Original Article

Oral paracoccidioidomycosis: Retrospective analysis of 55 Brazilian patients

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Summary
Paracoccidioidomycosis (PCM) is a rare fungal infection in the world, but endemic and acquired exclusively in Latin America, with the highest prevalence in South America and Brazil, particularly. Changes in oral cavity are common and constitute the first clinical manifestation in many patients. The aim of this study was to describe the prevalence of oral PCM and analyse the profile of the disease and patients. Retrospective research, consisting of information present in the medical records in the period 1998-2015, whose histopathological diagnosis was oral PCM. Fifty-five oral PCM cases were confirmed. Of these patients, 90.9% were males and 9.1% were females. The average age was 49.66 years and the most reported occupation was rural workers. The painful symptomatology was present in 61.82% of patients. Erythematous lesions were predominant in 73% of them. In single lesions (22 cases), the most common locations were jugal mucosa and tongue. In multiple involvement (30 cases), the most affected regions were lips, jugal mucosa and alveolar ridge. Epidemiology of PCM, was similar to several other studies, especially in Brazil. This is the most important fungal infection in Latin America and the recognition of oral lesions is extremely important, as it is often the first and in many cases the only manifestation of the disease.

Keywords
Brazilian patients, epidemiology, oral paracoccidioidomycosis, retrospective study

1 INTRODUCTION

Paracoccidioidomycosis (PCM) or South American blastomycosis is a deep fungal infection caused by the dimorphic fungus Paracoccidioides brasiliensis.1,2 It is a rare disease in the world, but endemic and acquired exclusively in Latin America, with the highest prevalence in South America and Brazil, particularly.3

This mycosis predominantly affects middle-aged male, engaged in rural activities.4 The incidence is higher in typically humid geographic areas, with rainfall high levels and acidic soils.1 According to epidemiological studies conducted in Latin America, around 50% of the inhabitants of endemic areas have been exposed to the fungus, but a small proportion of patients develop a clinical manifestation.5

Clinically, PCM presents two distinct patterns, according the incubation period and the profile of the affected individuals. The acute form, responsible for 10% of patients, is characterised by an abrupt and severe progression of infection that affects children and young people of both sexes. The chronic form, which is seen in 90% of cases, affects adults, mostly male and presents with primary pulmonary impairment and, secondary, mucosal lesions, skin, lymph nodes and adrenal glands.6

Changes in the oral region are quite common and constitute the first clinical manifestation in many patients. They are virtually pathognomonic and described as moriform lesions: granular, erythematous or ulcerated appearance contouring by jagged edges with a thin haemorrhagic dotted. They are located in various places: lips, gingiva, tongue, mouth floor, buccal mucosa, uvula, pharynx and cervical-facial regions.7,8

The treatment comprises addition of antifungal agents and the use of measures to improve the general condition of the patient. Some controlled studies and case series have shown that azoles fast action and sulfa derivatives are useful therapeutic options for milder forms of...
the disease while in moderate/severe cases, longer treatments or parenterally are needed, especially when there is mucosal involvement.9

The epidemiological approach to PCM is difficult, since its notification is not compulsory. The prevalence calculations, incidence and morbidity are based on reports of epidemiological studies and case series.10

The aim of this study was to assess the prevalence of oral PCM and analyse the profile of the disease and patients diagnosed at Maxillofacial Pathology Laboratory of the School of Dentistry in the Federal University of Minas Gerais, Brazil.

2 | MATERIALS AND METHODS

This is a retrospective and observational study. The sample consisted of information present in medical records of patients diagnosed with oral paracoccidioidomycosis (PCM) in Laboratory of Oral and Maxillofacial Pathology of the Faculty of Dentistry, Federal University of Minas Gerais, Belo Horizonte, Brazil, in the period 1998-2015 (18 years). The referred laboratory is an important diagnostic center and meets the demand for histopathological examinations of the public and private services, being a reference in the area.

The following variables related to patients were collected: gender, age, profession and skin colour. Regarding infection, the data were gathered about their location, colour, symptoms, early or recurrent signs and final diagnosis methods.

![Distribution of patients with oral paracoccidioidomycosis (PCM) according to gender](image)

**TABLE 1** Frequency, clinical characteristics and means of removal of lesions of paracoccidioidomycosis present in the oral cavity of patients attended at the Faculty of Dentistry of UFMG

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Manifestation</td>
<td></td>
</tr>
<tr>
<td>Primary lesion</td>
<td>46</td>
</tr>
<tr>
<td>Recurrent lesion</td>
<td>1</td>
</tr>
<tr>
<td>Not determined</td>
<td>8</td>
</tr>
<tr>
<td>Painful symptomatology</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>34</td>
</tr>
<tr>
<td>Absent</td>
<td>13</td>
</tr>
<tr>
<td>Not determined</td>
<td>8</td>
</tr>
<tr>
<td>Diagnosis tests</td>
<td></td>
</tr>
<tr>
<td>Incisional biopsy</td>
<td>47</td>
</tr>
<tr>
<td>Excisional biopsy</td>
<td>03</td>
</tr>
<tr>
<td>Not determined</td>
<td>5</td>
</tr>
<tr>
<td>Colourations of the lesions</td>
<td></td>
</tr>
<tr>
<td>Erythematous</td>
<td>40</td>
</tr>
</tbody>
</table>

Data were entered and tabulated using SPSS (Statistical Package for Social Sciences), version 22.0, which were statistically evaluated and converted to percentages, tables and graphs. This study was approved by the Ethics Committee of the School of Dentistry, Federal University of Minas Gerais (No. 51017615.7.0000.5149).

3 | RESULTS

From January 1998 to December 2015, 55 oral PCM total cases were confirmed. Of these patients, 50 (90.9%) were males and 05 (9.1%) were females, with a ratio of 10:1 (Figure 1). The average age was 49.66 years, range 06-81 years. In addition, the distribution for skin colour were as follows: Afrocaucasian 22 (40.0%), Caucasian 15 (27.27%) and black 12 (21.82%). These skin colour data were absents in 6 charts (10.90%).

Among the chips with information available, the most reported occupation was agricultural/rural workers (11 cases), followed by construction worker/builder (6 cases). Another 14 cases were various other professions such as surveyor, carpenter and trader.

![Histologic aspect of fungal structures of *Paracoccidioides brasiliensis*, indicated by the arrows: (A) Haematoxylin and eosin staining, (B) Grocott-Gomori staining (40X)](image)
TABLE 2 Oral Paracoccidioidomycosis (PCM) lesions distribution according to their location

<table>
<thead>
<tr>
<th>Injuries location</th>
<th>N</th>
<th>%</th>
<th>Multiple</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth floor</td>
<td>0</td>
<td>0.00</td>
<td>Mouth floor</td>
<td>6</td>
<td>7.69</td>
</tr>
<tr>
<td>Lip commissure</td>
<td>1</td>
<td>4.55</td>
<td>Lip commissure</td>
<td>3</td>
<td>3.85</td>
</tr>
<tr>
<td>Lobby fund</td>
<td>1</td>
<td>4.55</td>
<td>Lobby fund</td>
<td>2</td>
<td>2.56</td>
</tr>
<tr>
<td>Gingiva</td>
<td>2</td>
<td>9.09</td>
<td>Gingiva</td>
<td>5</td>
<td>6.41</td>
</tr>
<tr>
<td>Lip</td>
<td>2</td>
<td>9.09</td>
<td>Lip</td>
<td>15</td>
<td>19.23</td>
</tr>
<tr>
<td>Tongue</td>
<td>3</td>
<td>13.64</td>
<td>Tongue</td>
<td>3</td>
<td>3.85</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>2</td>
<td>9.09</td>
<td>Buccal mucosa</td>
<td>5</td>
<td>6.41</td>
</tr>
<tr>
<td>Jugal mucosa</td>
<td>7</td>
<td>31.82</td>
<td>Jugal mucosa</td>
<td>11</td>
<td>14.10</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0</td>
<td>0.00</td>
<td>Oropharynx</td>
<td>5</td>
<td>6.41</td>
</tr>
<tr>
<td>Hard palate</td>
<td>2</td>
<td>9.09</td>
<td>Hard palate</td>
<td>7</td>
<td>8.97</td>
</tr>
<tr>
<td>Soft palate</td>
<td>1</td>
<td>4.55</td>
<td>Soft palate</td>
<td>6</td>
<td>7.69</td>
</tr>
<tr>
<td>Alveolar ridge</td>
<td>1</td>
<td>4.55</td>
<td>Alveolar ridge</td>
<td>10</td>
<td>12.82</td>
</tr>
</tbody>
</table>

The used test for lesions diagnosis was incisional biopsy in 47 (85.45%) cases and excision in 03 (5.45%) of them. In five records, this information was not present. Figure 2A,B shows two histological staining methods used by service: haematoxylin–eosin (HE) and Grocott-Gomori (silver impregnation). Table 1 shows the clinical features findings of the 55 patients with PCM lesions.

In 46 cases (83.64%) the disease had a primary manifestation: There was only one case (1.81%) of recurrent manifestation, whereas in eight charts there was no indication of the type of manifestation of paracoccidioidomycosis: whether primary or recurrent. The painful symptomatology was present in 34 patients (61.82%), 13 (23.63%) was absent and was not determined in eight (14.55%). Erythematous lesions were predominant in 40 (73%) of the subjects, followed by white colour (7.27%). Normal mucosal-like colour was observed in 4 patients (7.27%). On the other hand, 3 patients (6%) of the lesions presented mixed coloration, be it a mixture of yellow, red and white. There was no information about the colour lesions in 4 charts (7.27%).

Of the 52 cases with available information as to their location and scope, 30 of them were multiple injuries and 22 had lesions in only one location. Table 2 shows the lesions distribution in the affected sites. It is observed that in individuals who had single lesions, the most common locations were jugal mucosa and tongue. Already in multiple involvement, the most affected regions were lips, jugal mucosa and alveolar ridge. Figures 3A,B,C shows the multiple oral manifestation of paracoccidioidomycosis in the gingiva, palate and oropharynx.

4 | DISCUSSION

Even though this study is showing the epidemiological aspects of paracoccidioidomycosis in Brazil, it is important to remember that some cases of the disease have already been diagnosed in other countries, such as Spain, Japan, Austria, and Germany. Although this disease is not endemic in those countries, these diagnoses may be related to the farmer or tourists who were traveling in Brazil or Central America.

There is a difficulty in determining the actual frequency of the disease. Notification is not always mandatory; a significant proportion of infected patients do not have clinical repercussions and many cases go undiagnosed because of lack of knowledge of health professionals, lack of patients access and disability laboratory diagnosis in some endemic areas.

According to Martinez, over 15 000 cases of PCM were reported in Latin America between the years 1930 and 2012 and more than 12 000 cases in Brazil. Their study, based on large data series of cases shows a high annual average number of cases reported in Brazil in endemic areas: southeast, south, central west and currently in the western Amazon region. Their incidence in Colombia, Venezuela and Ecuador, with an annual number of cases, is much smaller than in Brazil.

It is a disease that can be fatal and which manifests itself with a wide spectrum of clinical presentations, including frequent oral lesions. The oral mucosa manifestations often represent the main clinical symptom representing a spectrum of numbers between 39.38% and 50% of patients.

This study is an analysis of 55 patients with oral PCM in a period of 18 years. All cases were diagnosed by a single laboratory, located in the capital of Minas Gerais, which geographically is located in an endemic region in Brazil. Most affected individuals were men (90.9%), in the fourth decade of life and predominantly Afro-Caucasian (40%).

FIGURE 3 Clinical aspect of oral paracoccidioidomycosis (PCM) at multiple sites in the same patient: (A) Gingiva, (B) Palate, (C) Oropharynx. Note the morform appearance: granular and erythematous, contoured by jagged edges.
Paracoccidioidomycosis prevails among men, but the male:female ratio varies according to geographical region. In the Southeast and Midwest Brazil, it ranges from 3:1 to 10:1, reaching greater proportions, close to 100:1 in number of cases of southern Brazil and other South American countries. This study evaluated the manifestation of oral lesions and man relationship: found that women were 10:1, similar to previous work. Bicalho et al. found an even higher proportion of male involvement (30:1) that this work and stressed that although men and women are also infected with P. brasiliensis, women are protected by the inhibitory action of beta-estradiol on the fungus, which inhibits the formation of yeast cells of inhaled conidia and also modulates cellular immune responses, besides its low involvement in agricultural activities. It is interesting to remember that the primary infection occurs in the lungs, which may confound the diagnosis with tuberculosis. However, patients complain more commonly of dry cough, in contrast to tuberculosis which is accompanied by exudate and haemoptysis.

In general, PCM has been reported in patients, aged 2-102 years, but the prevalence is greatest between 30 and 60 years old and less frequent during the first decade of life and after age 70. The age of patients with oral manifestations ranged 06-81 years and the average age was 49.66 years. Some similar studies have found similar results with average age that also fall into the fourth decade of life, which can be explained by greater exposure to the fungus by adults in their work activities. Furthermore, it is believed that the great majority of the cases belongs to study chronic form of the disease which is seen in 90% of patients, it affects adults and often show secondary mucosal lesions.

With regard to patients skin colour, 22 (40.0%) were Afrocaucasian, 15 (27.27%) white and 12 black (21.82%). Large case series showed no racial predisposition to the development of paracoccidioidomycosis. However, in a retrospective study with 1219 patients in Brazil, it was observed that black and mulattoes tend to have an increased prevalence of acute/subacute and white patients showed a predominance of chronic disease.

The association between PCM with housing in rural areas and agricultural business activities is also described in the literature. Paniago et al. reported that 45.5% of 422 patients were rural workers, Bicalho et al. found this association in 53% of patients and Souza et al. found that 65.2% lived in rural areas or working with agriculture. Although the medical records were incomplete in the profession of infected patients, since some of them did not inform the profession, it can be observed that the majority of the patients were farmers (11 cases) and constructors (6 cases). These professions are related to the exploitation of the soil. Soil is the main habitat of P. brasiliensis and its filamentous form of infection is usually found in the soil or leaves of plants facilitating their inhalation by these professionals.

There are some laboratory diagnostic methods of the disease, including scaling analysis of the lesions, sputum or by biopsy. Paniago et al. emphasises that the diagnosis of ringworm when there are accessible lesion (skin, mucosa or superficial lymph node), the direct microscopic examination of material obtained from lesions should be preferred for its simplicity and accuracy. All the cases in question were diagnosed by histopathological examination of biopsied specimens of oral lesions. The incisional biopsy was the most used technique (85.45% of cases) for diagnosis, and shown to be effective in the diagnosis of oral lesions as demonstrated in other studies. Some differential diagnosis should be included to such injuries, especially squamous cell carcinoma, tuberculosis, sarcoidosis and Wegener’s granulomatosis.

Regarding the location of the oral lesions of 52 cases with available information, 30 of them were multiple injuries and 22 had lesions in only one location. Multiple injuries affected predominantly the lips, oral mucosa and alveolar ridge, while the only injuries were more present in the oral mucosa, tongue and alveolar ridge. As in the present work, Brazão-Silva et al. and Verli et al. evaluated only oral lesions and found multiple manifestation in most cases, the most frequent locations—gingiva and alveolar ridge, followed by the hard and soft palate, buccal mucosa and tongue.

In conclusion, this study revealed that the epidemiology of paracoccidioidomycosis, including the demographic profile of patients and their clinical presentations were similar to several other series of cases, especially in Brazil. This is the most important fungal infection in Latin America and the recognition of oral lesions is extremely important, as it is often the first and in many cases the only manifestation of the disease. Moreover, increasingly observed cases diagnosed outside of rural areas due to increased urbanisation and away from endemic areas related to globalisation and travel to South and Central America.

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CONFICT OF INTEREST

There are no conflicts of interest.

REFERENCES


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