnosis.

In Cushing's syndrome hypetension and hypokalemia are attributed to mineralocorticoid like activity of cortisol but not due to excess mineralocorticoid. The local cortisol conversion to cortisone by the action of 11 beta-hydroxysteroid dehydrogenase is the rate limiting step for the mineralocorticoid activity of cortisol.When cortisol levels are higher the action of this enzyme is insufficient and mineralocorticoid effects appear.[6] Ectopic

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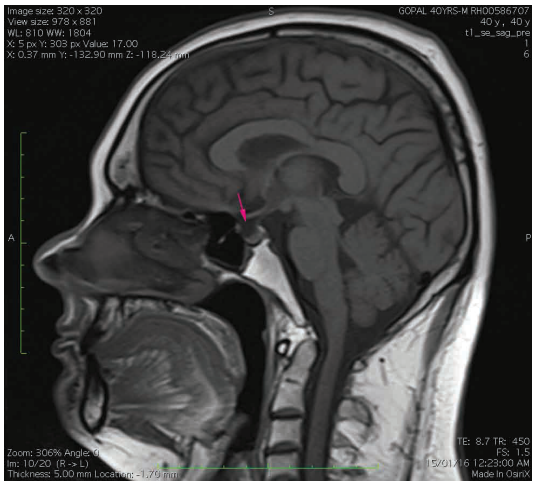

Figure-1: MRI of Pituitary (Arrow pointing normal pituitary)

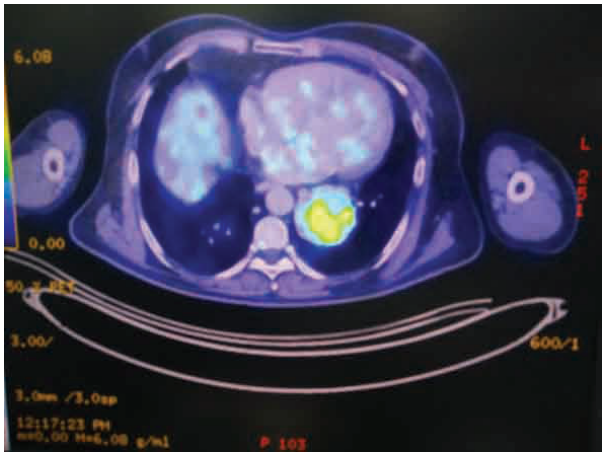

Figure-2 PET CT Showing Metabolically active Lesion in the left lower lobe of lung

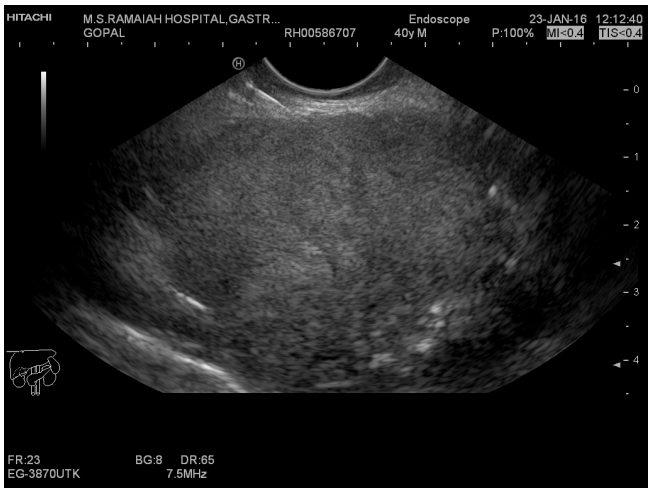

Figure-3: EUS showing A 6 X 5 cms lesion in the lung

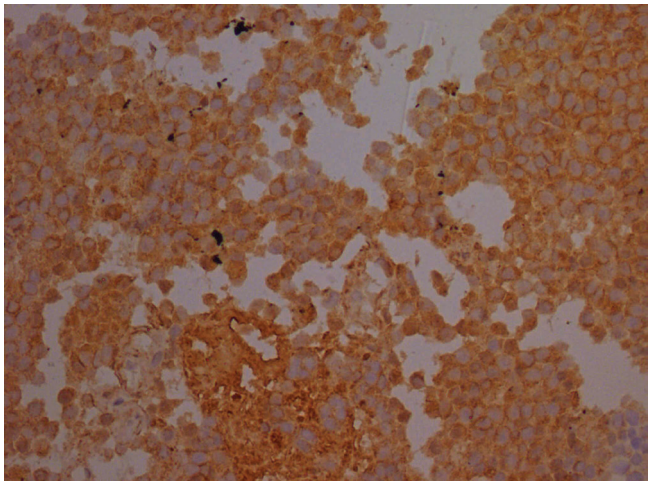

Figure-4: IHC suggestive of carcinoid tumor

Cushing's syndrome frequently presents a major diagnostic challenge. Ectopic source of ACTH production is located in the lungs in the majority of cases with small cell carcinoma and carcinoids being the commoner. Bronchial carcinoids account for about 10% of all causes of Ectopic ACTH syndrome. The incidence of bronchial carcinoids is 0.2 to 2 /100000.[1]

Diagnosing Ectopic ACTH syndrome is difficult as Dexamethasone suppression test and CRH stimulation test have a high false positivity. Recent data suggest Inferior petrosal sinus sampling to be the most accurate in the differentiation of pituitary from extra pituitary sources of ACTH.[4]

In our case diagnosis of Ectopic ACTH syndrome was made based on

a. High serum cortisol (43.38)
b. High serum ACTH (131)
c. Inability of high dose of dexamethasone to supress serum cortisol.
d. Normal MRI pituitary and CT abdomen(adrenals)
e. A 6X5 cm metabolically active lesion in lower lobe of left lung parenchyma.

Imaging modalities are the cornerstone of Ectopic ACTH syndrome because removal of the tumor is the only potential curative treatment. It has been described that in 30 % to 50% of patients with ACTH dependent cushings syndrome the source of ACTH could not be identified by conventional imaging like CT, MRI, PET, and SRS.[7,8]

The patient mentioned above was subjected to FDG PET scan in view of high suspicion of malignancy (Positive family history and Weight loss of 6kgs in 1 month). He was planned for surgical excision of the carcinoid but the patient lost to follow up.

Bronchial Carcinoid presenting with features of Cushing's syndrome without respiratory symptoms is rare. Most common presenting features are cough, hemoptysis, wheeze, dyspnea. About 1-2% of carcinoids manifest with features of Cushing's syndrome.[9,10] Excision of the tumor is the only potential curative modality.

CONCLUSION

The case is reported in view of rare occurrence of bronchial carcinoid and its rarity to present with features of Cushing's syndrome without any respiratory symptoms. By this case report we emphasise the need for complete evaluation of young hypertensives so that a treatable cause would not be missed.

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