

ORIGINAL ARTICLE

Ocular paracoccidioidomycosis in the Western Amazon: a case report

Sebastião Afonso Viana Macedo Neves^{a,b}, Natália Pimentel Moreno^{a,b}, Rogério Ferraz Baquette^c, Jesiane Rocha da Silva Maia^{a,d}, Danielly Moreira Gonçalves^{a,b}, Irenilce Souza de Matos^{a,b}, Amaro Nunes Duarte Neto^e



^aUniversidade de Brasília, Universidade Federal do Acre, Programa de Graduação em Medicina, Rio Branco, Acre, Brasil.

^bHospital das Clínicas de Rio Branco, em Rio Branco, Acre.

^cLaboratório DNA, Hospital das Clínicas de Rio Branco, em Rio Branco, Acre.

^dPrograma de Clínica Médica em Hospital das Clínicas de Rio Branco, em Rio Branco Acre.

^eHospital das Clínicas, Departamento de Patologia, da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil.

Corresponding author

tiaoviana.sebastiao@gmail.com

Manuscript received: may 2024

Manuscript accepted: june 2024

Version of record online: july 2024

Orcid Authors

Sebastiao Viana: <https://orcid.org/0000-0001-8500-952X>

Natália Moreno: <https://orcid.org/0000-0002-0254-5026>

Jesiane Rocha da Silva Maia: <https://orcid.org/0009-0007-9178-7425>

Rogério Ferraz Baquette : <https://orcid.org/0009-0004-9167-631X>

Danielly Moreira Gonçalves: <https://orcid.org/0000-0001-9830-8852>

Irenilce Souza de Matos <https://orcid.org/0000-0003-4216-1390>

Amaro Nunes Duarte Neto - <https://orcid.org/0000-0001-6659-7186>

Abstract

Background: *Paracoccidioidomycosis* (PCM), a systemic mycosis related to agricultural activities, is prevalent in Brazil. Its insidious evolution can have serious consequences when not diagnosed and treated early. This endemic disease affects several organs, but ocular lesions are uncommon. A bibliographic search on Scielo and Medline found very few confirmed cases. This report relates the case of a 58-year-old male patient with an ulcerated and secreting lesion on the eyelid and blurred vision. He is a resident of a rural area in the municipality of Bujari, Acre, in the Brazilian Amazon.

Keywords: Paracoccidioidomycosis; Palpebral; Paracoccidioides ocular; Amazon mycosis.

Suggested citation: Macedo Neves SAV, Moreno NP, Baquette RF, Maia JRS, Gonçalves DM, Matos IS, Neto AND. Ocular paracoccidioidomycosis in the western amazon: a case report. *J Hum Growth Dev.* 2024; 34(2):366-370. DOI: <http://doi.org/10.36311/jhgd.v34.16335>

Authors summary

Why was this study done?

Because it is an uncommon clinical case and because it is a fungal disease with an increasing incidence in areas of occurrence in Central and South America, where health services are not always prepared for fast diagnosis and effective treatment.

What did the researchers do and find?

A case report was made, where the clinical findings showed Paracoccidioidomycosis in the ocular and disseminated clinical form

What do these findings mean?

A contribution to internal medicine and infectiology, drawing attention to the unusual forms of paracoccidioidomycosis

INTRODUCTION

Paracoccidioidomycosis (PCM) is endemic, with clinical expression in localized, cutaneomucosal, ganglionic, or systemic forms, with particular severity in immunocompromised patients. The skin, mucous, cutaneomucosal, nasopharyngeal, laryngeal, pulmonary, and intestinal membranes, as well as bone, are the most commonly affected sites¹.

Limited to South and Central America and Mexico, the Paracoccidioides brasiliensis (species *P. americana*, *P. restrepiensis*, *P. venezuelensis*) and Paracoccidioides lutzii complexes are defined through nuclear gene sequencing and phylogenetic analysis in Latin American isolates^{2,3}. Found in the form of mycelium, this dimorphic fungus is adapted to temperatures between 22 and 26 °C and as budding yeast in the form of a large “mother cell surrounded by blastoconidia”⁴.

The II Consensus of the Brazilian Society of Tropical Medicine-2018, recognized the following classification: Paracoccidioidomycosis infection, acute disease, subacute (juvenile form) moderate to severe, and chronic form. PCM can also present in a residual or scar form. In chronic forms, the occurrence ratio in men/women is 13:1 due to the differentiated presence of the hormone 17-Beta-estradiol in women, which inhibits the mycelium-yeast transition.

Thus, ocular involvement, as well as the involvement of the eyelids and conjunctiva, are uncommon. A bibliographic search using the Cochrane Library, LILACS, Scielo, Medline, PubMed, and PMC (Pub Med Central) found few cited and confirmed cases of ocular involvement. As most of these cases were recorded decades ago, they generally do not present the confirmation stages of the diagnosis, including images and other identification techniques described here⁵.

Biopsy is indicated for a definitive diagnosis. Granulomas are found with giant cells and yeasts, almost 30 µm, and commonly followed by daughter spores. Grocott-Gomori methenamine-silver nitrate and Periodic acid-Schiff (PAS) staining are usually used to identify the microorganism; however, smear microscopy and culture can also be employed⁶.

CASE REPORT

The patient, J. S. S. N., was 58 years and 10 months old, married, brown, a teacher, and a resident of Bujari, a rural area of Acre in the Brazilian Amazon. He had no comorbidities or family history of aneurysm, diabetes mellitus, hypertension, and leukemia. He denied previous hospitalizations. When asked about his lifestyle habits, he

reported being a social drinker and smoking 20 cigarettes a day.

He presented with discomfort, mild pruritus, and low-intensity pain in the right eye, with evolution for one year, which had worsened in the last four months. The lower right eyelid later exhibited a purulent corneal ulcer (Figure 1). After initial medical and ophthalmologist evaluations, he was prescribed eye drops and antibiotics, but he could not recall the names of the medicines. These drugs did not improve the infection. He also observed a slight fever, intermittent, in the previous two months, which worsened and included photophobia and pain. In 30 days, he experienced progressive loss of vision of about 50% visual acuity loss, which was worse after sleeping but improved with cleaning of the eye. Thus, he underwent a lesion biopsy (conducted by an ophthalmologist), and histopathology were requested. The histopathology found the presence of Paracoccidioides spp (Figure 2).

The patient had ulcerated lesions on the lower right eyelid, was purulent secretion and hyperemia of the sclera. He also presented respiratory tract symptoms of a rough vesicular murmur, inspiratory crackles in the middle third of the lungs, and a respiratory rate of 16/min. A physical examination found no other compromised systems.

Laboratory tests were requested, which showed a nonspecific blood count, with a sedimentation rate (ESR) of 80 mm, C-reactive protein (CRP) at 60 mg/L. The chest CT scan indicated bronchial wall thickening, bilateral interstitial infiltrates, ground-glass opacity, and bilateral pleural thickening (Figure 3).

After clinical and histopathological examination, his doctors concluded that the patient was affected by disseminated chronic PCM with ocular and pulmonary involvement. The histological picture associated with epidemiological, clinical, and radiological data was conclusive for Paracoccidioidomycosis (Figure 1,2).

An ophthalmological examination found visual acuity without correction of 20/70 in the right eye (RE) and 20/30 in the left eye (LE). The best-corrected visual acuity of 20/20 and 20/25 in the right and left eyes, respectively. Dynamic refraction was RE +1.50 sph and LE+1.00 sph. A biomicroscopy found ulcerated vegetating lesions in the right eyelid’s inferior tarsal conjunctiva and inferior palpebral margin. The cornea was clear without anterior chamber reaction, and there were no signs of uveitis or incipient cataract in the right eye. The left eye had a clear cornea and incipient cataract. Fundoscopy and ocular pressure were normal in both eyes. The excisional biopsy



Figure 1: Paracoccidioidomycosis, chronic form with ocular, ulcerated papular lesion on the lower right eyelid.

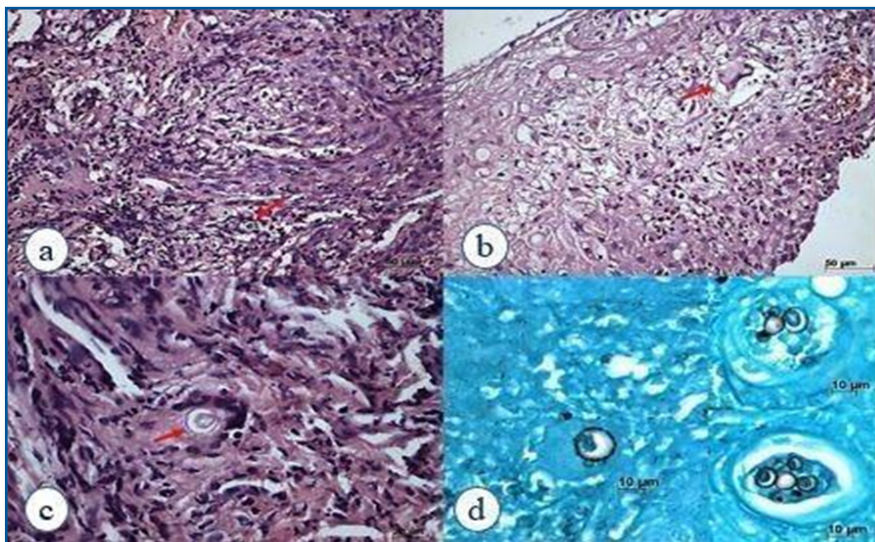


Figure 2: Histology of the palpebral mucosa demonstrates a chronic and ulcerated granulomatous inflammatory process, with some giant cells containing rounded and hyaline yeasts in the H&E stain, widely ranging in size with multiple and narrow-necked-budding. Figure d was stained with Gomori-Grocott methenamine silver.



Figure 3: Axial section of chest tomography in a parenchymal window, noting gross interstitial infiltrate and bilateral irregular micronodules, as well as thickening of the interlobular septa, notably the right one in a subpleural situation.

was performed on the right eye with a surgical margin.

He was medicated with itraconazole 200 mg twice a day for sixty days for thirty days and then maintained with 100 mg twice a day for another six months.

About sixty days after initiation of treatment, the patient showed progress toward a complete disappearance of the lesions on the right lower eyelid but still had a small papule. He also presented expressive regression of the lung lesions.

DISCUSSION

The dimorphic fungus *Paracoccidioides* spp causes systemic mycosis. Paracoccidioidomycosis is restricted to Latin America but is one of the main systemic mycoses in Brazil, frequent in the southern, southeastern, and central-western regions⁵. The disease is contracted through inhalation of fungal propagules. Acute infection occurs in childhood and involves the immune system. However, the chronic form with multifocal dissemination in adults is more common, affecting lungs, lymph nodes, skin, and mucous membranes.

The diagnosis of the chronic form is usually delayed, and cough, dyspnea, weight loss, and skin and mucous lesions are reported. Ocular lesions caused by PCM are very uncommon. They are clinically similar to several pathologies, such as the eyelid lesion that resembles a chalazion, with the appearance of a pruritic granuloma, with tearing and little or no purulent secretion or bleeding.

Cases have been described with granulomatous uveitis, preceded by a lesion in the oropharynx. After treatment with amphotericin, remission of the lesions was achieved. However, months later, a patient suffered paralysis of the III cranial nerve ipsilateral to the lesion, generalized involvement of the central nervous system, and death^{7,8}.

The chest X-ray may show diffuse reticulonodular infiltration, which is evidenced mainly in the middle lobes. Definitive diagnosis is made when *P. brasiliensis* is found in direct microscopic examination of specimens such as ganglion aspiration or BAL material, in addition to the growth of the *Paracoccidioides* in culture⁹. Histopathological analysis of tissue specimens may find a thickened and birefringent fungal cell wall and the typical exosporulation in the mother cell. According to recent guidelines, itraconazole is the best therapy for mild to moderate PCM clinical forms. Cotrimoxazole is a second option, and amphotericin B is used in severe cases of the disease¹⁰.

The form of involvement, the intensity, and the time it takes to diagnose and start treatment are the main

determinants of prognosis, which is directly proportional to the severity. Severe forms have high chances of developing sequelae, such as pulmonary fibrosis and emphysema, adrenal insufficiency, neurological involvement, cutaneous and mucosal fibrosis, and physical deformities. In the case reported here, the patient evolved well, with significant improvement of the lesion and no sequelae after being medicated.

The adult patient was from a rural area of the State of Acre, in Brazil's Western Amazon. This region has limited resources for the most accurate diagnoses of fungal diseases, especially in the public healthcare network, which includes few professionals specialized in tropical diseases, particularly fungal diseases. In addition, the availability of triazole drugs is restricted, which are now recognized as the first choice to treat Paracoccidioidomycosis. A case of extensive eye injury and bilateral lung involvement is considered a relevant public health case. Furthermore, its description could stimulate better diagnostic structures and access to treatment, which is time-consuming and expensive.

Extensive pulmonary cases, followed by disseminated forms, often evolve to fatal outcomes, mainly due to delayed diagnosis and therapy or even to the definitive loss of the patient's vision or respiratory and definitive functional impairment¹¹⁻¹³.

This case report discusses the diagnosis and therapeutic approach of a low-prevalence disease in an individual without previous comorbidities. The diagnosis required evaluation by multiple professionals. Pharmacological treatment was initiated with a good therapeutic response and progressive regression of lesions. The patient is still followed by an infectious disease specialist and maintaining progressive improvement.

Conflict of interest

The authors declare that they have no conflicts of interest.

Acknowledgments

To everyone who participated, directly or indirectly, in the development of this case report, where the objective is to disseminate information, share knowledge and experiences.

Financial Support

The submitted manuscript has not received any financial support from industry or other commercial sources.

REFERENCES

1. Palmeiro M, Cherubini K, Yurgel LS. Paracoccidioidomycose-revisão da literatura Paracoccidioidomycose-Revisão da Literatura Paracoccidioidomycosis-Literature Review. *Scientia Medica*. 2005.
2. Restrepo A, Gomez BL, McEwen JG, et al. Paracoccidioidomycosis. In: *Diagnosis and Treatment of Human Mycoses*, 3rd edition, Hospenthal DR, Rinaldi MG, Walsh TJ (Eds), SpringerLink, 2023.
3. Cocio TA, Nascimento E, von Zeska Kress MR, et al. Phylogenetic Species of *Paracoccidioides* spp. Isolated from Clinical and Environmental Samples in a Hyperendemic Area of Paracoccidioidomycosis in Southeastern Brazil. *J Fungi (Basel)* 2020.

4. Wanke B, Aidê MA. Capítulo 6-Paracoccidioidomicose* Chapter 6-Paracoccidioidomycosis. Vol. 35, J Bras Pneumol. 2009.
5. Shikanai-Yasuda MA, Mendes RP, Colombo AL, Telles FQ, Kono A, Paniago AMM, et al. II Consenso Brasileiro em Paracoccidioidomicose - 2017. Epidemiol Serv Saude. 16 de agosto de 2018;27(spe):e0500001.
6. Teixeira M de M, Cattana ME, Matute DR, Muñoz JF, Arechavala A, Isbell K, et al. Genomic diversity of the human pathogen Paracoccidioides across the South American continent. Fungal Genetics and Biology. 2020 July 1; 140.
7. Martinez R. Epidemiology of paracoccidioidomycosis. Revista do Instituto de Medicina Tropical de São Paulo. 2015 Sep;57(suppl 19):11–20.
8. Dantas AM, Yamane R, Camara AG. South American Blastomycosis: Ophthalmic and Oculomotor Nerve Lesions. The American Journal of Tropical Medicine and Hygiene. 1990;43(4):386-388.
9. Cruz AAV, Zenha F, Silva JT, Martinez R. Eyelid involvement in paracoccidioidomycosis. Vol. 20, Ophthalmic Plastic and Reconstructive Surgery. 2004. p. 212–16.
10. Oke I, Loporchio DF, Siegel NH, Subramanian ML, LaMattina KC. Chorioretinal paracoccidioidomycosis treated with intravitreal voriconazole and therapeutic vitrectomy. Am J Ophthalmol Case Rep. 2021 September 1; 23.
11. Valle ACF do, Guimarães RR, Lopes DJ, Capone D. Aspectos radiológicos torácicos na paracoccidioidomicose. Revista do Instituto de Medicina Tropical de São Paulo. 1992 Apr;34(2):107–15.
12. Cavalcante RS, Sylvestre TF, Levorato AD, de Carvalho LR, Mendes RP (2014) Comparison between Itraconazole and Cotrimoxazole in the Treatment of Paracoccidioidomycosis. PLoS Negl Trop Dis 8(4): e2793.
13. Campos EP de, Sartori JC, Hetch ML, Franco MF de. Características clínicas e sorológicas de 47 pacientes com paracoccidioidomicose tratados com anfotericina B. Rev. Med. Tropa. São Paulo [Internet]. 1984 August 1 [cited on 9 February 024];26(4):212-5.

Resumo

Introdução: A paracoccidioidomicose (PCM), micose sistêmica relacionada às atividades agrícolas, é prevalente no Brasil. Sua evolução insidiosa pode ter consequências graves quando não diagnosticada e tratada precocemente. Essa doença endêmica afeta vários órgãos, mas lesões oculares são incomuns. Uma busca bibliográfica no Scielo e Medline encontrou pouquíssimos casos confirmados. Este relato relata o caso de um paciente do sexo masculino, 58 anos, com lesão ulcerada e secretora na pálpebra e visão turva. Ele é morador de uma área rural no município de Bujari, Acre, na Amazônia brasileira.

Palavras-chave: Paracoccidioidomicose; Palpebral; Paracoccidioides ocular; Micose amazônica.

©The authors (2024), this article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.