



Case Report

Brain paracoccidioidomycosis in an immunosuppressed patient with systemic lupus erythematosus

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ABSTRACT

Background: Brain paracoccidioidomycosis (PCM) or neuroparacoccidioidomycosis (NPCM) is a fungal infection of the central nervous system (CNS) caused by *Paracoccidioides brasiliensis*, a dimorphic fungus. The CNS involvement is through bloodstream dissemination. The association between NPCM and systemic lupus erythematosus (SLE) is rare. However, SLE patients are under risk of opportunistic infections given their immunosuppression status.

Case Description: The aim of this case report is to present a 37-year-old female with diagnosis of SLE who presented with progressive and persistent headache in the past 4 months accompanied by the right arm weakness with general and neurologic examination unremarkable. The computerized tomography of the head showed left extra-axial parietooccipital focal hypoattenuation with adjacent bone erosion. The brain magnetic resonance imaging reported left parietooccipital subdural collection associated with focal leptomeningeal thickening with restriction to diffusion and peripheral contrast enhancement. The patient underwent a left craniotomy and dura mater biopsy showed noncaseous granulomatosis with multinucleated giant cells with rounded birefringent structures positive for silver stain, consistent with PCM. Management with itraconazole 200 mg daily was started with a total of 12 months of treatment, with patient presenting resolution of headache and right arm weakness.

Conclusion: The diagnosis of NPCM is challenging and a high degree of suspicion should be considered in patients with persistent headache and immunosuppression.

Keywords: Central nervous system, Neglected diseases, Neuroparacoccidioidomycosis, *Paracoccidioides*, Paracoccidioidomycosis

BACKGROUND

The paracoccidioidomycosis (PCM) is caused by the fungus *Paracoccidioides brasiliensis*, and it is the principal systemic fungal infection endemic to the Latin America^[9] and is not usually related to immunosuppression status.^[11,17] It mainly affects male individuals engaging in agriculture and in contact with soil.^[14] A PCM exhibits variable clinical presentation, with increased tendency to compromise multiple organs and systems.^[10,17,18] The lungs are the most common affected organ.^[7] However, the fungus can disseminate to any organ, including the central nervous system (CNS) in

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10–27% of times.^[2] In some reports, the CNS can be the only organ compromised by PCM.^[4,5] The CNS compromise by PCM is not common and when it happens, it is mostly associated with pulmonary and skin manifestation of the disease.^[2] Most of the cases presents with multifocal disease manifested as increased intracranial pressure and seizures.^[3] The CNS involvement is due to hematogenic dissemination from peripheral foci.^[15] PCM and neuroparacoccidioidomycosis (NPCM) are more prevalent in males in a 11:1 ratio.^[1,16,17] In a systematic review, 93% of patients were male living in rural areas.^[12]

In addition, CNS forms of PCM can be further characterized as pseudotumoral or parenchymal, and meningoencephalitic presentation.^[15] The pseudotumoral forms of NPCM (abscess, granulomas, and intraparenchymal cyst) are more frequent, with the meningoencephalitic counterparts presenting in 10% of the cases.^[12] The patient reported in this case featured a pseudotumoral form, however with extra-axial (subdural) compromising. The main symptom was persistent headache, which is unspecific presentation. Likely the small size of the subdural collection did not cause cortex compromise, which sometimes can manifest as seizures, as previous related.^[5,18]

The differential diagnose is broad for inflammatory subdural collections. On brain magnetic resonance imaging (MRI), single or multiple hypointense cystic lesions with peripheral enhancement are not specific.^[15] Additional histopathologic studies are required and are characterized by noncaseous granulomatous reaction with typical multinucleated giant cells.^[5] In addition, Grocott's methenamine silver stain is required to identify yeast-like forms, being the classic “pilot's wheel” characteristic of *P. brasiliensis*.^[13,16]

Patients with SLE are immunosuppressed and have a higher risk of developing fungal infection.^[6] The association of PCM and SLE is rare.^[8] From our knowledge, there is no mention in the literature of a case of NPCM associated with SLE under immunosuppression therapy in a female patient. It was not clear for us if the patient was previously exposed to the PCM, or it was clearly related to the immunosuppression status. Systemic lupus erythematosus (SLE) is a risk factor for invasive fungal infections, however, the association with PCM is rare.^[18] The aim of this study is to report a case of NPCM in an immunosuppressed patient diagnosed with SLE under prednisone and azathioprine, successfully treated with itraconazole for 12 months.

CASE DESCRIPTION

This is a 37-years-old female patient with recent diagnose of SLE, who presented with persistent pulsatile bitemporal headache started 4 months ago, daily, and progressively worse. Photophobia was present, however, no nausea or vomiting or phonophobia was reported. It was accompanied by weakness in the right arm noticed 1 week before presentation, which prompted her to come for evaluation. She was taking

prednisone 40 mg daily, azathioprine 50 mg twice daily, and hydroxychloroquine 400 mg daily. Family history was unremarkable. The physical examination, showed blood pressure 115/77 mmHg, heart rate 80 bpm, respiratory rate 20 ipm, and axillary temperature of 36.2°C. Bilateral rash was noticed in the malar area of the face. During neurologic examination patient was alert and oriented in time, place, and person. Speech and language appropriated. The pupils were reactive to light and accommodation bilateral. Fundoscopy without signs of papilledema. Other cranial nerves showed preserved function. Strength was 5/5 in all four extremities and with normal reflexes. Sensibility was globally preserved, and the gait was normal. No nuchal rigidity was appreciated.

Laboratory wise showed hemoglobin 13.3 g/dL, hematocrit 40%, leukocytes 7.143/mm³, platelets 223.300/mm³, creatinine 0.78 mg/dL, blood urea nitrogen 10 mg/dL, sodium 141 mEq/L, potassium 3.7 mEq/L, magnesium 2.09 mg/dL, ionized calcium 1.26 mmol/L, and C-reactive protein 2.4 mg/dL.

Computerized tomography of the head [Figure 1] showed left extra-axial parietooccipital focal hypoattenuation with adjacent bone erosion. Brain MRI [Figure 2] reported left parietooccipital subdural collection associated with focal leptomenigeal thickening. It was considered that the cerebrospinal fluid analysis would not add a definitive diagnose in this case, even though could potentially demonstrate arachnoiditis, so it was not performed, and the patient was taken for open surgery.

Neurosurgery was consulted and recommended craniotomy for evacuation of the subdural collection. During the procedure, the collection was not purulent, which raised no concerns for subdural empyema. However, given bone erosion and concerns for chronic osteomyelitis on imaging, it was opted for partial bone resection. The adjacent dura mater was resected showing noncaseous granuloma with multinucleated giant cells and asteroids bodies on histopathology [Figure 3]. In addition rounded birefringent

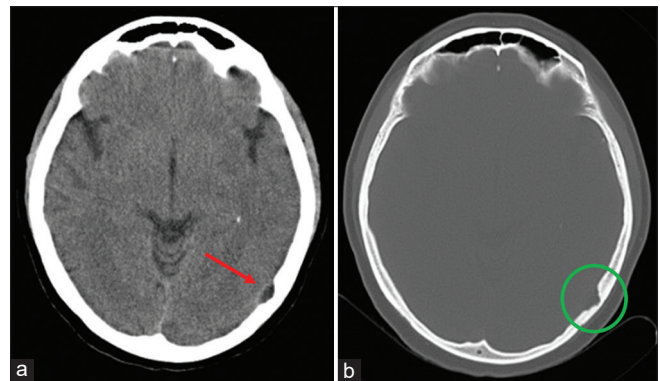


Figure 1: Computed tomography of the head showing in a (small arrow) left extra-axial parietooccipital focal hypoattenuation and in b (green circle) adjacent bone erosion.

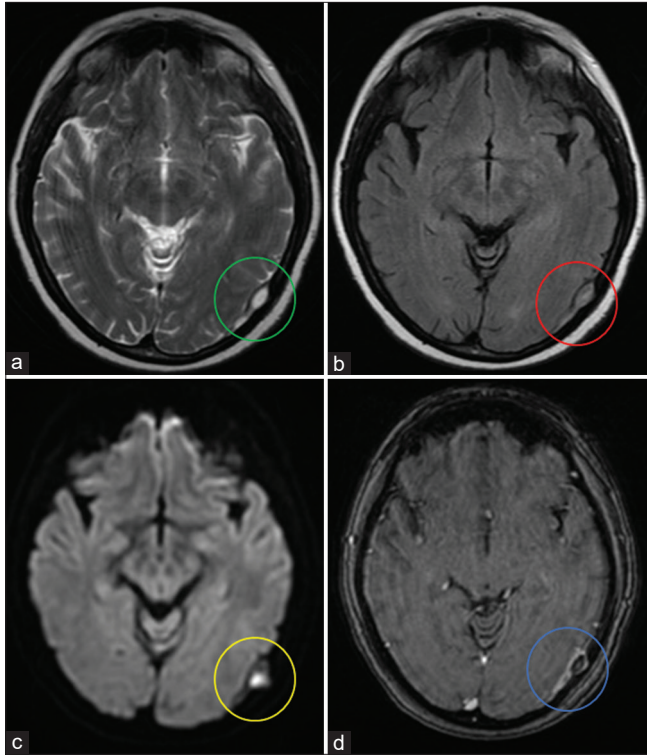


Figure 2: Brain magnetic resonance imaging sequences. In a (green circle), T2 weighted. In b (red circle), fluid attenuation imaging recovery acquisition (FLAIR). In c (yellow circle), diffusion-weighted sequence (DWI). In d (blue circle), gadolinium-enhanced T1 acquisition. One can see left parietooccipital subdural collection well demarked with hypersignal in T2 and intermediate signal in T2/FLAIR with water restriction to diffusion in DWI and peripheral enhancement after contrast.

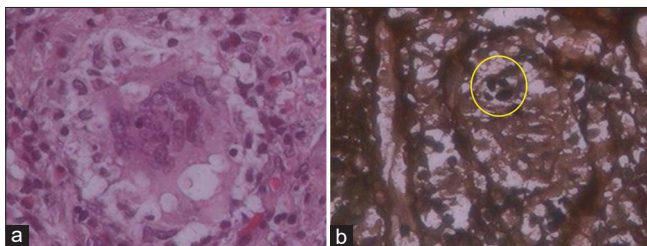


Figure 3: Left parietooccipital dura mater biopsy. In a, noncaseous granuloma with multinucleated giant cells. In b, silver stain showing rounded birefringent structures consistent with paracoccidioidomycosis (circle).

structures with positive silver stain consistent with PCM were noticed. Infectious disease was consulted and itraconazole was started 200 mg daily for 12 months. After procedure, the patient showed improvement of headache and of the weakness. Follow-up was unremarkable and the patient completed treatment without side effects. After 12 months of treatment, there were no residual lesions on imaging.

CONCLUSION

PCM is a systemic fungal infection endemic in Latin America, especially in Brazil. It is common in males working in an agricultural setting or in direct contact with soil. It is rare in females not involved with those activities. Usually, there is no association with immunosuppression. In addition, there are multiple clinical presentations, however, NPCM is not frequent. When isolated, the diagnosis is challenging and requires histopathologic analysis, given imaging test is not conclusive. The treatment is based on long-term antifungal therapy with itraconazole.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Banushree CS, Madhusudhan NS. Pathogenesis of fungal infections. In: Turgut M, Challa S, Akhaddar A, editors. *Fungal Infections of the Central Nervous System: Pathogens, Diagnosis, and Management*. Berlin/Heidelberg: Springer International Publishing; 2019. p. 31-42.
- Da Silva CE, Cordeiro AF, Gollner AM, Cupolilo SM, Quesado-Filgueiras M, Curzio MF. Paracoccidioidomycosis of the central nervous system: Case report. *Arq Neuropsiquiatr* 2000;58:741-7.
- De Macedo PM, Falcão EM, Freitas DF, Freitas AD, Coutinho ZF, Muniz MM, *et al.* Neuroparacoccidioidomycosis: A 13-year cohort study, Rio de Janeiro, Brazil. *J Fungi (Basel)* 2020;6:303.
- Francesconi E, da Silva MT, Costa RL, Francesconi VA, Carregal E, Talhari S, *et al.* Long-term outcome of neuroparacoccidioidomycosis treatment. *Rev Soc Bras Med Trop* 2011;44:22-5.

5. Gonzalez-Lara MF, Ostrosky-Zeichner L. Fungal Infections of the brain. In: Hasbun HR, Bloch PH, Bhimraj A, editors. *Neurological Complications of Infectious Diseases*. Berlin/Heidelberg, Germany: Springer International Publishing; 2021. p. 201-24.
6. Jeong SJ, Choi H, Lee HS, Han SH, Chin BS, Baek JH, *et al.* Incidence and risk factors of infection in a single cohort of 110 adults with systemic lupus erythematosus. *Scand J Infect Dis* 2009;41:268-74.
7. Kauffman CA. Central nervous system infection with other endemic mycoses: Rare manifestation of blastomycosis, paracoccidioidomycosis, talaromycosis, and sporotrichosis. *J Fungi (Basel)* 2019;5:64.
8. Londero AT, Santos W, Silva LA, Ramos CD. Paracoccidioidomycose associada por droga imunossupressora em paciente com lupus eritematoso sistêmico. *J Pneumol* 1987;13:224-9.
9. Martinez R. Epidemiology of paracoccidioidomycosis. *Rev Inst Med Trop Sao Paulo* 2015;57 Suppl 19:11-20.
10. Mendes RP, Cavalcante RS, Marques SA, Marques ME, Venturini J, Sylvestre TF, *et al.* Paracoccidioidomycosis: Current perspectives from Brazil. *Open Microbiol J* 2017;11:224-82.
11. Neto EG, Coletto A, Biazus PG, Dos Santos IP, Rieder CR, de Castro Ribeiro M. Neuroparacoccidioidomycosis. *Neurol Neuroimmunol Neuroinflamm* 2019;6:e519.
12. Pedroso VS, Mde CV, Pedroso ER, Teixeira AL. Paracoccidioidomycosis compromising the central nervous system: A systematic review of the literature. *Rev Soc Bras Med Trop* 2009;42:691-7.
13. Rahman R, Davies L, Mohareb AM, Peçanha-Pietrobon PM, Patel NJ, Solomon IH, *et al.* Delayed relapse of paracoccidioidomycosis in the central nervous system: A case report. *Open Forum Infect Dis* 2020;7:ofaa077.
14. Riechelmann RS, Rodrigues LH, Avelar TM, Xander PA, da Costa GH, Cannoni LF, *et al.* Isolated neuroparacoccidioidomycosis as a pseudotumoral lesion in the absence of systemic disease. *In Surg Neurol Int* 2020;11:151.
15. Rosa M Jr, Baldon IV, Amorim AF, Fonseca AP, Volpato R, Lourenço RB, *et al.* Imaging paracoccidioidomycosis: A pictorial review from head to toe. *Eur J Radiol* 2018;103:147-62.
16. Shikanai-Yasuda MA, Mendes RP, Colombo AL, Queiroz-Telles F, Kono AS, Paniago AM, *et al.* Brazilian guidelines for the clinical management of paracoccidioidomycosis. *Rev Soc Bras Med Trop* 2017;50:715-40.
17. Shikanai-Yasuda MA, Mendes RP, Colombo AL, Telles FQ, Kono A, Paniago AM, *et al.* Brazilian guidelines for the clinical management of paracoccidioidomycosis. *Epidemiol Serv Saude* 2018;27:e0500001.
18. Silva MF, Ferriani MP, Terreri MT, Pereira RM, Magalhães CS, Bonfá E, *et al.* A multicenter study of invasive fungal infections in patients with childhood-onset systemic lupus erythematosus. *J Rheumatol* 2015;42:2296-303.

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