

Case Report

Paracoccidioidomycosis simulating brain tumor

Gustavo R. Isolan^{1,2}, Daniel M. Vieira¹, Francine Hehn³, Ápio C. M. Antunes^{1,2}

¹Departments of Neurology, ³Pathology, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos 2350, 90035-903, ²Graduate Program in Medicine: Surgical Sciences, School of Medicine, Universidade Federal do Rio Grande do Sul, Rua Ramiro Barcelos 2400, 90035-003, Porto Alegre, RS, Brazil

E-mail: *Gustavo R. Isolan - gisolan@yahoo.com.br; Daniel M. Vieira - dmvieira21@hotmail.com; Francine Hehn - francine_hehn@yahoo.com.br; Ápio C. M. Antunes - apioantunes@hotmail.com

*Corresponding author

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Abstract

Background: Paracoccidioidomycosis (PCM) is a systemic granulomatous disease caused by *Paracoccidioides brasiliensis*. Involvement of the central nervous system (CNS) occurs in about 10% of cases.

Case Description: A 57-year-old white man presented with the complaint of headache and an episode of focal seizure 1 month earlier. Magnetic resonance imaging (MRI) revealed a ring-enhancing lesion in the right parietal lobe with peri-lesional vasogenic edema suggestive of a primary neoplasm. The patient underwent craniotomy and the intraoperative finding was a yellowish, hard lesion with thick content and yellow inside. Anatomic-pathological findings were pathognomonic of PCM: large, thick-walled, spherical yeast cells with multiple peripheral buds. The patient tested negative for human immunodeficiency virus (HIV). Encephalitis and meningitis were ruled out by cerebrospinal fluid analysis. Culture confirmed the diagnosis of PCM and the patient was treated with amphotericin B. The patient responded well to treatment with resolution of the headache and clinical improvement, despite a bitemporal hemianopia. He was clinically stable and then discharged in good general condition.

Conclusions: Radiographic findings of PCM with CNS involvement may suggest neoplasia, making diagnosis difficult. In endemic areas, the diagnosis of PCM should be promptly considered when a ring-enhancing mass associated with peri-lesional edema is observed on MRI.

Key Words: Brain neoplasms, central nervous system, magnetic resonance imaging, paracoccidioidomycosis

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INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic granulomatous disease caused by a dimorphic fungus known as *Paracoccidioides brasiliensis*.^[1,7] The fungus presents as a mycelium in the environment, with temperatures around 25°C, and as a yeast on its parasitic

form and in cultures under temperatures of 37°C.^[17] The mycelium is the infecting form of the organism and contaminates people when there is contact with soil.^[23] The disease is endemic to Central and South America, most notably Brazil, which accounts for approximately 80% of reported cases.^[4] Living in rural areas and being a male are the main risk factors for being

infected.^[12] Infection is often subclinical, but the fungus can proliferate, causing severe disease. The chronic adult form occurs in more than 90% of patients, being more common in adult males in their fourth to sixth decades of life and affecting mainly the lungs, mucus membranes, skin, and lymph nodes.^[4,21] Less frequently, in about 10% of cases, PCM affects the central nervous system (CNS), with a mortality rate of 53%.^[10,16] Its clinical course remains unclear and the diagnosis can be elusive. Radiographic images may provide nonspecific findings that can be suggestive of neoplasia. We report a case of PCM simulating a neoplasm in the brain on magnetic resonance imaging (MRI).

CASE REPORT

A 57-year-old white man presented to the neurosurgery outpatient clinic at a tertiary care hospital located in the city of Porto Alegre, southern Brazil, with the complaint of headache. The patient reported an episode of focal seizure that had occurred 1 month earlier. Neurological examination revealed no abnormalities, except for left hemianopia on confrontation visual field test.

Brain MRI showed an expansive, relatively well-defined mass in the right parietal lobe [Figure 1a and b]. The lesion was heterogeneously hypointense on T2-weighted images and isointense on T1-weighted images. The mass measured 5.0 cm in diameter, showing peripheral contrast enhancement with peri-lesional vasogenic edema suggestive of a primary neoplasm. Dexamethasone therapy was initiated and the patient was referred for surgery.

Preoperative chest X-ray film revealed multiple bilateral micro-nodules, with emphysema bubbles in the apices. The patient underwent craniotomy and the intraoperative finding was a yellowish, hard lesion with good cleavage plane, thick content, and yellow inside. There was a hypothesis of brain abscess. The patient tested negative for human immunodeficiency virus (HIV) antibodies.

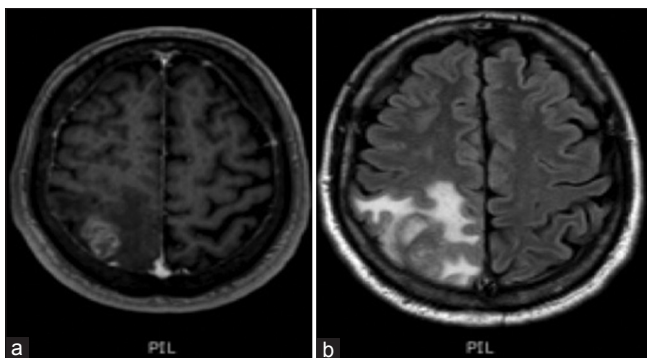


Figure 1: Brain magnetic resonance imaging (MRI). (a) Contrast-enhanced T1-weighted MRI showing a lesion with mass effect in the right parietal lobe and (b) the same image using the fluid-attenuated inversion recovery (FLAIR) sequence

On anatomic-pathological examination, the findings were pathognomonic of PCM: large, thick-walled, spherical yeast cells with multiple peripheral buds, with the capsule wall thickness giving the impression of a double capsule, although it was a single capsule [Figure 2a and b].

Serum and cerebrospinal fluid (CSF) specimens were negative for cryptococcal antigen by the cryptococcal latex agglutination test (Crypto-LA; Wampole Laboratories, Cranbury, NJ, USA). Gram-stained CSF contained 4 leukocytes/mm³, 8 mg/dl of glucose, and 4 mg/dl of total protein. Four days later, gram-stained CSF contained 2 leukocytes/mm³, 46 mg/dl of glucose, and 33 mg/dl of total protein. No microorganisms were detected on Gram stain of the CSF. Fibrotic bronchoscopy (FOB) performed 1 day later revealed bleeding at the carina and pus in the right upper lobe (RUL). Analysis of cells obtained from RUL broncho-alveolar lavage (BAL) fluid showed a negative smear for acid-fast bacilli (AFB), negative Gram stain, and presence of *Strongyloides stercoralis* larvae and yeast cells compatible with *P. brasiliensis*.

Abdominal computed tomography (CT) scan showed a nodule in the prostate and a left adrenal nodule. Chest CT scan showed cavitated apical lesions and diffuse micro-nodular infiltrates in the mid-upper lobe with some areas of atelectasis and ground-glass pattern.

In the immediate postoperative period, the patient had worsening of proprioception and impairment in left-side motor coordination, which improved later. Headache improved with surgery.

Culture of the lesional material confirmed the diagnosis of disseminated PCM (including a right adrenal nodule and lung injury) and the patient was treated with liposomal amphotericin B.

The patient responded well to amphotericin B therapy with resolution of the headache and clinical improvement. Echocardiography showed no abnormal findings. Thyroid ultrasound examination revealed a simple cyst (0.36 cm in diameter) at the junction of the isthmus and the right lobe and another simple cyst (1.31 cm in diameter) located in the lower pole of the left lobe. There were no

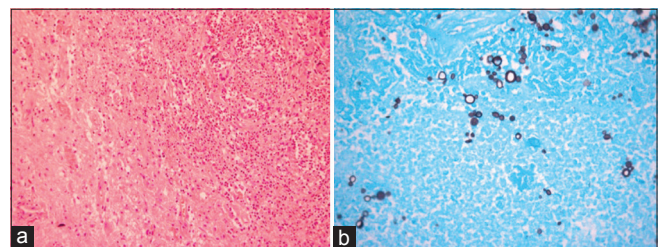


Figure 2: Histological sections showing (a) the edge of brain parenchyma with reactive infiltrate of lymphocytes and giant cells with central necrosis gliosis (H and E, ×100) and (b) presence of characteristic helm-shaped yeasts compatible with paracoccidioidomycosis (Gomori methenamine silver stain, 600×)

solid nodules. Visual field testing (perimetry) performed by an ophthalmologist showed bitemporal hemianopia. The patient was clinically stable and was then discharged in good general condition.

DISCUSSION

PCM may have a broad spectrum of speed of disease spread, form, and aggressiveness, ranging from acute to chronic and from self-limited to a fatal disease.^[17] In the chronic form, the lungs are the most common site of clinical manifestation, being affected in 90% of patients. In these cases, a plain chest radiograph may show the classic image of “butterfly wings.”^[21] Diagnosis is often accomplished by the identification of *P. brasiliensis* in direct mycological examination, which shows multiple gemmulation in “pilot” wheel, culture, histopathological or cytopathological examination, and serological tests. The gp43 is the most important serum marker for diagnosis.^[17]

Involvement of the CNS is more common in the chronic form of PCM, occurring in the progressive phase of the disease, often after the third decade of life.^[10] The prevalence of CNS involvement ranges from 3.4 to 13.9% of cases,^[5,3,11] with rates also ranging from 9.9 to 27.3% of cases in some reports.^[2,6,9,14,18] In PCM with CNS involvement, the disease can present as meningitis, meningoencephalitis, meningoradiculitis, and as a pseudo-tumoral form.^[11,17] In 66.8% of cases, the fungus affects the supratentorial region, especially the frontal and parietal lobes.^[15]

The diagnosis of PCM with CNS involvement is difficult and clinical suspicion may help achieve the correct diagnosis by ordering proper diagnostic imaging studies. The most common symptoms of neurological involvement are intracranial hypertension, cranial nerve deficits, motor deficits, gait disturbances, altered consciousness, hemiparesis, headache, ataxia, and seizures.^[10,11,16] Differential diagnosis should include neoplasms (particularly malignant gliomas and metastatic tumors), tuberculosis, bacterial and parasitic abscesses, neurocysticercosis, and infections such as histoplasmosis and cryptococcosis.^[10]

The regimen of choice for PCM with CNS involvement is preferably a combination of oral fluconazole and trimethoprim–sulfamethoxazole for long periods, ranging from 12 to 84 months.^[11,21] However, amphotericin B and intravenous sulfamethoxazole are indicated for severe manifestations of the disease, at least in the initial phase of treatment, in order to prevent unfavorable outcomes.^[8,13,21] Some azoles have also been used in the treatment of PCM, such as itraconazole and voriconazole. Itraconazole does not have a good penetration into the CNS, but voriconazole has been successfully used in the treatment of fungal infections of the CNS, such as blastomycosis^[22] and aspergillosis,^[20] and may be considered

in patients who cannot tolerate the treatments of choice. However, there is insufficient evidence to support the use of azoles as first-line therapy for PCM with CNS involvement. In addition, these drugs are not available in the public health system in all states of Brazil.^[21]

MRI with intravenous contrast injection often reveals the lesion. However, because the radiological presentation of PCM may be suggestive of neoplasia, patients are commonly referred for cancer treatment and tumor resection, thus delaying diagnosis and definitive treatment. Therefore, in the presence of neuroimaging findings that are characteristic of PCM (ring-enhancing lesion), culture should be considered to confirm the diagnosis of PCM. Whenever possible, stereotactic biopsy should be performed as a less-invasive way to obtain the tissue samples needed for histopathology.^[19]

In conclusion, PCM should be promptly considered in the differential diagnosis of brain tumors in endemic areas when a ring-enhancing mass associated with peri-lesional edema is observed on MRI. Treatment should be introduced as early as possible, with amphotericin B and intravenous sulfamethoxazole for severe manifestations of the disease.

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