

Case Reports

Pituitary apoplexy due to mucormycosis infection in a patient with an ACTH producing pulmonary tumor

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Abstract

Rhinocerebral mucormycosis is an acute, fulminating form of invasive fungal sinusitis occurring principally in individuals who are immunologically or metabolically compromised. The incidence of pituitary apoplexy ranges from 6% to 17%, presenting as a capsule rupture in up to 1.7–2.0%. Isolated cases of mucormycosis are associated with solid tumors and Cushing's syndrome. A 42-year-old, diabetic woman, with Cushing's syndrome of 5 years duration presented with hemiplexy, hemiparesis and altered speech following a syncope episode and fall. Brain CT scan showed a left temporal lobe infarction. The patient deteriorated rapidly and she died 4 days later. Autopsy findings included: plurihormonal pituitary adenoma with extension to the sphenoid bone and sellar erosion; many thick, septated, mucormycosis hyphae; and recent fronto-temporal brain infarction. Also, a solitary adrenal corticotrophic hormone (ACTH)-producing neuroendocrine tumor, 3 cm in diameter, was found in the left lung. This patient illustrates the correlation between ACTH-producing ectopic pulmonary tumor, pituitary apoplexy and mucormycosis.

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1. Introduction

Pituitary apoplexy refers to the clinical picture resulting from hemorrhagic infarction or ischemic necrosis of the anterior lobe of the hypophysis, usually associated with a pituitary adenoma.¹ Pituitary apoplexy is a well-defined clinical entity. Some authors have identified hypoxic pituitary infarction, even in the absence of tumor after delivery; most cases of pituitary apoplexy occur spontaneously, although precipitating factors have been suggested. Magnetic resonance imaging is the investigation of choice.¹

Rarely pituitary apoplexy is secondary to fungal infection;^{2,3} brain abscesses have also been reported. This is uncommon and is also associated with Cushing's syndrome (CS).^{4,5} CS results from an increase of adrenal corticotrophic hormone (ACTH) due to: excessive adrenal production; adrenal hyperplasia and adrenal tumors either benign or malignant; ectopic ACTH-production due to extra-adrenal tumors (particularly lung, ovary). Extensive radiological and hormonal investigation is necessary to detect extrapituitary sources of ACTH. Differentiation between pituitary and non-pituitary (ectopic) sources of ACTH secretion may be extremely difficult in some patients despite the wide diagnostic armamentarium available.⁶

A 42-year-old, diabetic woman, with CS of 5 years duration, due to an ACTH-producing lung tumor, is presented. Pituitary apoplexy was associated with a plurihormonal pituitary adenoma secondary to mucormycosis.

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2. Case report

We present a 42-year-old woman with a history of hypertension and type 2 diabetes mellitus of 10 years duration, under pharmacological management. Five years before her current illness she developed stress-related lumbar pain and facial and lower limb edema; itching and skin darkening were later observed, and a pituitary adenoma was detected. Surgical treatment was proposed, which she refused. Three years later, she noticed hirsutism, frequent and spontaneous ecchymosis, increase in abdominal girth and weight gain; 2 years before her current illness she noticed progressive decrease of visual acuity.

She then presented with left hemiplexy, left hemiparesis and altered speech, after a syncopal episode and fall.

On physical examination, the patient looked older than she was, with hirsutism, melasma and moon face. She was obese and her blood pressure was 160/100 mmHg. She presented with multiple ecchymosis, violet-spotted skin, dysrhythmic tachycardia (150 bpm), an enlarged abdomen with violaceous striae, asymmetric hypotrophic lower limbs and incoherent speech.

Neurological examination revealed optic atrophy, with facial asymmetry and there was diminished strength and hypoesthesia on the right.

Her hormone profile was thyrotrophin 1.0 microU/mL (0.35–4.94), free thyroxine 9.3 pmol/L (9.0–19.0), thyroxine 50 nmol/L (62.5–150.0), follicle stimulating hormone (FSH) 27.2 mU/mL (26.0–135), luteinizing hormone (LH) 3.4 mU/L (7.7–59.0), prolactin 9.8 ng/mL (3.4–24.1), growth hormone 8.4 ng/mL (0.0–20.0) and morning cortisol 65.5 ng/mL (8.7–22.4).

Four days after her admission, she deteriorated, with anemia and sepsis. Surgical resection of the pituitary adenoma was attempted, but she deteriorated into coma and had a cardiac arrest during surgery.



Fig. 1. Necrotic tissue removed from the sella turcica at autopsy.

2.1. Radiological findings

Brain CT scan showed a cortical hypodense area, which suggested a recent infarction in the left temporal lobe. The sphenoidal sinus had destructive lesions with inflammatory characteristics with wall remodeling that infiltrated the sellar region.

A CT scan of the thorax showed a well-defined, homogeneous, 2-cm nodule in the basal lobe of the right lung, which was also seen on abdominal CT.

An MRA showed narrowing of the superficial branches of the left middle cerebral artery.

2.2. Autopsy findings

The skull base structures showed minor softening, and the meninges were slightly swollen and pale. No abnormalities were found in the coronal sections of the brain. Some friable, soft, whitish necrotic matter destroying the sellar region and the sphenoid sinus was removed (Fig. 1).

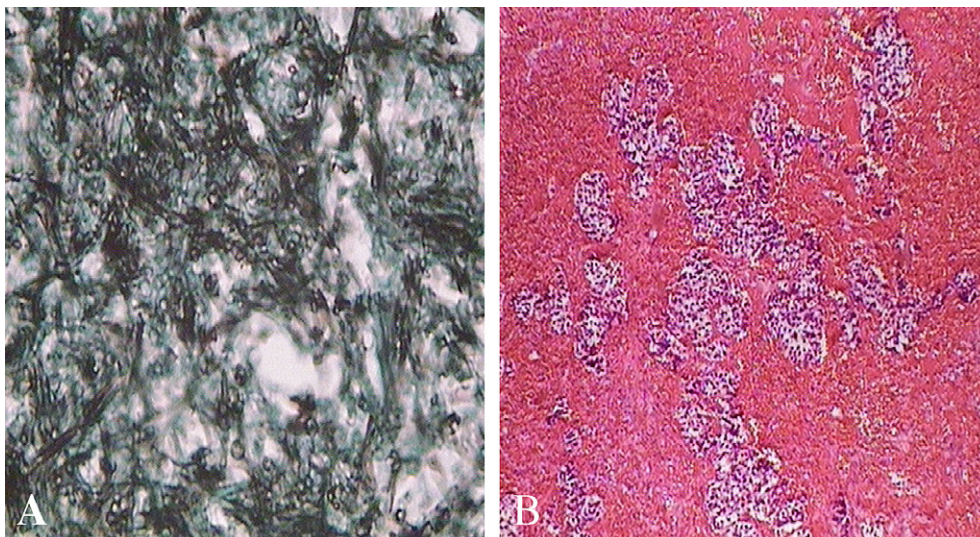


Fig. 2. A: Tissue removed from the sellar region showing necrosis and mucormycosis hyphae (Grocott stain, original magnification $\times 400$). B: Pituitary adenoma with necrotic and hemorrhagic areas consistent with pituitary apoplexy (Hematoxylin and eosin, original magnification $\times 400$).

2.3. Histological findings

Histological examination showed congested meninges with ischemic changes in the left temporal-parietal cortex. In the necrotic sellar contents, septate, densely clustered Periodic Acid Schiff (PAS) and Grocott positive mucormycosis hyphae were found (Fig. 2A). The pituitary gland showed necrosis and hemorrhage consistent with apoplexy; features of adenoma were observed in the preserved areas (Fig. 2B). The pituitary adenoma was immunoreactive for growth hormone, FSH and LH.

The lungs were congested and a 3 × 3 cm, yellowish, soft, homogeneous nodule was found in the right lower lobe; histological features corresponded to a neuroendocrine tumor (Fig. 3A) with positive immunoreactivity for neuron-specific enolase and ACTH (Fig. 3B). The remainder of the lungs showed edema, hemorrhage and pneu-

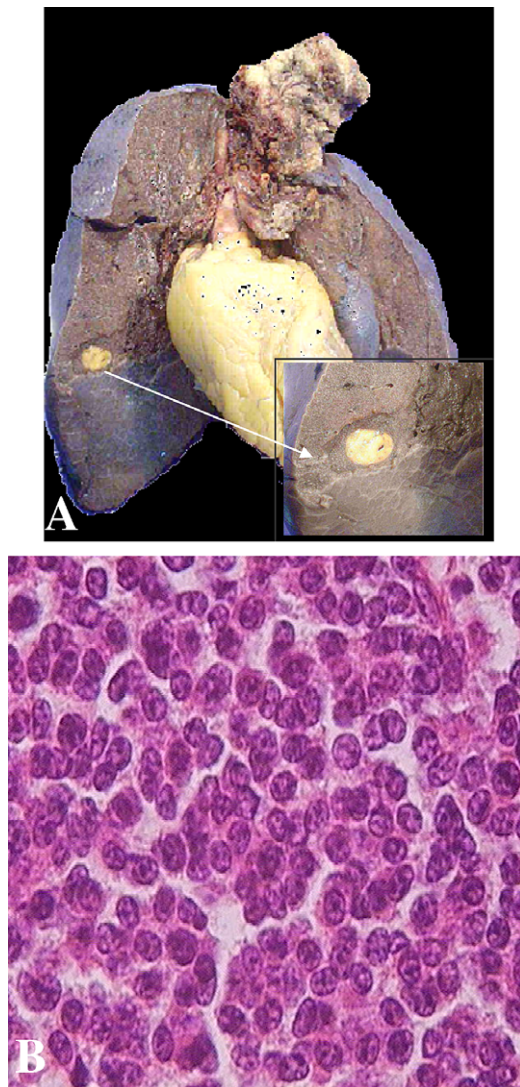


Fig. 3. A: Lung tumor, gross examination. B: Histological features of the pulmonary nodule which was immunopositive for adrenal corticotrophic hormone (ACTH) (Immunohistochemistry for ACTH, original magnification × 400).

monic foci. The heart weighed 400 g and there was left ventricular hypertrophy.

3. Discussion

Pituitary abscesses are uncommon and are due to fungi or bacterial infections; the diagnosis is made only by histopathological examination and cultures to identify the causative organism as the clinical and radiological findings, including MRI, are not specific.¹

Rhinocerebral mucormycosis can affect the paranasal and mastoid sinuses, but it rarely affects the brain parenchyma.² It is usually associated with immunosuppressed states; including diabetes mellitus (as in our patient), AIDS, and hematological malignancies.² The incidence of surgical complications after a transsphenoidal approach for pituitary lesions is low.² Calli et al.⁷ reported pontine infarction secondary to thrombosis of the basilar artery and brain hematoma due to mucormycosis. Keane et al.⁸ reported a 42-year-old woman, with epistaxis and mucormycosis, where the diagnosis of pituitary apoplexy was established on CT scan.^{1,8}

The involvement of the pituitary gland by aspergillosis is extremely rare and can be misdiagnosed as a pituitary tumor; most cases reported are associated with sphenoid sinusitis.^{3,7} Mortality in intracranial aspergillosis approximates 100%, especially in immunosuppressed patients where it is often misdiagnosed and therefore left untreated.^{9,10}

Mucormycosis and aspergillus are very similar fungi, the only differences are thickness and the presence of septae.^{2,3,9,10} Mucormycosis hyphae are thicker, less septated and do not cause granulomas.^{2,7-9} Due to their special affinity for blood vessels, particularly for the elastic membrane, they tend to present as arterial thromboses.⁹ These fungi invade and destroy the arterial walls, causing occlusion and rupture, which in turn can lead to brain hemorrhage.⁷⁻⁹ Even though our patient had no evidence of sinusitis, mucormycosis hyphae may have passed through the bone along vascular channels causing osteomyelitis of the skull base with secondary pituitary apoplexy.⁸

Endogenous CS is a clinical state resulting from prolonged, inappropriate exposure to excessive endogenous secretion of cortisol and hence excess circulating free cortisol, characterized by loss of the normal feedback mechanisms of the hypothalamic-pituitary-adrenal axis and the normal circadian rhythm of cortisol secretion.^{6,11} Bronchopulmonary carcinoid tumor is one of the most common causes of ectopic secretion of ACTH, and accounts for approximately 1% of all the patients with CS.⁶ The differentiation of Cushing's disease and non-pituitary ACTH-secreting tumors is rarely straightforward.¹¹ Current knowledge is based upon a limited number of reports including a small number of patients with opportunistic infections, such as cryptococcus, nocardiosis and aspergillus.⁶ However thromboembolic complications are recognized in endogenous CS; they are usually associated with severe hypercortisolemia and carry a high mortality.^{11,12}

Patients with active CS present a remarkable increase in cardiovascular risk, mainly due to dilated-hypertrophic cardiomyopathy¹ with systolic dysfunction, which increases the risk for thrombo-embolic events in these patients.¹ Also, there is an increase in the vascular risk secondary to atherosclerotic and lipid-related vascular damage,¹² which may explain the brain infarction in our patient.¹²

4. Conclusions

A 42-year-old, diabetic woman with CS of 5 years duration, secondary to an ectopic ACTH-producing lung tumor with a neurological profile secondary to a brain infarction in the left middle cerebral artery territory, is presented. A destructive lesion in the sphenoid sinus and sellar region was shown on CT and MRI. Plurihormonal pituitary adenoma, as well as pituitary apoplexy and features of a mucormycosis infection, were observed. Mucormycosis should be included in the differential diagnosis of lesions in the parasellar region and in CS.

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Two-level total *en bloc* lumbar spondylectomy with dural resection for metastatic renal cell carcinoma

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Abstract

Only five reports of multilevel spondylectomy for tumor have been reported in the literature, mostly in the thoracic spine. We report a successful two-level spondylectomy with *en bloc* dural resection in a patient with metastatic renal carcinoma to the L3 and L4 vertebrae. © 2006 Elsevier Ltd. All rights reserved.

Keywords: Spondylectomy; Lumbar spine; En bloc; Dural resection; Reconstruction; Tumor

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1. Introduction

The vertebral column is the most common destination for skeletal metastases.¹ *En bloc* spondylectomy has been