A CASE OF SMALL CELL CARCINOMA WITH ECTOPIC ACTH SYNDROME

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ABSTRACT

We report a case of ectopic ACTH syndrome in a 50-year old woman with small cell carcinoma of the lung. Ectopic ACTH syndrome from small cell carcinoma often presents with hypokalemia, metabolic alkalosis and muscle wasting. This patient presented with Cushingnoid features which is unusual in such cases.

Keywords: Small cell carcinoma, Ectopic ACTH syndrome, Cushingnoid features, Hypokalemic alkalosis

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INTRODUCTION

Small cell carcinoma comprises 20% of all lung cancers (1). This cancer fascinates clinicians because of its unique behaviour, especially with regards to ectopic hormone secretion. Brown first described a patient with Cushing's syndrome from bilateral adrenal hyperplasia in 1928 in a patient with small cell carcinoma of the lung (2). The ectopic ACTH syndrome was described by Liddle in 1962 (2).

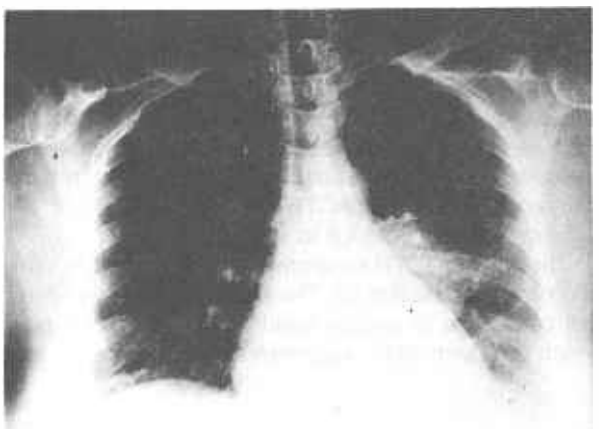
CASE REPORT

LPH, a 50-year old Chinese housewife was seen at the Department of Medicine, Singapore General Hospital on 16 June 1986 for dyspnoea and weakness in both lower limbs for a month. Diabetes mellitus was diagnosed by a private practitioner just prior to patient's presentation. A random blood sugar was 366 mg%. Patient had no past history of diabetes mellitus or bronchial asthma.

Clinical examination revealed typical cushingnoid features - facial flushing, mild hirsutism, truncal obesity and a very marked proximal myopathy involving both the upper and lower limbs. Patient was dyspnoeic at rest. Generalised expiratory rhonchi were present over both lungs. Examination of the abdomen, cardiovascular and central nervous systems were normal. Lymphadenopathy was absent.

Investigations revealed hypokalemic alkalosis, hypercortisolism and raised ACTH. Serum potassium was 1.7 mmol/l on admission. Blood gases showed metabolic alkalosis with a pH of 7.544, standard bicarbonate level of 30.7 mmol/l. There was loss of circadian rhythm of the 8 am and 12 midnight cortisol levels, the 8 am cortisol level being 31.6 ug/dl and the 12 midnight cortisol level being 32.9 ug/dl. The serum ACTH level was markedly raised to 569 pg/ml (N - 20 to 80 pg/ml). There was no evidence of inappropriate ADH secretion. The 24-hour urinary HIAA was 6.4 mg/day (normal). On chest X-ray, a mass lesion was seen in the left lower zone (Fig 1). CT Scan of the thorax revealed a tumour mass invading the left lung (Figs 2,3). Small cell carcinoma was confirmed by percutaneous lung biopsy. A CT Scan of the brain was normal.

Fig 1



The patient was treated with two courses of intravenous cyclosphosphamide 600 mg; methotrexate 40 mg; vincristine 1 mg and adriamycin 50 mg. The diabetes mellitus was controlled with insulin, and bronchodilators were prescribed for broncho-constriction. The diabetes mellitus and symptoms of broncho-constriction improved remarkably after the second course

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of chemotherapy. ACTH level after therapy was 169 pg/ml. Metastases to the lumbosacral spine was demonstrated on isotope bone scan following the patient's complaint of backpain. Patient subsequently refused further chemotherapy and was treated conservatively. Patient's condition deteriorated and she died on 14 October 1986.

Fig 2

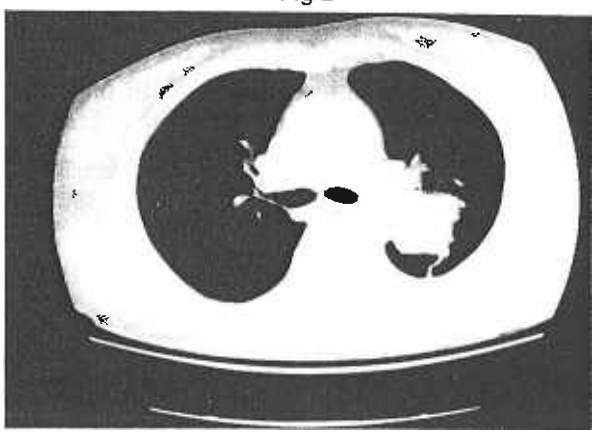
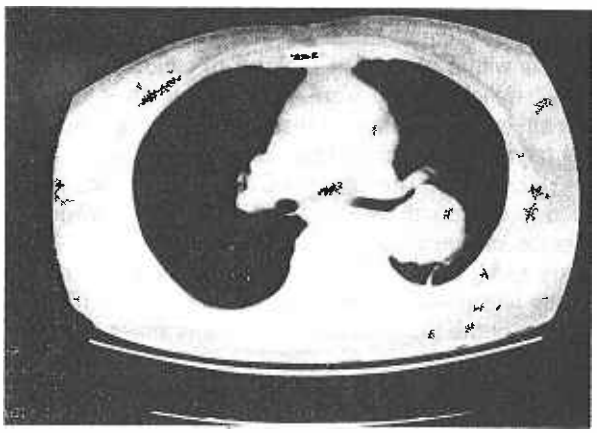


Fig 3



DISCUSSION

Most cases of ectopic ACTH syndrome are associated with small cell carcinoma of the lung (3). Other tumours producing a similar clinical picture include endocrine tumours of the foregut, phaechromocytoma, other adrenal tumours and some ovarian neoplasms. The relative frequency of ectopic ACTH production in small cell carcinoma varies from 4.8 to 19% (3).

The ectopic ACTH syndrome has two distinct patterns of clinical presentation (2). The type associated with small cell carcinoma is usually rapidly fatal. A second type, which is much less aggressive, is associated with bronchial or thymic carcinoids, pancreatic tumours or phaechromocytomas.

It is rare for the ectopic ACTH syndrome associated with small cell carcinoma of the lung to present with typical cushingnoid features despite high levels of cortisol production. It can be explained by the fact that patients with small cell carcinoma often do not live long, as it takes about two months for cushingnoid features to develop. Besides the rapid weight loss due to the carcinoma may also mask the cushingnoid features. These patients therefore, usually present with ankle oedema or with ACTH induced hyperpigmentation. Muscle weakness from hypokalemia, and thirst and polyuria from diabetes mellitus are other common complaints.

Investigations of these patients often reveal the presence of hypokalemic alkalosis and diabetes mellitus. There is also high plasma ACTH and cortisol, which is unusual in other types of Cushing's syndrome. The plasma corticosteroids and ACTH levels show no circadian fluctuation.

The present patient fits the clinical picture of ectopic ACTH syndrome. However, typical cushingnoid features were present ie. ankle oedema, skin pigmentation, hirsutism, proximal myopathy, truncal obesity and diabetes mellitus of recent onset. This is unusual in small cell carcinoma presenting with the ectopic ACTH syndrome. The other unusual feature is the recent onset of bronchospasm. This was attributed to the patient having been a chronic heavy smoker.

Management of the ectopic ACTH syndrome, besides treatment of the underlying tumour, includes supportive measures including correction of severe hypokalemia and control of diabetes mellitus. Until recently, small cell carcinoma was considered to confer the worst prognosis amongst lung cancers (4). However, the natural history of this cancer has been altered substantially over the past decade by application of combined modality therapy ie. combination chemotherapy and chest irradiation (5-7). Patients are reported to have survived as long as three years. In a recent review, the author reported that the addition of irradiation to chemotherapy produced little effect on median survival (8).

CONCLUSION

A case of ectopic ACTH syndrome with typical cushingnoid features from small cell carcinoma of lung is described. This is unusual in ectopic ACTH syndrome from small cell carcinoma which often presents with hypokalemia and metabolic alkalosis, and muscle wasting with muscle weakness. Overall prognosis is poor but our patient showed improvement with chemotherapy. However, widespread metastases developed resulting in death.

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