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A rare case of Ectopic Cushing's syndrome from a Benign Thymoma

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ABSTRACT

Ectopic ACTH production leading to ectopic ACTH Syndrome (EAS) accounts for a small percentage of all Cushing's syndrome cases. Ectopic Adrenocorticotropic hormone (ACTH) secretion is primarily from small cell carcinoma and carcinoid of the lung, these two comprises half of cases [1], others are mostly from tumors of the thymus, and the pancreas [2] , therefore the majority of ectopic secretion cases originate from the lungs which make them the first place to be searched to find the ectopic spot. Here we present the case of a 30-year-old male who presented with complaints of generalized body swelling, increase in weight, facial puffiness, striae on both thigh. Clinical and laboratory findings were suggestive of Ectopic ACTH syndrome. CT scan of thorax revealed a soft tissue density lesion in anterior mediastinum suggestive of a benign thymoma. The main purpose is to present a case of ectopic Cushing's syndrome and show how thorough investigation, early diagnosis and careful management are crucial to reduce morbidity and mortality.

Keywords: ACTH Syndrome, Ectopic Adrenocorticotropic hormone

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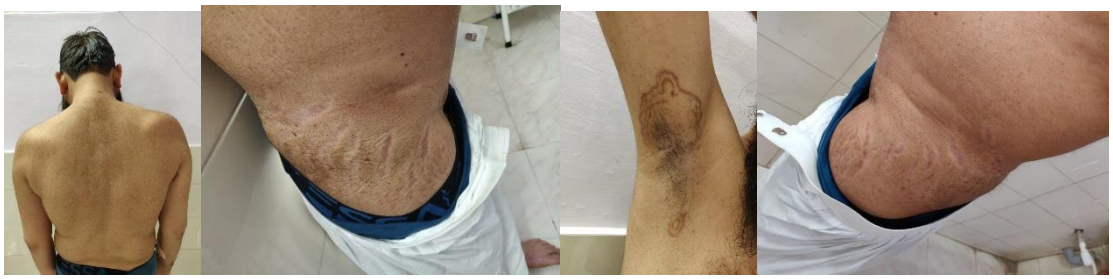
INTRODUCTION

Cushing's syndrome is a constellation of clinical features that result from excess of glucocorticoids in body. The incidence of endogenous CS varies from 0.2 to 5 cases per million per year, with a median age of onset around 41.4 years and a female preponderance in a 3:1 ratio [3]. Cushing's disease is further classified as ACTH dependent or ACTH independent. Cushing disease (CD) due to an ACTH-secreting pituitary adenoma are more commonly seen compared to ectopic ACTH syndrome (EAS), while corticotropin-releasing hormone producing tumors causing CS are exceedingly rare (<1%)[4]. Ectopic adrenocorticotropic hormone secretion (EAS) is responsible for 5–15% of all CS cases [5]. The major causes of EAS include small cell lung carcinoma, bronchial carcinoid, pancreatic tumor, thymic carcinoid, medullary thyroid cancer and non-small cell lung carcinoma [6]. Liddle and colleagues first described 'ectopic 'adrenocorticotropin' produced by nonpituitary neoplasms as a cause of Cushing's syndrome' in 1962 [7]. Once ACTH dependent Cushing's is confirmed, a negative high dose dexamethasone suppression test indicates Ectopic ACTH syndrome (EAS). As the clinical presentation of Cushing's is highly variable it makes the diagnosis challenging. It is crucial to find the source of ectopic ACTH and treat it in a timely manner.

CASE PRESENTATION

A 30 year old male, not a known case of any comorbidity, teacher by profession presented with complaints of generalized body swelling, weight gain, facial puffiness and striae on both thigh since the last four months. All the complaints were insidious in onset and gradual in progression. There was no significant past history or family history. He was not on any medication. On examination, patient was conscious, cooperative and well oriented to time, place and person. Blood pressure of the patient was 154/90 mmHg and random blood sugar was 280 mg/dl and post prandial blood sugar was 410 mg/dl. Chest Xray and echocardiography were within normal limits.



Following investigations were done:

Hb	13.6 gm/dl
Total counts	6200 cells per cu mm
Platelets	1.54 Lacs per cu mm
Urine Sugar	+3

Na	140
K	3.0
Cl	98
S creat	0.8
SGPT	34
HbA1c	7.8
Total Cholesterol	200
Triglycerides	128
LDL	133
HDL	40

Further the patient was investigated keeping in mind the clinical picture of Cushing's syndrome. A 24-hour urinary free cortisol excretion was raised, low dose DEX test was done after which serum cortisol levels were 36.31 µg/dl. Serum ACTH level were 155 pg/ml (7.2-63.6) and so the diagnosis of ACTH dependent Cushing's was confirmed. MRI brain with pituitary was normal and High dose DEX test was negative. Further as Ectopic ACTH syndrome (EAS) was suspected contrast enhanced computed tomography of abdomen was done which showed mildly bulky adrenal glands without any nodular lesion, cholelithiasis and left renal calculus. Contrast CT of thorax revealed a well-defined, heterogeneously enhancing, smoothly marginated soft tissue density lesion in anterior mediastinum measuring 19mm X 31mm possibility of benign Thymoma. Patient was managed symptomatically and advised for thymectomy.

DISCUSSION

Ectopic ACTH syndrome represents a minority of all cases of Cushing's syndrome [2]. With high ACTH level, ectopic ACTH syndrome (EAS) progresses with severe clinical deterioration. Delay in diagnosis and management leads to significant morbidity and mortality.

High-dose DST can be used to discriminate ectopic ACTH syndrome from classic Cushing's disease; a suppression of more than 50% of the basal cortisol level can be observed in more than 80% of patients with Cushing's disease [8]. However, the diagnostic utility of high-dose DST is limited, and this test is not recommended when IPSS is available [8]. IPSS can demonstrate the ratio of the ACTH level in the central sinus relative to the peripheral sinus. A central/peripheral ratio of 2 before the administration of corticotropin-releasing hormone and a ratio of ≥3 after its administration strongly suggests Cushing's disease [9]. Positive results are highly suggestive of Cushing's disease, but false negative results may be seen. In cases of a negative response, clinicians should perform a careful search for an ectopic source (10). In our case, high ACTH levels and a negative high dose DEX test directed the diagnosis towards ectopic Cushing's syndrome.

The source of ectopic ACTH secretion should be established after diagnosis because the excision of an ACTH-producing tumor can be curative [11]. The most likely site of ACTH-producing tumors is the thorax, and these tumors are frequently bronchial carcinoid tumors. Locating these tumors can be challenging; they are relatively small and slow-growing, and conventional imaging studies, such as CT and MRI, identify the tumor in only 50% of cases [12]. The tumor can remain occult long after the diagnosis of Cushing's syndrome [13]. The use of a single imaging tool may not be sufficient to diagnose ectopic ACTH-secreting tumors; conventional and functional imaging studies should be used in combination when needed [12]. In our case, the ectopic lesion was detected on contrast enhanced CT thorax.

CONCLUSION

We report this case of benign Thymoma associated with ectopic ACTH. Diagnosis of EAS is often difficult and requires multidisciplinary approach. Urgent surgical evaluation remains the mainstay of treatment following tumor localization and can result in a cure. EAS is a rapidly progressive and life-threatening situation that can be fatal if diagnosis or timely intervention is delayed [14].

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