Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Endocrinology

Cushing's Syndrome Revealing a Malignant Pheochromocytoma: A Case Report

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DOI: 10.36347/sjmcr.2022.v10i02.015 | **Received:** 06.01.2022 | **Accepted:** 10.02.2022 | **Published:** 15.02.2022

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Abstract **Case Report**

The most unusual cause of Cushing's syndrome (< 0.5% of cases) is a pheochromocytoma due to ectopic secretion of ACTH. Approximately 80% of cases are related to inappropriate corticotropin (ACTH) secretion and most of these patients have a pituitary adenoma (Cushing's disease). This is mostly a pulmonary or thymic carcinoid tumour, a pancreatic neuroendocrine tumour or a small cell lung cancer. 66 year old patient with a 20 years history of cannabis consumption, weaned 3 years ago. Admitted for etiological evaluation of a right adrenal mass, examination revealed abdominal pain over the last 6 months, intense in the right flank without any pressure sensation within a major weight loss context, asthenia and anorexia associated with generalized, disabling, and insominating skin pruritus; no Menard's Triad, no cramps or paresthesia. Pelvic abdominal CT scan: a 70×32 mm adrenal mass in contact with the inferior vena cava, segment I of the liver and the upper pole of the kidney with loss of the fatty border, it encircles the renal pedicle which remains permeable, associated with pre-aortic and aorto-caval adenopathies. Endocrine assessment: ACTH-dependant cushing syndrome. Management: due to the highly invasive nature of the tumour the patient benefited from a biopsy of the mass as well as a skin biopsy associated with heparinotherapy management of the partial thrombosis of the vena cava. Pathological and immunohistochemical examination of the mass biopsy: compatible with a pheochromocytoma with a score of Pass = 10, probably aggressive pheochromocytoma.

Keywords: Cushing's syndrome, malignant pheochromocytoma, inappropriate corticotropin (ACTH) secretion, invasive adrenal mass, brain metastasis, pulmonary metastasis, score of Pass..

INTRODUCTION

The most unusual cause of Cushing's syndrome (< 0.5% of cases) is a pheochromocytoma due to ectopic secretion of ACTH. This is a challenging entity for both diagnosis and management. Cushing's syndrome or endogenous hypercorticism is a rare disorder, occurring in about 3-4 new cases per million inhabitants each year [1-5]. Approximately 80% of cases are related to inappropriate corticotropin (ACTH) secretion and most of these patients have a pituitary adenoma (Cushing's disease) [1, 4, 5]. Another extremely rare cause of hypercorticism is ectopic secretion of ACTH from a benign or malignant neuroendocrine tumour (about 10% of cases) [6, 7]. This is mostly a pulmonary or thymic carcinoid tumour, a pancreatic neuroendocrine tumour or a small cell lung cancer. Exceptionally, cases of pheochromocytoma have been reported in the literature, with about 50 cases. We report a case of a silent malignant ACTH-secreting pheochromocytoma.

OBSERVATION

66 year old patient with a 20 years history of cannabis consumption, weaned 3 years ago, with no other personal or family, medical or surgical history. Admitted for etiological evaluation of a right adrenal mass, examination revealed abdominal pain over the last 6 months, intense in the right flank without any pressure sensation within a major weight loss context, asthenia and anorexia associated with generalized, disabling, and insominating skin pruritus; no Menard's Triad, no cramps or paresthesia.

Examination: normotension, 12.5% weight loss over 6 months, grade II of malnutrition, no clinical signs of cushing's syndrome, very pruritic skin papules on the back, the thorax, the flanks and the pelvis. During his

hospitalisation, the patient presented generalised tonic-clonic convulsions.

Assessment: Pelvic abdominal CT scan: a 70×32 mm adrenal mass in contact with the inferior vena cava, segment I of the liver and the upper pole of the kidney with loss of the fatty border, it encircles the renal pedicle which remains permeable, associated with pre-aortic and aorto-caval adenopathies, whose largest size is 32×27 mm.

Completed by a TAP

Right apical pulmonary lesion process associated with suspicious mediastinal adenopathies, sub pleural intra parenchymal nodules more prominent at the upper lobes.

Right adrenal tissue mass with irregular contour and heterogeneous enhancement after injection of contrast agent measuring 53.3×65.2×64.8 mm. Top: Intimate contact with the visceral surface of the IV and V liver segments. Top and front: Contact with the hepatic hilum and the head of pancreas, which are compressed with dilatation of the PVB measuring 11.6 mm in maximum caliber and loss of the fatty interface. Down and out: it invades the homolateral superior polar renal parenchyma. Nodular lesions in the liver which may be related to angiomas.

Doppler ultrasound of the IVC: partial thrombosis of the IVC extending to the iliac confluence.

Cerebral CT: temporal and fronto-polar process with secondary aspect.

Endocrine assessment: Minute inhibition test with dexamethasone (1mg at 11pm): no suppression of morning cortisol: 9. 18 ug/dl (normal value < 1.8), Urinary Free Cortisol: 1761.80 nmol/24 H (normal value: 100-379) 4.6 times normal. High ACTH: 89.2 ng/l (10,3- 48.3 ng/l). Chromogranin An elevated: 149 ng/ml (<102 ng/ml), 3 normal kaliemias: 4 - 4.40 -3.32 mmol/l, Urinary Metoxylates: Normetanephrine: 0.26 mg/ 24 h (0.07- 0.46), Metanephrine 0.06 mg/ 24h (0.04-0.30).

Other tests: Gly: 0.91, Total cholesterol: 1.37, HDL cholesterol: 0.33, Triglycerides: 1.11, LDL cholesterol: 0.82, Calcium: 95mg/l, Phosphorus: 40mg/l, Alb: 34.6g/L, ECG: normal, ETT: LV size and systolic function preserved LVEF: 65, Renal function: Urea: 0.31g/l, Creatin: 5.7mg/l, CRP: 164.31.

Management: due to the highly invasive nature of the tumour the patient benefited from a biopsy of the mass as well as a skin biopsy associated with heparinotherapy management of the partial thrombosis of the vena cava.

Pathological and immunohistochemical examination of the mass biopsy: compatible with a pheochromocytoma with a score of Pass = 10, probably aggressive pheochromocytoma.

Histological examination of the skin biopsy: non-specific dermatitis that could be part of a paraneoplastic syndrome.

In view of these results, we concluded to a silent malignant pheochromocytoma with ectopic ATCH secretion.

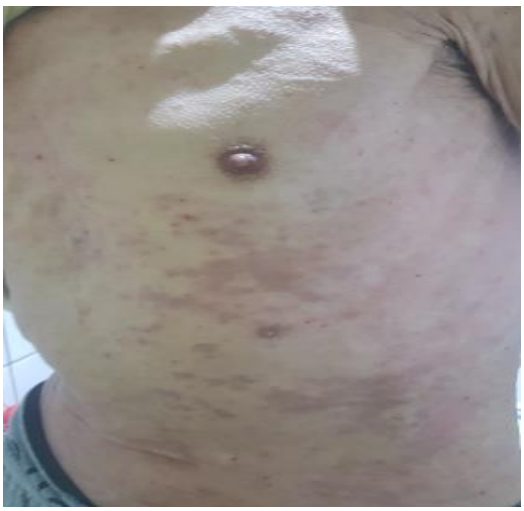


Image-1: Chest skin lesions

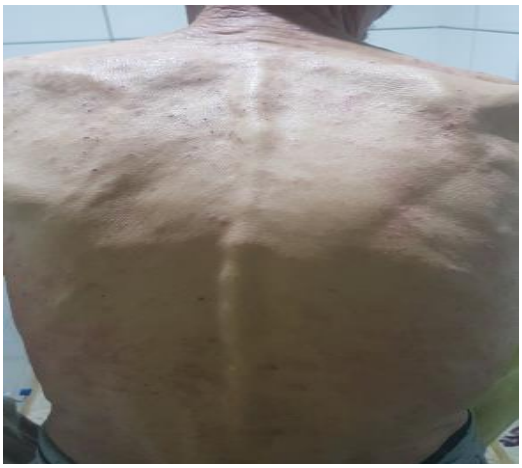


Image-2: back skin lesions

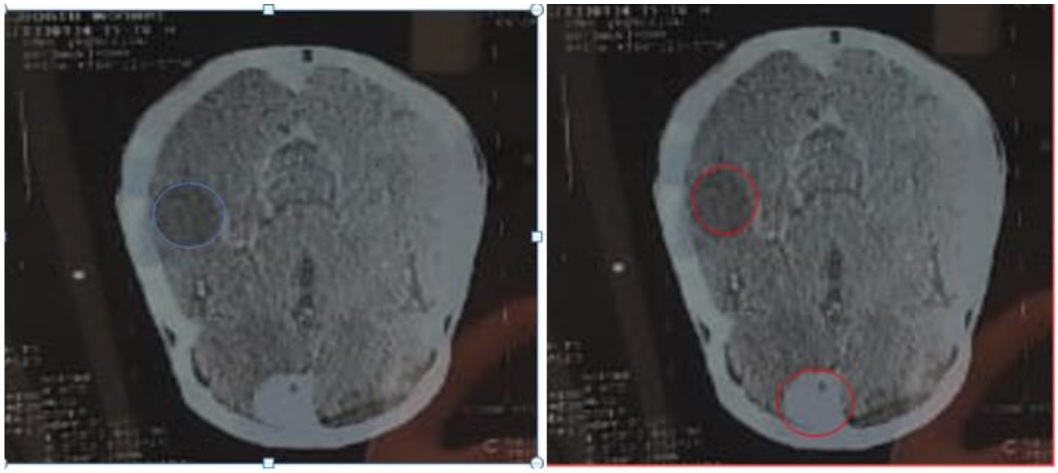


Fig-1: Brain CT

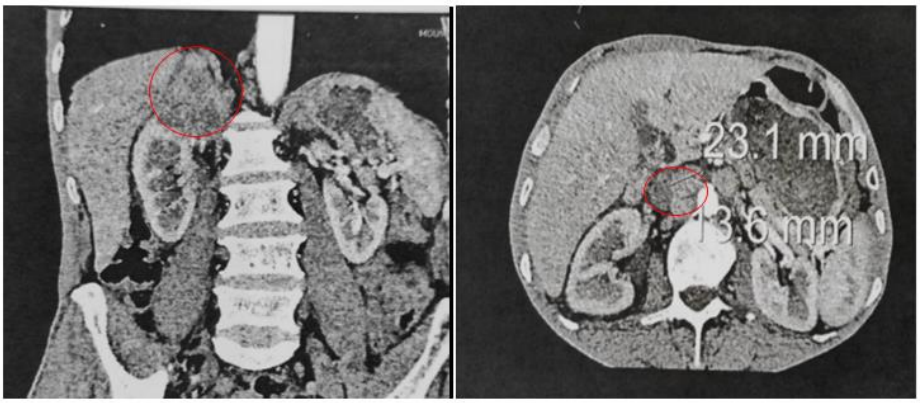
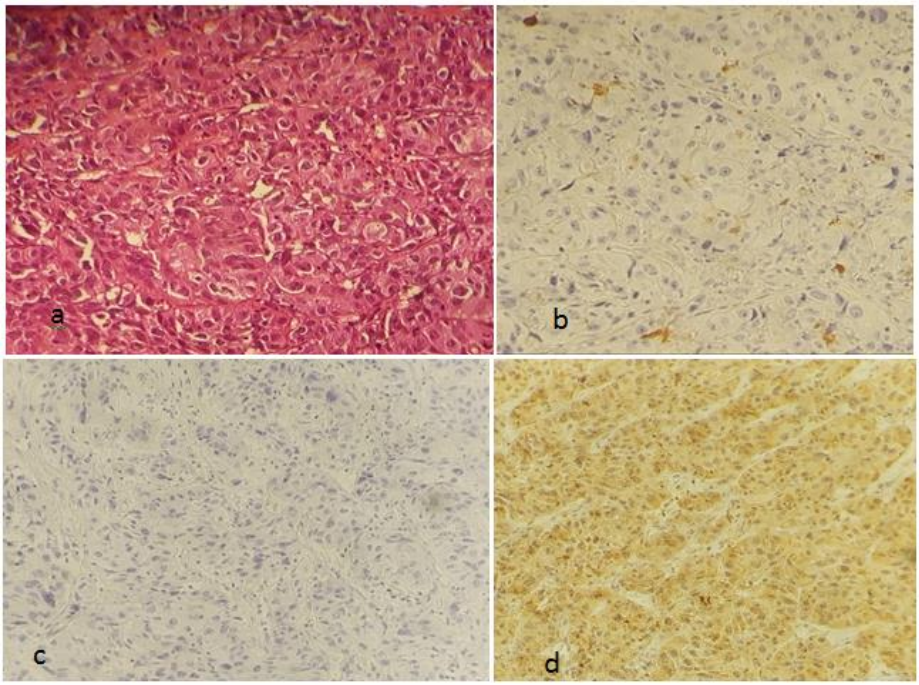


Fig-2: Abdominal CT



Anatomopathological study of the adrenal biopsy
a- Pleomorphic tumour proliferation
b- Cytoplasmic and nuclear expression of supratentacular stem cells
c- Absence of tumour cell expression of anti-Melan A antibody
d- Moderate and diffuse cytoplasmic expression of anti-Synaptophysin antibody in tumour cells

DISCUSSION

The occurrence of Cushing's syndrome due to ectopic ACTH secretion from an active pheochromocytoma is rare. About 50 similar cases have been described in the literature [8-14]. A pheochromocytoma causes ectopic ACTH secretion in only 5% of cases [9]. Symptoms can be clinically various, including those of chronic hypercorticism or pheochromocytoma, and most commonly a combination of both [8-10].

Criteria for malignancy include invasion of neighbouring organs, large tumour, and presence of adenopathy, imaging or scan fixation. Pheochromocytoma metastases are rare and occur in 10% of cases and tend to be localised within the lung, bone and liver. Srinivan *et al*. described a case of cutaneous metastasis [16] and other cutaneous manifestations such as finger necrosis with cryoglobulinemic, disseminated vascular coagulation associated with pheochromocytoma.

The CT scan of our patient shows a heterogeneous tumour process, with invasion of neighbouring organs, liver, pancreas and vena cava, associated with a hepatic nodule and adenopathies, as well as pleuropulmonary and cerebral injury. Eleven cases of cerebral metastasis of a pheochromocytoma have been found in the literature, at the peridural, subdural and intraparenchymal level [17] Brahim *et al*. found a case of brain metastasis of subclinical pheochromocytoma in the context of a genetic mutation of the beta dehydrogenase subunit gene, this genetic component is mainly found within paediatrics.

The prognosis of metastatic pheochromocytomas is guarded with a 5-year survival of 50% or less. However, it is difficult to predict metastatic potential on the basis of histopathological findings only, and no proposed histological scoring system can accurately predict the level of metastasis [18]. Survival depends on age of diagnosis over 50 years, male gender, disease progression, whether the tumour is resected or not and the size of the primary tumour [19].

CONCLUSION

Pheochromocytoma is an exceptional cause of Cushing's syndrome (< 0.5% of cases), by ectopic secretion of ACTH. Malignancy is defined by the presence of metastases; its prognosis depends on the age at diagnosis, its size and its initial surgical management. Anatomopathological findings cannot predict metastatic potential.

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