Neuroparacoccidioidomycosis: Case reports and review

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Abstract. Cerebral and cerebellar masses occurred in patients with paracoccidioidomycosis. Correct diagnosis was delayed due to overlooking the abnormal lung roentgenograms and the history of previous disease in a different localization. The fungus was identified through biopsy and direct examination of the samples. In two patients necropsy confirmed the diagnosis. None of the patients responded to amphotericin B or cotrimoxazole. A 10 year English and Latin American literature review on neuroparacoccidioidomycosis was performed through a MEDLINE and LILACS (Latin American Literature Search System) database system.

Key words: Central nervous system mycosis, Neuroparacoccidioidomycosis, Paracoccidioidomycosis

Introduction

Paracoccidioidomycosis is a chronic granulomatous infection caused by the dimorphic fungus, Paracoccidioides brasiliensis. The disease is endemic in Central and South America [1] and is more frequently seen in middle-aged male patients of low socioeconomic status [2]. In the central nervous system (CNS), P. brasiliensis has produced basal meningitis or isolated granulomas (pseudo-tumor form) in the spinal cord, brainstem, cerebellum or, most commonly, in cerebral hemispheres [3, 4]. The frequency of neurological disease is unknown because neither the brain or the spinal cord is routinely studied in necropsies and there are silent clinical forms [5–7].

Case reports

Case 1. A 48 year old man was admitted at the Dr Domingo Luciani Hospital (DDLH), Caracas, Venezuela, on 24 February 1992, because of instability on walking, falling forward to the right, diplopia and loss of 4 kg of weight of 2 months duration. He resided in Petare, he worked as a garbage collector in Mariches and gave a history of heavy smoking. A magnetic resonance image (MRI), which had been performed 3 weeks before admission, showed multiple hypodense lesions in the left frontoparietal region and in the right cerebellar hemisphere (Fig. 1), with mass effect. Physical examination revealed decreased breath sounds in the lower two thirds of the right lung, scarce fine rales in both lungs, dysmetria and ataxia. The rest of the examination was unremarkable. Routine laboratory studies including hemogram, ESR, urea, creatinine, glucose, VDRL, and liver tests were normal or negative. A chest film showed linear densities on both middle lung fields, and bullae toward the bases (Fig. 2). A presumptive diagnosis of cerebral metastasis from primary lung carcinoma was made and dexamethazone (24 mg/day, iv) was given. Twenty seven days later, a sputum sample, the bronchoalveolar lavage and the transbronchial biopsy revealed multiple budding yeasts. The cerebrospinal fluid (CFS) showed 16 mononuclear cells with the rest of the cytochemical values being normal. On 4 March a consultation was made to the infectious disease specialist and amphotericin B (AMB) at the dosage of 0.6 mg/kg/day was initiated.

Patient had a protracted evolution. A dry cough ensued, followed by vertigo, fever and dyspnea. A new chest film showed alveolar densities in both middle lung fields. He developed a right pneumothorax and a bronchiopleural fistulae. Direct examination of sputum and pleural fluid continued to show multiple budding yeasts and the Ziehl Nielsen stain was nega-
tive. The blood and pleural fluid cultures were always negative. Complement fixation test for *P. brasiliensis* in pleural fluid was positive. On 6 April, trimethoprim 160 mg and sulfamethoxazole 800 mg, intravenously, twice a day, was initiated but the patient finally died on 21 April. Autopsy revealed subdural and intraparenchymatous necrotic nodules in both cerebral hemispheres. Direct smear and histopathology of the lesions showed the fungus.

**Case 2.** A 62 year old man was admitted to DDLH on 18 May 1992, because of cephalalgia, dizziness and incoordination of three months duration, plus nausea and vomiting for the last two weeks. He was a farmer who was a native of, and resided in, Capaya (Miranda State) and gave a history of right otitis media three months before. The only positive finding on physical examination, as stated on the patient’s record, was ataxia. Routine laboratory studies were normal. The chest film showed linear densities in the upper two thirds of the right lung with small cavities. CNS computer tomographic scanning (CT-scan) revealed hypodense lesions in vermix which enhanced with contrast in a ring-like pattern, and dilated ventricles. Dexamethazone (24 mg/d, iv), acetazolamide (1 g/day, po), penicillin G (18 MU/day iv), chloramphenicol (4 g/day, iv), and metronidazole (750 mg tid, iv) was initiated on 25 May. Acetazolamide and dexamethazone were withdrawn ten days later. Two new CT-scans performed in June and July did not show any changes. Antibiotics were withdrawn on 2 July and a craniectomy was performed on August 10. A cerebellar abscess was found, which was completely removed, and the direct examination of the lesion showed multiple budding yeasts. A consultation was made with the infectious disease specialist and AMB was initiated but the patient died 48 hours after surgery. Autopsy was not authorized.

**Case 3.** A 55 year old man was admitted to the DDLH Neurosurgery Service on 6 September 1992, because of cephalalgia, dysphonia, dysphagia, and 30 kg weight loss of one year evolution. He also had an outward deviation of the right eye, left palpebral ptosis, trembling of the right arm, and ataxia for the last three months. The patient was a sailor from La Guaira, who resided in Caracas, and he gave a history of heavy smoking and drinking habits. A diagnosis of ‘laryngeal mycosis’ had been made 2 years before and he had been treated with ketoconazole for 2 months. On admission, physical examination revealed an emaciated male with a Glasgow of 15, paralysis of left third and sixth nerves, and of vertical gaze, paresis and continuous tremor of the right arm. Coarse rales could be heard on both lungs and the breath sounds were diminished. Routine laboratory studies were normal. The chest film showed bilateral linear densities. The CNS CT-scan and MRI (Fig. 3) disclosed a hypodense lesion in the midbrain which extended to the hypothalamus, thalamus, pons and left middle cerebellar peduncle which enhanced with contrast in a ring-like pattern. There was perifocal edema, third ventricle compression, and supratentorial ventricu-