Central Nervous System Paracoccidioidomycosis: A Case Report

Paracoccidioidomicose do sistema nervoso central: relato de caso

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ABSTRACT

Paracoccidioidomycosis (PCM) is an endemic systemic mycosis in Latin America but occurs sporadically in North America and Europe. Neurological involvement is rare and a potential severe complication of the disease. Herein, we report a case of a young Brazilian whose diagnosis was established only after development of neurological manifestations. We also briefly review the most critical aspects of the disease and the patterns of neurological involvement.

RESUMO

A paracoccidioidomicose (PCM) é uma micose sistêmica endêmica na América Latina, podendo ocorrer de forma esporádica na América do Norte e na Europa. O envolvimento neurológico é raro e uma complicação potencialmente grave da doença. Neste artigo, relatamos o caso de um jovem brasileiro cujo diagnóstico foi estabelecido apenas após o desenvolvimento de manifestações neurológicas. Também revisamos brevemente os aspectos mais críticos da doença e os padrões de envolvimento neurológico.

Keywords – Paracoccidioidomycosis, Central Nervous System Infections, Brain Abscess.

Palavras-chave – Paracoccidioidomicose, Infecções do Sistema Nervoso Central, Abscesso Cerebral

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Contributorship statement

- VE: acquisition of data, drafting the manuscript, interpreting the results and critical review.
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- MMS: interpreting results and critical review of the final version.
- MAL: drafting the manuscript, interpreting the results, and critical review.

CASE REPORT

A 38-year-old non-smoker previously healthy Brazilian man presented with a two-week history of dry cough, night sweats, and weight loss. On initial evaluation at a local clinic, physical examination findings were not fully documented, and no extrapulmonary manifestations were reported at that time. Initial laboratory investigation included sputum acid-fast bacilli smear, mycobacterial culture, and GeneXpert MTB/RIF, all of which were negative. A chest computed tomography (CT) scan performed during this initial assessment revealed bilateral ground-glass opacities, reticular changes, and multiple pulmonary nodules. Based on these findings, along with the constitutional and respiratory symptoms, pulmonary tuberculosis was suspected, and empirical anti-tuberculosis therapy was initiated.

After one month of treatment without clinical improvement, the patient developed new neurological symptoms, including headache, nausea, vomiting, and progressive cognitive changes, described by family members as forgetfulness and disorganized behavior. He was then referred to our institution.

On admission, physical examination revealed asymmetric cervical lymphadenopathy, diffuse crackles on pulmonary auscultation, and an ulcerated oral lesion with a characteristic mulberry-like appearance (Figure 1A - arrow).

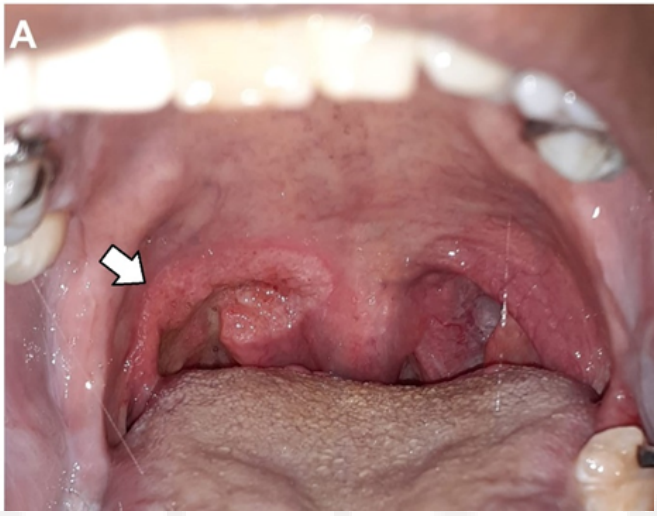

Figure 1 A) palatal mulberry-like appearance lesion

It is unclear whether this lesion was present during the initial evaluation at the local clinic. Neurological examination demonstrated delirium, characterized by inattention, disorientation, and a fluctuating level of awareness, without focal neurological deficits. Fundoscopy revealed papilledema.

He underwent a repeat chest CT scan, which again demonstrated ground-glass and reticular opacities, as well as multiple pulmonary nodules, findings similar to those described in the initial imaging. However, in contrast to the initial interpretation at the referring clinic, these findings were considered more suggestive of paracoccidioidomycosis (Figure 1B). This interpretation was supported by the presence of a mixed interstitial and nodular pattern, bilateral distribution, and the association with extrapulmonary features such as lymphadenopathy and mucocutaneous involvement, which are more characteristic of paracoccidioidomycosis than tuberculosis.

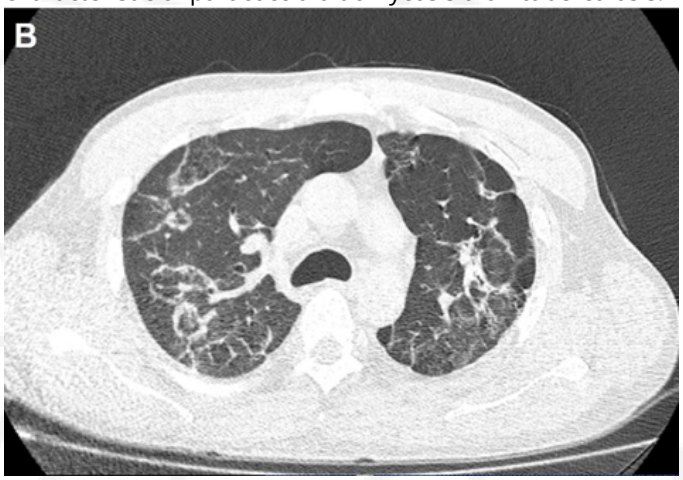

Figure 1 B) Chest CT scan showing diffuse ground-glass opacities and nodules in both lungs.

Brain MRI revealed multiple contrast-enhancing expansive lesions in the left cerebral hemisphere (Figure 1C). Direct microscopy of scrapings from the oral ulcer demonstrated the characteristic yeast forms of *Paracoccidioides brasiliensis*, establishing the diagnosis.

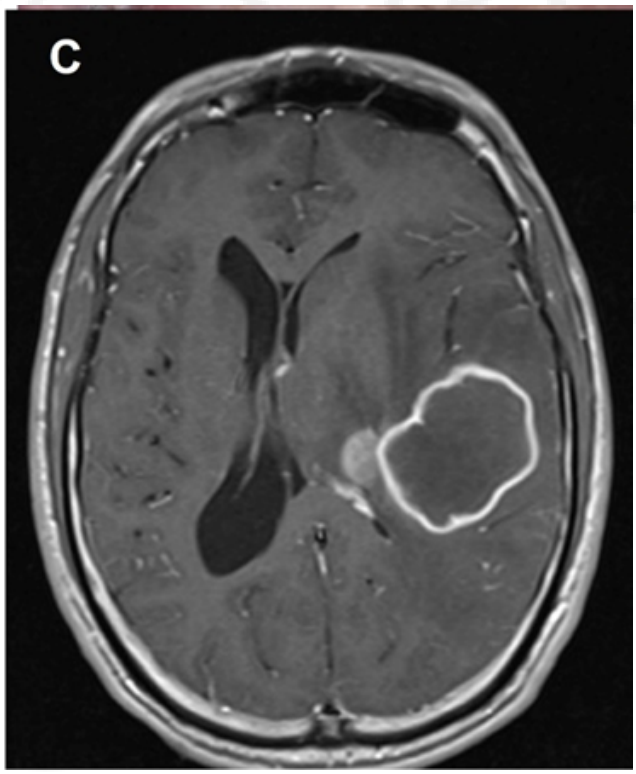

Figure 1 C) T1-weighted brain MRI showing a large contrast enhancing lesion with mass effect in the left hemisphere.

The largest brain lesion was initially drained, and analysis of the abscess fluid confirmed the presence of Paracoccidioides yeasts on direct examination (Figure 1D). The patient was started on amphotericin B, followed by oral trimethoprim-sulfamethoxazole. However, despite treatment, the follow-up brain MRI performed 33 days later showed no significant improvement. The patient subsequently underwent surgical excision of the lesion (Figure 1E), with marked improvement in cognitive symptoms thereafter.

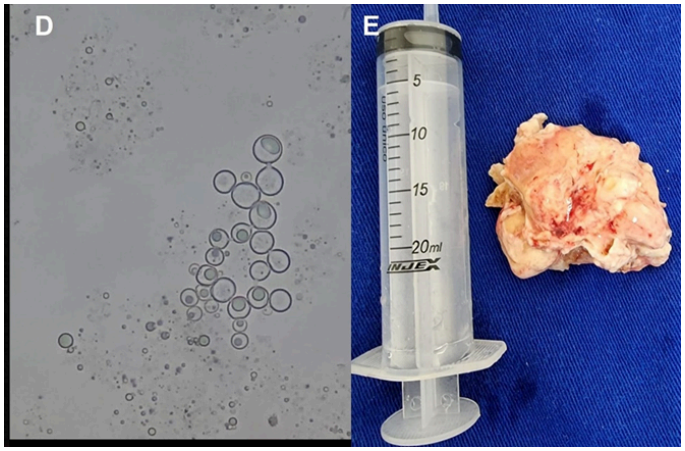

Figure 1 D) Paracoccidioides brasiliensis yeasts on direct visualization of the brain lesion aspirate**. E)** Brain abscess after surgical excision.

DISCUSSION

Paracoccidioidomycosis (PCM) is a systemic mycosis caused by fungi of the genus *Paracoccidioides*. It is the most prevalent endemic systemic mycosis in Latin America, although sporadic cases have been reported in other regions, including Europe, the United States, and Canada.[1] It predominantly affects men aged 30 to 60, particularly those with rural exposure. Unlike many other systemic mycoses, PCM does not appear to be strongly associated with immunosuppression.[2]

Infection occurs through inhalation of fungal propagules, leading to a primary pulmonary focus in a minority of exposed individuals. From there, the disease may disseminate via hematogenous and lymphatic routes, evolving into either an acute/subacute form (approximately 10% of cases) or a chronic form (approximately 90%). The acute form typically affects younger individuals and presents with systemic manifestations such as fever, lymphadenopathy, hepatosplenomegaly, and bone marrow involvement, often with minimal pulmonary disease.[3] In contrast, the chronic form represents reactivation of latent infection. It is characterized by insidious onset and progressive involvement of the lungs and mucous membranes, frequently manifesting as respiratory symptoms and painful oral lesions. Other organs, including the adrenal glands and central nervous system, may also be affected.[4]

When it does affect the nervous system, neurological involvement is an uncommon but potentially severe manifestation of chronic PCM, resulting from hematogenous dissemination. It may occur in isolation or in association with pulmonary and systemic disease. The most frequent presentation is the pseudotumoral form, characterized by granulomatous, expansive lesions that most commonly affect the frontal lobes. However, other brain regions and the spinal cord may also be involved. Clinical manifestations include headache, seizures, cognitive impairment, and focal neurological deficits.[5] Neuroimaging typically demonstrates parenchymal lesions with perilesional edema and heterogeneous signal characteristics, often with ring or nodular patterns of contrast enhancement.[6]

In this context, paracoccidioidomycosis should be systematically considered in patients presenting with brain abscesses or expansive lesions, particularly when accompanied by pulmonary abnormalities or mucocutaneous findings such as oral ulcers. The coexistence of these features represents an important clinical clue, as this combination is more suggestive of a disseminated fungal infection than isolated central nervous system disease. In the present case, early red flags—including constitutional symptoms, pulmonary imaging abnormalities, lymphadenopathy, and the later recognition of a characteristic oral lesion—were initially overlooked or underappreciated, contributing to diagnostic delay. Greater attention to the integration of neurological, pulmonary, and mucocutaneous findings may facilitate earlier recognition of PCM and improve clinical outcomes.

A key challenge in PCM is its nonspecific clinical and radiological presentation, which often overlaps with that of other infectious and neoplastic conditions. In the present case, the initial clinical picture—constitutional symptoms associated with pulmonary findings—combined with nonspecific chest CT abnormalities, led to an initial diagnostic suspicion of tuberculosis. This reflects a common diagnostic pitfall in endemic settings, where tuberculosis is often prioritized due to its higher prevalence. However, a retrospective analysis suggests that certain features, such as the presence of pulmonary nodules and a typical oral ulcer, may have raised earlier suspicion of PCM.

This case also highlights the importance of a thorough physical examination. The identification of a characteristic mulberry-like oral lesion was a key diagnostic clue, as mucosal involvement is highly suggestive of PCM. It remains unclear whether this finding was present at the initial evaluation, but its early recognition could have prompted more targeted investigation and potentially avoided diagnostic delay.

Given the overlap with other conditions, the differential diagnosis of central nervous system lesions in this context includes tuberculosis, sarcoidosis, syphilis, cryptococcosis, and neoplastic processes. Definitive diagnosis relies on direct identification of the organism

through microscopy, culture, or histopathology, as well as serological testing. Clinical specimens may include sputum, abscess fluid, lymph node aspirates, and scrapings or biopsies of mucocutaneous lesions.[7]

Treatment depends on disease severity. Itraconazole is the drug of choice for mild to moderate disease. In contrast, severe cases, particularly those with central nervous system involvement, require more aggressive therapy with amphotericin B or trimethoprim-sulfamethoxazole (SMZ-TMP). SMZ-TMP is often preferred in neuroparacoccidioidomycosis due to its ability to penetrate the central nervous system. Recent data suggest that combination therapy with SMZ-TMP and fluconazole may be associated with improved outcomes. Treatment duration is variable and often prolonged, sometimes extending to 24 months or more, depending on clinical and radiological response.[5]

CONCLUSION

We report a case of paracoccidioidomycosis with delayed diagnosis, ultimately progressing to severe central nervous system involvement. This case illustrates the diagnostic challenge posed by the disease's nonspecific clinical and radiological features, which may overlap with those of more prevalent conditions such as tuberculosis, particularly in endemic settings.

It also highlights the importance of thorough clinical evaluation, including careful physical examination, as key diagnostic clues—such as mucocutaneous lesions and lymphadenopathy—may be overlooked during early assessment. Recognition of these findings, in conjunction with pulmonary and neurological manifestations, may facilitate earlier diagnosis.

Clinicians should maintain a high index of suspicion for paracoccidioidomycosis in patients from endemic regions presenting with expansive CNS lesions, especially when associated with pulmonary abnormalities or suggestive extrapulmonary features. Early consideration of this diagnosis is essential to avoid delays in treatment and to reduce the risk of severe neurological sequelae and mortality.

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