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Case Report

Isolated neuroparacoccidioidomycosis as a pseudotumoral lesion in the absence of systemic disease

Ricardo Salemi Riechelmann, Leonardo Henrique Rodrigues, Tiago Marques Avelar, Paulo Adolfo Xander, Guilherme Henrique da Costa, Luiz Fernando Cannoni, Guilherme Brasileiro de Aguiar, Jose Carlos Veiga

Department of Surgery, Santa Casa de Sao Paulo School of Medical Sciences, Rua Dr. Cesário Motta Júnior, São Paulo, Brazil.

E-mail: Ricardo Salemi Riechelmann - ricardoriechel@gmail.com; Leonardo Henrique Rodrigues - leonardohsrodrigues@hotmail.com; Tiago Marques Avelar - avelar.tm@gmail.com; Paulo Adolfo Xander - pauloawx@yahoo.com.br; Guilherme Henrique da Costa - guilhermecosta@outlook.com; Luiz Fernando Cannoni - luiz2603@terra.com.br; *Guilherme Brasileiro de Aguiar - guilhermebraguiar@yahoo.com.br; Jose Carlos Veiga - jcemveiga@uol.com.br

***Corresponding author:**
Guilherme Brasileiro de Aguiar, Surgery, Santa Casa de Sao Paulo School of Medical Sciences, Rua Dr. Cesário Motta Júnior, São Paulo - 01221020, Brazil.

guilhermebraguiar@yahoo.com.br

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ABSTRACT

Background: Paracoccidioidomycosis (PCM) is a systemic, progressive, noncontagious, and often chronic disease caused by the fungus *Paracoccidioides brasiliensis* that rarely affects the central nervous system (CNS). The condition is usually treated using antifungal drugs, and some cases may require surgery.

Case Description: A 55-year-old man, a smoker, without known comorbidities, was referred to the neurosurgery team with a history of a single epileptic seizure a week before hospital admission followed by progressive right-sided hemiparesis. Head computed tomography and brain magnetic resonance imaging showed an intra-axial expansive lesion affecting the left parietal lobe, associated with extensive edema and a regional compressive effect producing slight subfalcine herniation that was initially managed as an abscess. After the failure of antibiotic treatment, the patient underwent a neurosurgical procedure for excision of the lesion. Histopathological analysis revealed that it was PCM and there was no evidence of impairment of other systems due to the disease.

Conclusion: PCM can be a serious, debilitating disease and is potentially fatal. Although isolated CNS involvement is rare, it must be considered, especially in endemic areas, as late diagnosis and treatment severely decreases good outcome rates.

Keywords: Central nervous system infections, Neurosurgical procedures, Paracoccidioidomycosis

INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic, progressive, noncontagious, and often chronic disease caused by the fungus *Paracoccidioides brasiliensis* that affects mainly Latin American men engaged in agriculture and in contact with soil.[2] It is the most common systemic mycosis in Latin America, accounting for about 80% of the cases.[9] Although the primary infection occurs in the lungs, there can be secondary lesions in other organs.[2]. The central nervous system (CNS) is not commonly affected, but when it is, the chronic form is most common and is associated with cutaneous or pulmonary manifestation of the disease.[2,7] CNS involvement leads to mortality that can reach 50% of cases.[5,7] When manifested in the pseudotumoral form, it most often affects the supratentorial compartment,[7] and this isolated form, without systemic involvement, is a rare event. We report on a case of a 55-year-old man diagnosed with the pseudotumoral form of

neuroparacoccidioidomycosis (NPCM), without systematic involvement, who underwent successful surgery. We will also undertake a brief review of the topic.

CASE REPORT

A 55-year-old man, a recycler, smoker, and alcoholic, without known comorbidities, was referred to the neurosurgery division with a history of a single epileptic seizure 1 week before hospital admission followed by progressive right-sided hemiparesis. On initial evaluation, muscle strength was graded as III and IV in the proximal and distal right upper limb, respectively, and IV in the right lower limb. There was also tactile hypoesthesia in the right hemibody. On visual examination, the patient's remaining teeth were in a very bad hygienic condition, and most of them were missing. Head computed tomography (CT) and brain magnetic resonance imaging (MRI) showed an intra-axial expansive lesion affecting the left parietal lobe, associated with extensive edema and a regional compressive effect producing slight subfalcine herniation. A pyogenic abscess was the main diagnostic hypothesis and given the poor oral condition and lack of other findings, the primary infection site was presumed to be odontogenic.

Antibiotic therapy (ceftazidime + metronidazole + vancomycin) and administration of dexamethasone were then initiated. Approximately 10 days later, the patient developed a high fever followed by one generalized tonic-clonic seizure despite the use of phenytoin. Within a few hours, he suffered a cardiopulmonary arrest and only returned to spontaneous circulation after 38 min of cardiopulmonary resuscitation and was admitted to the ICU, where he managed regain consciousness overtime, while maintaining previous deficits and radiologic findings.

After a new brain MRI showed lesion growth despite the antibiotic therapy for 40 days, stereotactic surgical treatment was indicated and successfully performed, but the histopathological analysis was inconclusive. A control CT scan showed a small reduction in perilesional edema and signs of a remnant lesion.

The patient was discharged without antibiotic therapy after 3 months of hospitalization and maintained clinical stability in a follow-up evaluation 20 days later with mild improvement in the right hemibody strength and a single focal seizure episode.

Three months later, the patient returned with an increase in the frequency of focal seizures and an increase in the remnant lesion, observed by a CT and MRI performed on readmission [Figures 1 and 2], this time with a length of over 3 cm. Antibiotic therapy was restarted and a new surgical approach was employed, this time with complete resection of the lesion [Figure 3].

The anatomopathological study showed brain tissue with an inflammatory process characterized by granulomas with multinucleated giant cells next to extensive areas of necrosis. In the middle of the process and, sometimes, in the giant cells, histological examination using the Grocott-Gomori's

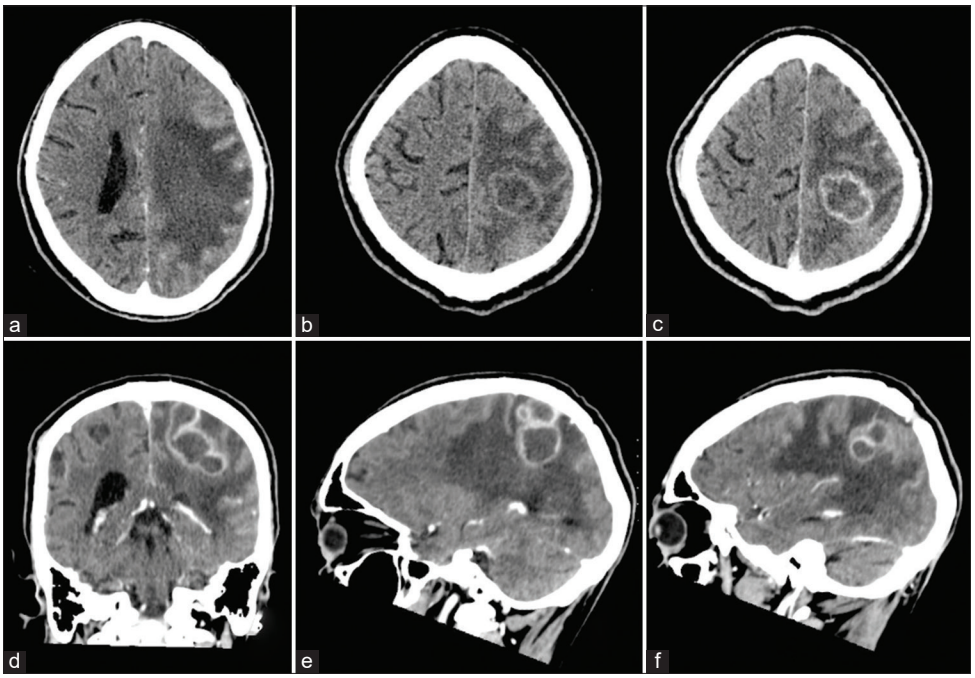

Figure 1: Computed tomography scan before (a and b) and after (c-f) contrast injection. Significant perilesional edema and isodense peripheral aspect of multinodular subcortical left parietal lesion with hypodense content to normal parenchyma with moderate mass effect to the left lateral ventricle (a and b). Ring peripheral postcontrast enhancement in axial, coronal, and sagittal views (d-f).

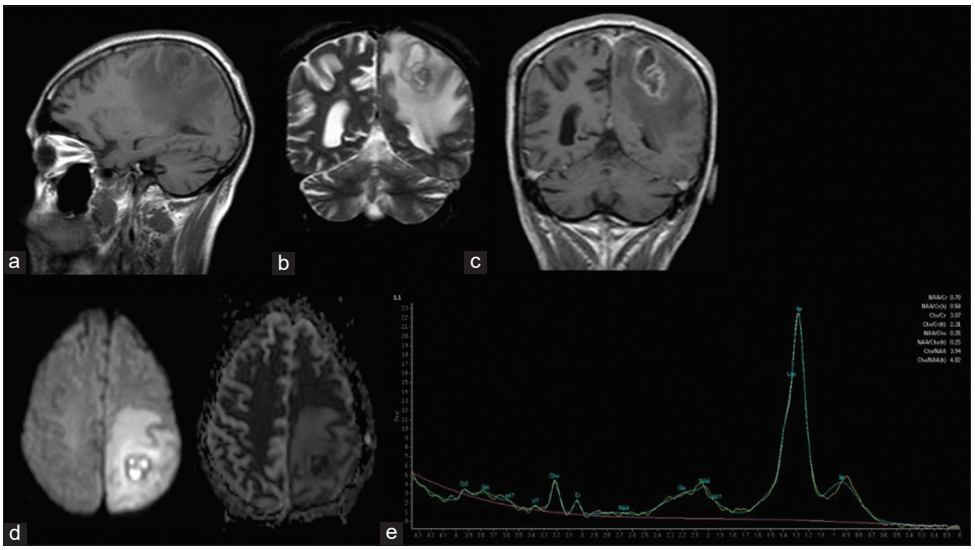

Figure 2: Magnetic resonance imaging findings: perilesional edema, iso/hyperintense periphery with hypointense content on T1WI (a), hypointense periphery with hyperintense content on T2WI (b), postcontrast periphery enhancement (c), restricted diffusion (d), and lipid peak at 1.3 ppm in spectroscopy (e).

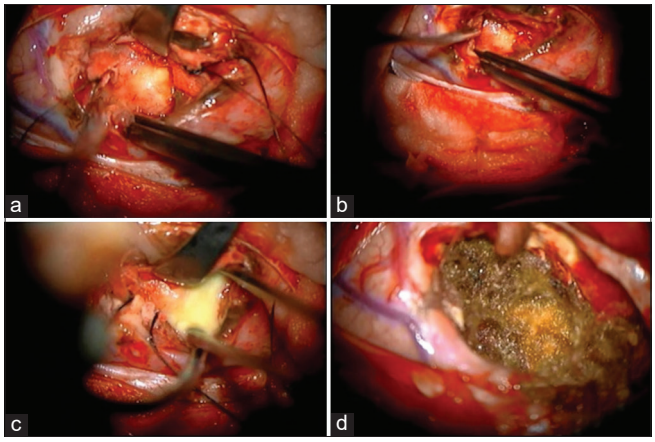

Figure 3: Intraoperative findings of the lesion. (a) Firm capsulated lesion. (b) Microdissection in the cleavage plane between the capsule and with matter tissue. (c) Break of the capsule with liquefactive necrotic material leakage. (d) Final aspect with resection cavity lined by fibrillar hemostatic.

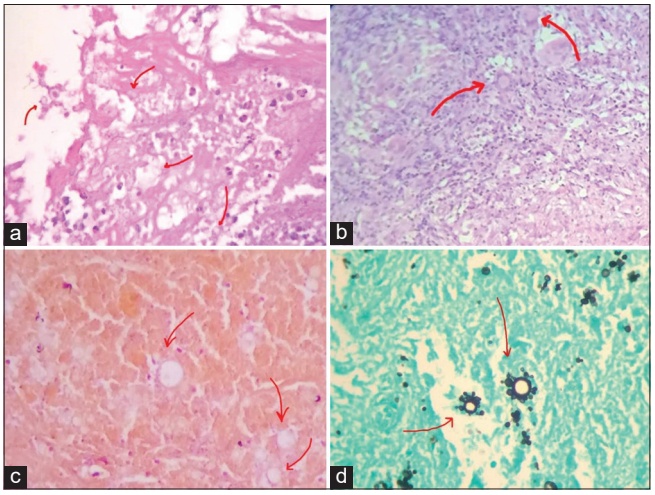

Figure 4: Histological study: (a-c) brain parenchyma with reactive infiltrate of lymphocytes and giant cells with central necrosis gliosis (red arrows) (Hematoxylin and Eosin); (d) presence of characteristic helm-shaped yeasts (multiple budding) compatible with paracoccidioidomycosis (Gomori's methenamine silver stain).

methenamine silver nitrate stain method showed highly specific signs of cerebral PCM similar to a ship's wheel or Mickey Mouse ears [Figure 4].

Itraconazole was then prescribed after the suspension of the antibiotic therapy. The patient was discharged from hospital and after responding well to treatment and making a partial recovery of his neurological deficits.

DISCUSSION

Brazil is the country with the most cases of PCM in Latin America with a prevalence estimated at between 5.6 and 17.5%, with an age peak of 30–50 years of age.[1,2,9,11] The disease is caused by inhaling fungal spores, resulting in a primary pulmonary complex that can spread through the lymphatic and/or hematological pathways to various extrapulmonary foci. Initial infection is usually asymptomatic and rapidly resolves by itself, leaving residual lesions that may contain viable fungi for many years (latent or quiescent foci) that eventually reactivate (adult form – 90% of cases) due to immunosuppression in tandem with a debilitating disease. On rare occasions, the primary infection acquires a progressive character, evolving to severe acute/subacute forms (juvenile form).[2,10,12]

NPCM can be manifested as meningitis, meningoencephalitis, meningoradiculitis, or pseudotumoral forms,[5,7] most commonly presenting as granulomas, abscesses, lumps, or intraparenchymal cysts.[10] It usually starts with a primary lesion in the lungs followed by lymphatic and blood dissemination to various organs and systems.[6] In approximately 20% of cases, the onset of neurological symptoms takes place before systemic symptoms, in 33%, it appears simultaneously, and in 46%, it starts after systemic manifestations.[9] In the majority of NPCM cases, simultaneous lung impairment and common abnormalities (opacities, consolidations, nodules, or cavitations) are seen in chest X-rays.[2,8,11,12] Despite what the literature shows, the present case had no systemic manifestations of the disease. The symptoms regarding the disease can vary according to the site of the lesion in the brain.[6] The frontal and parietal lobes are the most commonly affected areas, but the involvement of the posterior fossa is not unusual.[5] The most common manifestations appear to be headaches and cerebellar symptoms such as gait ataxia and hemiparesis. Other frequent symptoms are intracranial hypertension, ocular motility deficits and generalized seizures, or alteration of consciousness.[2,5,9,10,11] Our case followed the majority of findings in the literature, presenting with hemiparesis and generalized seizures.

The most important differential diagnosis is tuberculosis, a disease that may coexist with the mycosis in 8% of patients. Other diseases that should be considered are cancer and neoplastic disorders (including lymphoma), histoplasmosis, leishmaniasis, leprosy, and syphilis. Since symptoms and radiological findings are nonspecific,[5,8] only laboratory testing is capable of establishing the correct diagnosis.[4] Cerebrospinal fluid (CSF) analysis is also not efficient and is rarely positive,[2,5,9] thus a histopathologic study of biopsy tissue is required to make an accurate diagnosis. The microscopic findings in Grocott-Gomori's methenamine silver nitrate stain are characteristic and highly specific for PCM, with multiple budding and cells arranged in a shape similar to a ship's wheel or Mickey Mouse's ears, as happened to our patient.[2,4,5,6,8,9,11] It is possible to analyze circulating *P. brasiliensis* antigens (gp43 and gp70) in body fluids using inhibition enzyme-linked immunosorbent assay, which can be helpful for confirmation of the diagnosis of NPCM.[8] Antigen concentrations are higher in CSF (gp43 antigen higher than gp70) than in serum, with high sensitivity.[3,5] Antigen detection may be preferred for early diagnosis in immunocompromised individuals or when antibody detection appears inconclusive and is also useful as a way of measuring the effectiveness of treatment in any follow-up analysis.[3,4] These tests, however, are expensive and not available in most PCM endemic regions. In terms of image evaluation, MRI is considered the best imaging examination to define the location and extent of the lesion since it allows precise analysis of meningeal and parenchymal involvement and can help differentiate it from other possible diagnoses.[2,6,10]

Findings in MRI studies reveal an iso- to hyperintense signal on T1WI sequences and a hypointense signal on T2WI sequences at the periphery of the lesions, frequently associated with significant perilesional edema (hypointense on T1WI and hyperintense on T2WI), as demonstrated in the present case. Contrast (gadolinium) enhancement is also present, mainly as a peripheral ring enhancement but also a heterogeneous enhancement. The interior of the lesions is hypointense on T1WI and hyperintense on T2WI. As in granulomatous diseases such as neurotuberculosis, restricted diffusion is usually absent in NPCM due to solid caseation and associated fibrosis, but can be present, as happened in this case. MRI spectroscopy showed lipid peaks (1.3 ppm) that could be useful to differentiate NPCM from other lesions such as pyogenic abscesses (where peaks of succinate at 2.4 ppm, acetoacetate at 1.9 ppm, and alanine at 1.4 ppm may be seen).[13]

Treatment for PCM is mainly clinical with antifungal drugs such as trimethoprim/sulfamethoxazole (with low toxicity and easily availability)[11,12] in association with an azole agent such as itraconazole or fluconazole (the only azole that can cross the brain–blood barrier) as the therapy of choice for a period of 12–84 months according to the literature.[1,4,5,6,8,9] Immunocompromised or severely ill patients can be treated with amphotericin B and sulfadiazine.[14] Drug therapy should be initiated as soon as possible after diagnosis and should be in place before any surgical procedure to prevent dissemination of the fungus caused by manipulation of the lesion.[12] Since the at-risk population is often socioeconomically disadvantaged, maintenance of adequate outpatient drug therapy can be a challenge, increasing the risk of disease impairment, as happened to our patient. Surgery is a therapy of last resort, although in cases of NPCM, it can often occur since there is frequently uncertainty about the diagnosis, and the presence of intracranial hypertension or focal neurological deficits, requiring removal of the expansive intraparenquimatous lesion. When the condition is resistant to drug treatment, a surgical procedure should be considered.[5,7,8,9] Our patient went through complete resection of the subcortical left parietal brain abscess before the diagnosis through biopsy because of the serious nature of the clinical presentation and doubt regarding etiology. There was an improvement in functional status after surgery.

The prognosis is not very good, especially in disseminated forms and cases of late diagnosis, in which mortality can reach up to 20%.[5,14]

CONCLUSION

Paracoccidioidomycosis can be a serious debilitating disease and potentially fatal if untreated, especially because patients

are often immunodepressed. Early diagnosis is, therefore, necessary for a good response to treatment and better prognosis. PCM in the CNS is not a common condition but the possibility of it occurring in the CNS should not be overlooked by clinicians, neurologists, and neurosurgeons, especially those who work in endemic areas as there is a specific treatment and real potential to cure the condition. Late diagnosis and treatment severely decrease good outcome rates. Our case progressed well, mainly because of rapid hospital admission and surgical resection of the lesion. Drug therapy was promptly initiated and adjusted after the biopsy results for the lesion were available.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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