

Disseminated paracoccidioidomycosis diagnosis based on oral lesions

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Abstract

Paracoccidioidomycosis (PCM) is a deep mycosis with primary lung manifestations that may present cutaneous and oral lesions. Oral lesions mimic other infectious diseases or even squamous cell carcinoma, clinically and microscopically. Sometimes, the dentist is the first to detect the disease, because lung lesions are asymptomatic, or even misdiagnosed. An unusual case of PCM with 5 months of evolution presenting pulmonary, oral, and cutaneous lesions that was diagnosed by the dentist based on oral lesions is presented and discussed.

Keywords: Infection, oral disease, oral mycosis, paracoccidioidomycosis

Introduction

Paracoccidioidomycosis (PCM), also known as South American blastomycosis, is a chronic mycosis caused by *Paracoccidioides brasiliensis*.^[1] PCM more commonly affects farm workers and/or people who live in rural areas, people between 30 and 50 years of age, particularly males. The disease is more prevalent in South and Central Americas, especially in regions with wet climate, high rainfall, and acid soils.^[2,3]

In general, PCM manifests firstly in lungs, and later may spread systemically, affecting lymph nodes, skin, oral and nasal mucosae, adrenal glands, gastrointestinal tract and central nervous system through lymphatic and blood vessels.^[1,4] Expectoration, cold, dyspnea, thoracic pain, fever, hemoptysis, anorexia, and weight loss are observed in most cases.^[4] Oral lesions commonly affect gums, palate, and labial and buccal mucosae.^[1,4]

The treatment requires administration of antifungals, lasting between 6 and 12 months.^[4] Differential diagnosis includes other deep mycoses, and squamous cell carcinoma.^[1]

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This study presents a case report of PCM with lung, skin and oral manifestations whose diagnosis was reached based mainly on oral lesions, by the dentist.

Case Report

A 41-year-old mulatto, male, bricklayer, reported to our institution with a chief complain of an ulcer located in the palate with 5 months of duration that, in his own words, “caused a nuisance during meals”. He reported that he smoked 20 cigarettes a day for 20 years and that lived at rural area of the city. The patient also reported having lost weight (4 kg in the previous month), nocturnal sudoresis and dry cough. General clinical examination revealed an ulcer and a nodule, on the right shoulder skin [Figure 1a]. Intraoral examination revealed an ulcerative lesion with punctuate and hemorrhagic appearance involving gum and palate [Figure 1b and c] and poor oral hygiene habits. He also referred itching and discomfort in the throat for the previous month. The first diagnosis hypothesis was “infectious disease”.

An incisional biopsy of the palate lesion was performed. A sample was retrieved from the posterior portion of the palate, near midline [Figure 1c]. Then, the specimen was fixed in 10% neutral buffered formalin and paraffin embedded. Histological sections were submitted to hematoxylin and eosin staining for routine diagnosis. Histopathological examination revealed pseudoepitheliomatous hyperplasia with microabscesses. Moreover, it was observed granulomatous inflammation with epithelioid macrophages and multinucleated giant cells. These cells presented small round birefringent structures indicating presence of fungi, whose size and morphology were suggestive of PMC [Figure 2].

Blood test indicated leukocytosis and neutrophilia, suggesting the presence of infection. Radiographs of the thorax revealed reticulonodular infiltrate distributed in lungs, reinforcing the presence of infection.

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Taken together, clinical, histopathological, laboratory, and radiographic findings led to a final diagnosis of PCM. The patient was referred to pneumology treatment, which included itraconazole (200 mg/day for 6 months). The patient was also referred to dental practitioner to perform scaling and root planning procedures, but he did not follow the recommendation. After 5 months, the follow-up consultations were recover, and patient showed regression of skin [Figure 3a] and oral [Figure 3b and c] lesions, which leaved scar areas. Radiographs of the thorax confirmed the remission of lung lesions. After 12 months, there was no signal of recurrence.

Discussion

PCM is a systemic mycosis, noncontagious, acquired from soils contaminated with the microorganisms. It often has oral manifestations and eventual skin lesions. Therefore dentists must be capable to recognize its clinical features, in order to establish an accurate diagnosis.^[3] Our patient presented the disease for five months prior to diagnosis, and had attended to some health professionals who did not manage the disease properly, even though South Brazil is an endemic area for PCM.

The presence of cough, tiredness and weight loss raise the hypothesis of a chronic infectious lung disease followed by the emergence of skin and oral lesions. These could be fungal, bacterial, or viral.^[5] Among infectious diseases, PCM and tuberculosis are those that usually present lung and oral manifestations concurrently.^[6,7] The most common oral manifestations of these diseases are ulcerative lesions, especially in the palate and gums.^[3] Another possibility is that the patient had a lung disease unrelated to these mucocutaneous lesions, such as recurrent pneumonia.^[6]

The radiographic findings indicated lung infection. However, it is well-known that the radiological changes observed in PCM are diverse and unspecific.^[6,8] Other diagnostic aids such as computed tomography and pulmonary scintigraphy could contribute in diagnosis. Regardless, it should be emphasized that multidisciplinary efforts become evident, in order to achieve the definitive diagnosis.^[8]

Skin lesions associated with PCM are polymorphic, presenting as papulae, plaques or nodules, which sometimes become verrucous or ulcerative.^[3] The diverse clinical presentation regarding frequency, number, distribution, and morphology of the skin lesions is related to the interaction between agent and host.^[5] About 60% of cases, presents concomitantly in oral mucosa and skin. However, skin lesions often occur in head and neck region.^[9] The present case is unusual, because the patient had skin and oral lesions, simultaneously. Moreover, skin lesions ranged in appearance, presenting as ulcer and as nodule. Interestingly, these lesions were located on upper limbs, which are reported in only 15% of cases.^[9]

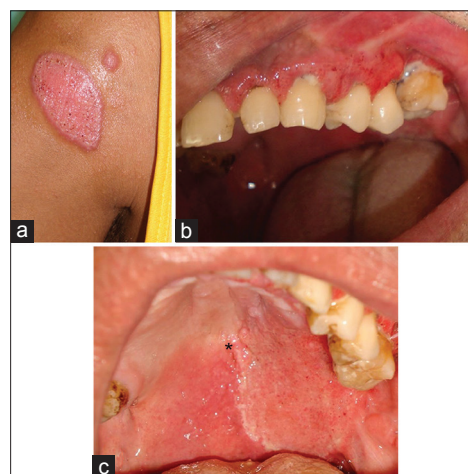


Figure 1: (a) Cutaneous lesions presenting as a sessile papule, covered by apparently normal skin and as an ulcer with punctate and hemorrhagic appearance. (b) Gingival lesion showing punctate and hemorrhagic appearance. (c) Palatal view showing an extensive ulceration with necrotic areas extending from midline to gingival margin. Asterisk indicates the biopsied area

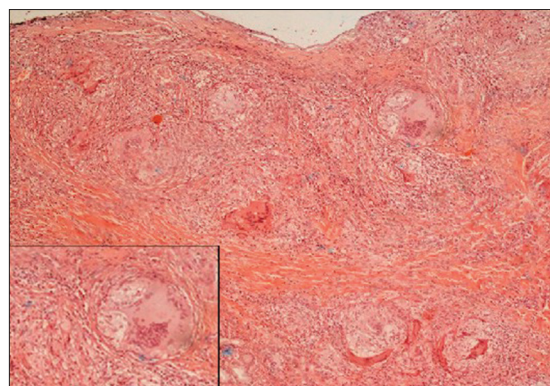


Figure 2: Microscopic view presenting granulomatous inflammation characterized by collections of epithelioid macrophages and multinucleated giant cells with small round structures indicating presence of fungi (detail)

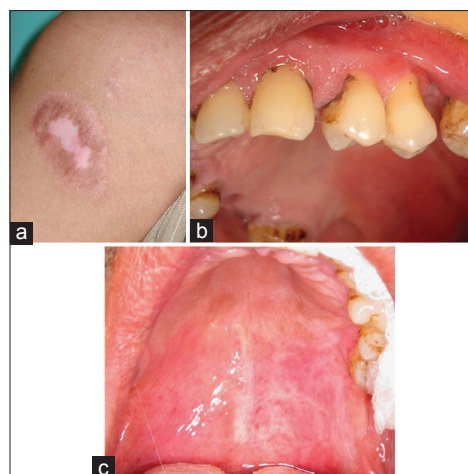


Figure 3: Clinical appearance after treatment, showing lesion remission. (a) Skin, (b) Gingiva, (c) Palate

This case attempts to highlight the importance to include a strict evaluation of general health conditions during clinical examination, which is sometimes neglected by a significant number of the general dentists. Particularly in our case, the observation of the skin lesion manifested as fine granular ulcers and pinpoint hemorrhages was strongly contributory, since these may be considered as pathognomonic sign of PCM.^[9]

Since our patient showed multiple oral lesions, squamous cell carcinoma (often included in differential diagnosis of PMC) was not considered, since it presents typically as a single lesion. On the other hand, the occurrence of an extensive oral ulcer includes leishmaniasis, cryptococcosis, histoplasmosis, tuberculosis and aspergillosis^[7] as differential diagnosis. The observation of moriform lesions in the gums was helpful, since these characteristics are described in 76% and 50% of PCM cases, respectively.^[10] In spite of that, the diagnosis could only be confirmed based on the biopsy and histological findings. This specific evaluation addresses morphological characteristics of the pathogen as to spore size, type of gemulation, and presence of septate hyphae.^[11]

Exfoliative cytology exams may be useful in diagnosis, but it requires experienced and training of professionals.^[4] Serological investigation, besides potentially contributory, is not routinely used in oral medicine in these cases.^[12] Several serological and molecular assays, like enzyme-linked immunosorbent assay and polymerase chain reaction, may also be useful for that purpose. Sensitivity and specificity of these assays may vary between 73.4-100% and 87.5-100%, respectively.^[12] Although sensitive and specific, serological assays are not reliable as a cure parameter, since high titers may be found even after cure. In this sense, definition of clinical criteria for resolution is difficult, and should be based on careful clinical evaluation.^[5]

Although PCM is a well-known disease, there are reports of cases whose diagnosis was difficult.^[1,5] In most cases addressed correctly, diagnosis is reached in approximately 3 months.^[13] In the present case report, the time interval elapsed between emergence of lesions on skin and definition of diagnosis based on oral lesions was 5 months. This delay may be explained in the light of the fact that symptoms of lung manifestations were unspecific, and that the clinical picture progressed slowly, since skin lesions were not appropriately diagnosed. The delay in reaching an accurate diagnosis may lead to disease spreading to abdominal lymph nodes, spleen, liver, suprarenal glands, urogenital tract, bones, gastrointestinal tract or brain, and eventually life risk. This complications were not observed in the present case.^[5]

Smoking may increase the susceptibility to PCM. One possible reason is acrolein, a cigarette component, which may cause inflammation, bronchoconstriction, increase of mucous secretion favoring respiratory infections like PCM.^[14]

The treatment recommended for PCM includes the oral administration of antifungal drugs. The drug choice is based on the severity and degree of dissemination of the disease, as well as on the immune status of the host. Itraconazole, amphotericin B and sulfonamides are the most commonly drugs prescribed. In our case, the treatment was itraconazole.^[3,7] In the case reported here, the infection subsided after 7 months, and the patient remained under follow-up. Since PCM is a systemic disease, the treatment is conducted by the physician and the regression of oral lesion must be followed by dentist.^[11] Multidisciplinary management allows the adoption of the best supporting measures to address the systemic changes associated to disease, like malnutrition and other comorbidities, as well as dental treatment. In addition, it should be emphasized that follow-up for extended periods is mandatory.^[15]

The present case report shows that the dentist has an important role in the patient's general health evaluation. The adoption of the all steps of clinical examination as routine decreases the chances of misdiagnosis and wrong therapeutic approaches. Early diagnosis is extremely important to prevent the more severe manifestations of the disease, which may lead to higher morbidity or even mortality.

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