



# Oral Paracoccidioidomycosis, Clinical Characteristics, Diagnosis and Treatment

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## Abstract:

Paracoccidioidomycosis (PCM) is an infection caused by the dimorphic fungus *Paracoccidioides brasiliensis*, which has a predilection for hot and humid places; thus, this disease has a particularly high incidence in Brazil. Children, adolescents, and adults can be affected by acute/subacute or chronic PCM. To describe the clinical-pathological characteristics and treatment of a case of chronic PCM oral lesion. The oral examination of a 57-year-old male patient revealed moriform stomatitis on the perioral region (irregular shape), lips vermilion, and continuity with the jugal mucosa. After an incisional biopsy, the anatomopathological analysis confirmed the diagnosis of PCM. The patient was referred to a reference center for tropical diseases and treated with 400mg sulfamethoxazole and 80mg trimethoprim twice a day. Since some adverse effects were observed, the treatment was switched to 100mg of itraconazole twice a day. The follow-up examination revealed accelerated healing of the oral lesions and reduction of the inflammatory process. Stomatologists play a key role in the identification of PCM oral lesions and referral for adequate treatment by an infectious disease specialist.

**Keywords:** Paracoccidioidomycosis; Oral manifestations; Diagnosis; Fungi

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## INTRODUCTION

Paracoccidioidomycosis (PCM) is an infection caused by the dimorphic fungus *Paracoccidioides brasiliensis*, which has a predilection for hot and humid places; thus, this disease has a particularly high incidence in the south, southeast, and central-west regions of Brazil. In addition to lung infection, the fungus can spread through both bloodstream and lymphatic stream, and affect other organs<sup>6,11,15</sup>.

Children, adolescents, and adults over 30 years of age can be affected by acute/subacute or chronic PCM, which can vary from mild up to life-threatening cases. Its anatomopathological aspect is characterized by a suppurative granulomatous pattern mainly observed in lungs, mucous membranes of the upper respiratory tract and mouth, skin, and lymph nodes<sup>3</sup>. Patients with chronic oral PCM present sialorrhea and slowly evolving and painful ulcerative lesions (moriform stomatitis) that predominantly occur in the palate, gingiva, and tongue<sup>7,14</sup>.

Direct mycological examination, culture, and serology are methods to diagnose PCM. The investigation of potentially contaminated sites such as the lung, oral mucosa, and lymph nodes can speed up the definitive diagnosis and consequent treatment of PCM<sup>4</sup>. Since fungal morphology

can not be observed through hematoxylin and eosin (H&E) staining of tissue sections, Grocott-Gomori methenamine silver stain (GMS) is needed<sup>7</sup>. The first signs of PCM are usually observed by dentists, particularly stomatologists, which are expected to minimize the occurrence of sequelae by referring these patients to infectious disease physicians<sup>9,13</sup>. The following case report describes the clinical-pathological characteristics and treatment of a chronic PCM oral lesion.

## CASE REPORT

A 57-year-old white-skinned male, rural resident, with a smoking and alcoholism history presented to the Integrated Service of Oral Diagnosis and Dental Care for Special Patients of the Federal University of Pará (SIDOPE-UFPA) and complained about pain in the ulcerated labial and jugal mucosa. The patient reported the habit of chewing wood sticks and that the initial burning symptom started six months before.

The oral examination revealed moriform stomatitis on the perioral region (irregular shape), lips vermillion, and continuity with the jugal mucosa (Fig. 1A, B, C, and D). After an incisional biopsy, the analysis of H&E stained tissue sections revealed mucosal fragments



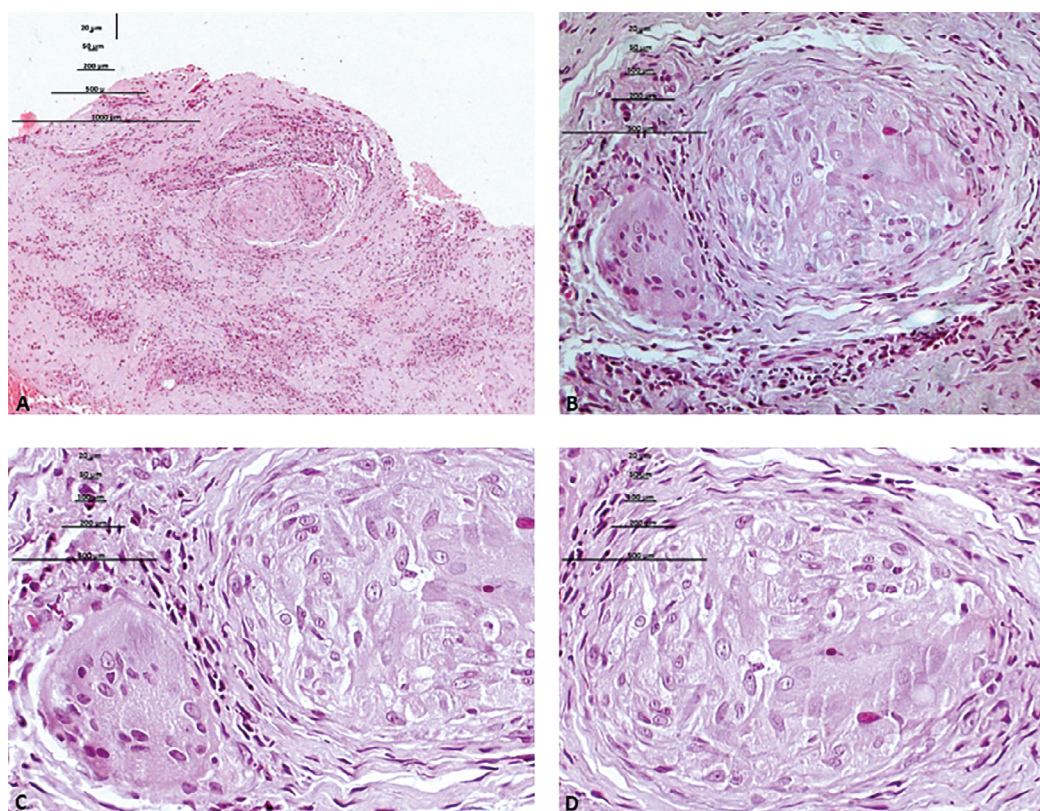
**Figure 1.** Clinical aspect of PCM oral lesions. Moriform stomatitis on the (A) lower lip mucosa, (B) perioral region and lips vermillion, (C) upper and lower labial mucosa, labial commissure, and tongue (erythematous pattern), and (D) left jugal mucosa.

coated by parakeratinized squamous epithelium and the presence of exocytosis and hydropic degeneration. The lamina propria presented a dense connective tissue, with chronic inflammation, lymphocytes, and macrophages. Yeast-like structures were observed throughout the lesion (Fig. 2A, B, and C). The anatomopathological examination revealed the presence of *Paracoccidioides Brasilienses* and a granulomatous inflammatory process with oval periodic acid-Schiff (PAS)-positive inclusion bodies inside multinucleated giant cells; therefore, the diagnosis was compatible with PCM.

The patient was referred to a reference center for tropical diseases in the Brazilian northern region and treated with 400mg sulfamethoxazole and 80mg trimethoprim twice a day. Since some adverse effects such as gastrointestinal discomfort, diarrhea, nausea, and mouth lesions were observed, the treatment was switched to 100mg of itraconazole twice a day. The follow-up examination revealed accelerated healing of the oral lesions and reduction of the inflammatory process.

## DISCUSSION

PCM is a deep infection caused by the dimorphic fungus *Paracoccidioides brasiliensis*. This rare and endemic disease has a high prevalence in Brazil<sup>6,11,18</sup>. Since the soil is the main natural source of infectious conidia, people living in rural areas have a higher risk of developing acute/subacute or chronic PCM, which depends on the incubation period and individual characteristics. The acute/subacute PCM mainly affects both males and females under 30 years of age, while the chronic form represents about 80% of the cases and is mainly observed among adult male rural workers<sup>2,9,12,15</sup>, which corroborates this case report. Souza et al<sup>17</sup> also reported that this infection has a predilection for men. This difference is explained by the hormone protective factor in women, in which estrogen receptors in *Paracoccidioides brasiliensis* inhibits its transformation from mycelial (infective) to yeast phase (parasitic)<sup>10</sup>. Moreover, Moreira<sup>6</sup> and Silva et al<sup>15</sup> reported that most of the individuals diagnosed with PCM are Caucasians, which is in line with this case report.



**Figure 2.** The microscopic findings showed a marked granulomatous inflammation characterized by collections of epithelioid macrophages. Multinucleated giant cells and growing fungus can be observed in the central region (H&E, 10x and 40x magnification).

In accordance with Souza et al<sup>16</sup> and Souza et al<sup>17</sup>, etiological factors of PCM such as age (between 30 and 70 years), soil-related occupation, and deleterious oral habits were observed in this case report. Araújo et al<sup>1</sup> also reported that chewing leaves/vegetables and tooth picking with wood sticks represent an additional risk for fungal contamination.

Oral lesions are the most frequent clinical manifestation of chronic PCM<sup>12</sup> and an essential aspect of its diagnosis<sup>3</sup>. In this case, ulcerated lesions known as moriform stomatitis were observed on the perioral region in addition to lips vermilion and jugal mucosa as described by Marques et al<sup>5</sup> and Neville et al<sup>7</sup>. However, the definitive diagnosis of PCM required the confirmation of fungal presence in the tissues through histopathological examination<sup>7,8,17</sup>. Firstly, tissue sections stained with H&E showed mucosal fragments with pseudoepitheliomatous hyperplasia and a chronic granulomatous inflammatory infiltrate with multinucleated giant cells in the lamina própria. Then, the use of PAS evidenced the acid-reactive circular structures, while GMS revealed silver-impregnated circular structures in the lamina propria.

The treatment of PCM is usually conducted by an infectious disease specialist that prescribes an adequate dosage of systemic antifungal drugs such as itraconazole<sup>11,12</sup> and sulfonamide derivatives<sup>13</sup>. In this case, the use of sulfamethoxazole and trimethoprim was replaced by itraconazole due to adverse effects, and marked regression of PCM clinical signs was observed.

## CONCLUSION

Stomatologists play a key role in the identification of PCM oral lesions and referral for adequate treatment by an infectious disease specialist.

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