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CASE REPORT

Oral paracoccidioidomycosis affecting the buccal mucosa

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Abstract

Paracoccidioidomycosis (PCM) is a disease caused by the fungus *Paracoccidioides brasiliensis*, common in Brazil and in some other areas of Latin America. We report a case of a 50-year-old male patient, farm worker, smoker, presenting with asymptomatic ulcerated lesion with moriform appearance in the left buccal mucosa. The patient underwent incisional biopsy and diagnosed with PCM. He was referred to the infectologist for treatment of the lesion. Although PCM primarily affects the lungs, it is often diagnosed through oral manifestations. Thus, dentists play a fundamental role in the identification of these lesions and referral for appropriate treatment.

Keywords: diagnosis, oral; oral manifestations; paracoccidioidomycosis.

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Introduction

Paracoccidioidomycosis (PCM), also known as South American blastomycosis, is a tropical disease caused by the dimorphic fungus *Paracoccidioides brasiliensis,* initially described by Adolfo Lutz in 1908[1,2]. Although a rare disorder from a global perspective, the disease is endemic in Latin America and is estimated to infect about 10 million Latin Americans. In Brazil, PCM is the main cause of death by systemic mycosis, and the eighth cause among infectious diseases[1,3], with an estimated incidence of approximately 1 to 3.7 cases per million individuals annually[1].

PMC more commonly affects farm workers and/or people who live in rural areas, particularly males, smokers and/or chronic alcoholics, aged between 30 and 50 years[2,3]. Although the primary route of PCM infection is pulmonary, the disease is often diagnosed by oral manifestations[4]. Oral mucosal lesions may be the first visible clinical manifestation of the disease, often even preceding lung lesions[1]. The oral cavity may be affected at one or multiple sites, with the gingiva/alveolar ridge and palate being the most frequent anatomical sites[1,2]. Classic clinical presentations are granular, erythematous or ulcerated lesions, with irregular borders and moriform appearance[2,5]. Furthermore, biopsies of PCM oral lesions are still uncommon in routine dentistry[1], which leads to many cases being diagnosed late, causing serious damage to the patient. Thus, dentists play a fundamental role in the diagnosis of these lesions and referral for appropriate treatment[5]. Herein, we report a case of PMC in buccal mucosa.

Case report

A 50-year-old male was referred to a private clinic for evaluation of a painless lesion on the buccal mucosa. Extraoral examination was unremarkable. The intraoral examination revealed an ulcerated lesion with moriform appearance in the left buccal mucosa, measuring approximately 2.0 cm in diameter (Figure 1A), and uncertain time of evolution. No other symptoms were present. The patient worked in farming, and that he was smoker and alcohol drinker. Considering all clinic features, a provisional diagnosis of PCM was established and an incisional biopsy was performed. Macroscopic examination revealed two fragments of fibrous soft tissue, yellowish in color, and with an irregular surface (Figure 1B). Microscopic examination of HE-stained histological slices revealed a fragment of oral mucosa lined by parakeratinized stratified squamous epithelium exhibiting acanthosis, exocytosis, spongiosis, and pseudoepitheliomatous hyperplasia. The lamina propria consisted of dense connective tissue, with an intense non-caseiform granulomatous inflammatory reaction, with the formation of numerous epithelioid histiocytes and Langhans giant cells (Figure 1C, 1D, and 1E). Histological sections stained in Grocott showed the presence of rounded yeasts, organized singly or forming multiple buds that resemble images classically described as "rudder wheel" or "Mickey mouse head", interpreted as yeasts of *Paracoccidioides brasiliensis* (Figure 1F and 1G). The diagnosis was PCM. The patient was referred to the infectologist for proper management of the lesion.

Discussion

PMC more commonly affects farm workers and/or people who live in rural areas, particularly males in the ratio of 15:1, smokers and/or chronic alcoholics, aged between 30 and 50 years[2,4,5]. This unequal distribution has been attributed to two main factors, namely: 1) the greater exposure of men to soil and 2) the role of estrogen, which inhibits the transformation of the mycelial form of the microorganisms to the yeast form, which is pathogenic[2,4]. These factors corroborate with the case reported here since the 50 years old patient was a smoker for over thirty years, alcoholic and worked in rural areas.

Most cases of PCM begin with pulmonary involvement after exposure to spores[4]. Inhalation of *P. brasiliensis* leads to infection even without manifestation of active disease[2]. The development of the disease depends on the virulence of the microorganism and the hormonal, genetic, nutritional, and immune conditions of the individual[2,4]. There may also be reactivations of latent foci. The latency period is quite variable, having been reported up to 60 years for the manifestation of the disease[1].

The clinical classification of infection includes acute/subacute (juvenile), chronic, and residual forms. The acute form is characterized by depression of the immune cellular response with low levels of IFN-γ production[4,5]. It usually affects young men and women, compromising liver, spleen, bone marrow, and lymph nodes[2]. The chronic form is much more common in men over 30 years of age, and its development is slow and gradual, affecting a single organ (unifocal) or several organs or systems (multifocal)[1,5]. Lung lesion is usually bilateral and symmetrical, giving a "butterfly wing" appearance in

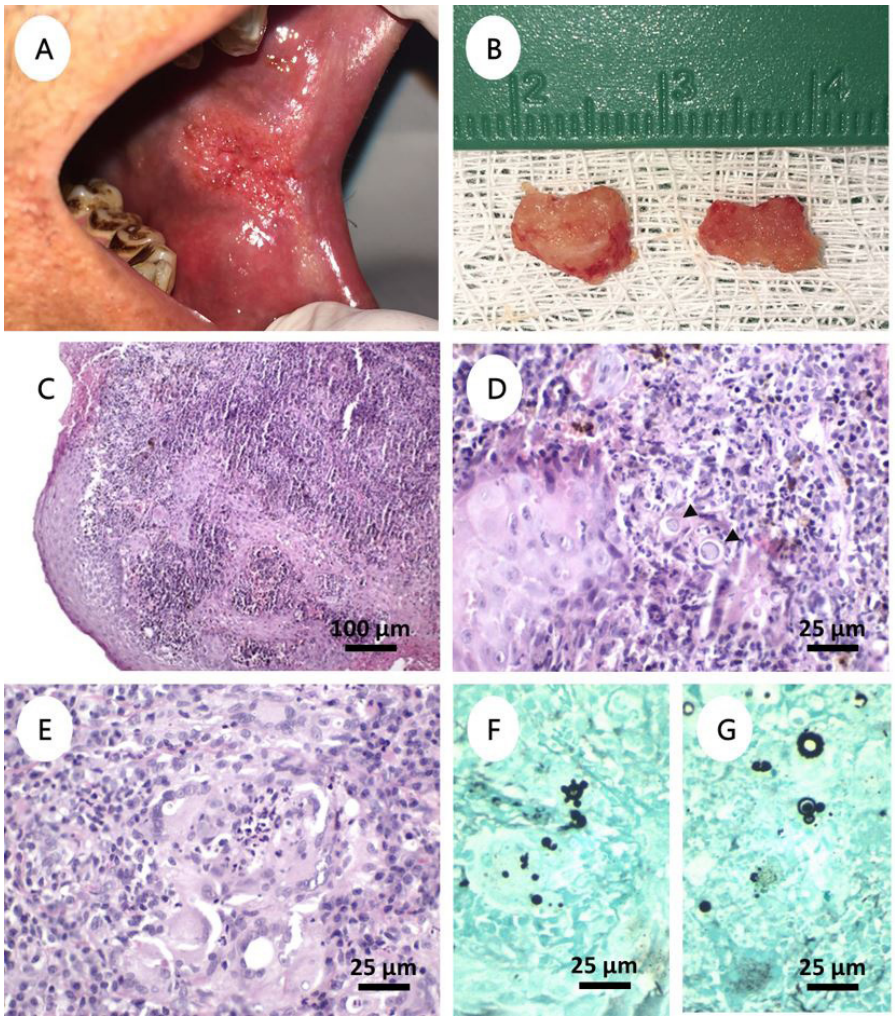

Figure 1. (A) Clinical aspect of the lesion. Multiple finely granular hemorrhagic pinpoint erosions with a mulberry-like appearance presented in the left buccal mucosa; (B) Macroscopic appearance of surgical specimens; (C, D, and E) Histological features of oral paracoccidioidomycosis; (C) The overlying mucosa showing pseudoepitheliomatous hyperplasia and an intense subepithelial inflammatory infiltrate; (D) Ovoid yeasts with birefringent membrane were also evidenced (arrows); (E) Non-caseiform granulomatous inflammatory reaction, with the formation of numerous epithelioid histiocytes and multinucleated giant cells (hematoxylin and eosin stain); (F and G) Grocott-stained sections showing the presence of microorganisms exhibiting multiple buddings (ship's wheel appearances) (F) and double buddings (Mickey Mouse ears) (G).

radiographic imaging[2]. The central and basal regions of the lungs can be affected, and the apex is usually spared[3].

Oral lesions frequently appear in the chronic form of PCM[1,2]. Clinically, the lesions are infiltrative, ulcerated, and with a moriform aspect. The anatomical sites most involved are the gingiva/alveolar ridge, tongue, palate, buccal mucosa, and lips[1-3]. Often, one or multiple sites of the oral cavity may be affected[1,5]. The nonspecific clinical presentation of PMC makes differential

diagnosis wide, including a spectrum of benign lesions, potentially malignant and malignant, with distinct biological behaviors. Squamous cell carcinoma, traumatic ulcer, lymphoma, oral tuberculosis, sarcoidosis, Wegener's granulomatosis, leishmaniasis, actinomycosis, and primary syphilis are some of the lesions that may have similar clinical characteristics[2].

The diagnosis of PCM is based on the identification of *P. brasiliensis* by histopathological examination or exfoliative cytology[5]. Histologically, lesions are represented by a fragment of oral mucosa lined by parakeratinized stratified squamous epithelium, which exhibits pseudoepitheliomatous hyperplasia and ulcerated areas[1,2,5]. The lamina propria is characterized by the presence of chronic granulomatous inflammation, rich in epithelioid macrophages and multinucleated giant cells, but usually without central necrosis[1,2]. The fungi appear as spherical structures with sizes ranging from 2 to 30 μm and may be dispersed by the inflammatory infiltrate or within multinucleated giant cells[1]. These yeasts can be identified by the Hematoxylin-Eosin staining technique, or more easily by special staining methods such as periodic acid–Schiff (PAS) and Grocott-Gomori[2,5]. Spore-forming microorganisms are sometimes seen, conferring a "Mickey ear" or "rudder" appearance; this data also coincides with our findings[2,4].

The main treatment options are sulfamide derivatives, trimethoprim, amphotericin B, azole derivatives, and terbinafine[2,3,5]. Treatment is always prolonged, and careful follow-up of the patient is necessary, even when "clinical cure" is achieved, due to the possibility of reactivation of the fungus. If not treated properly, PMC can be fatal[2,5].

In summary, PMC is an endemic and systemic disease. Although the primary route of infection is pulmonary, by inhalation of spores or fungal particles, several anatomical sites may be affected by lymphohematogenous dissemination, including the buccal mucosa. Thus, dentists play a fundamental role in the identification of these lesions, in the correct diagnosis and referral to the appropriate treatment. Careful clinical evaluation and complementary exams, such as exfoliative cytology and incisional biopsy, are valuable procedures in the diagnosis of this disease.

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