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Severe disseminated paracoccidioidomycosis

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Abstract

Paracoccidioidomycosis is a systemic fungal disease with a highly variable distribution, endemic to Central and South America with the highest prevalence in Brazil, Argentina, and Colombia. The chronic presentation of the disease is commonly observed in adult men and they manifest with pulmonary and mucocutaneous lesions. We report a fatal case of disseminated paracoccidioidomycosis in a 68-year-old immunocompetent man, with pulmonary, skin, mucosal, and cerebral involvement. Mucocutaneous lesions were decisive for the etiological diagnosis.

Keywords: fungal disease, paracoccidioidomycosis, systemic mycosis

Introduction

Paracoccidioidomycosis (PCM) occurs mainly in tropical areas of Brazil, Argentina, Colombia, Ecuador and Venezuela. This disease is more prevalent in adult men who carry out agricultural activities [1]. The etiological agent is a dimorphic fungus, classified in the *Paracoccidioides brasiliensis* complex, composed of four species: *P. brasiliensis sensu stricto*, *Paracoccidioides americana*, *Paracoccidioides restrepiensis,* and *Paracoccidioides venezuelensis* [2].

The disease has two presentations: acute (juvenile type) and chronic (adult type). The juvenile type is more serious, affecting mainly young patients and immunosuppressed adults. The chronic form represents more than 90% of cases, with pulmonary involvement and the presence of ulcerated lesions on the skin and mucous membranes (oral and nasal), [3]. Paracoccidioidomycosis is the main cause of death from fungal disease in immunocompetent people in Brazil [4]. A serious case of chronic PCM in an immunocompetent adult man is reported herein, with lung, brain, skin and mucosal involvement.

Case Synopsis

A healthy 68-year-old man, born in Rio de Janeiro, worked as house painter and had home farming habits. In April 2023, an ulcerated lesion appeared on the right fifth toe and plantar region of the same foot; he also noted moderate difficulty swallowing food. A month later, lesions appeared on the mucous membrane and skin of the nose (**Figure 1**).

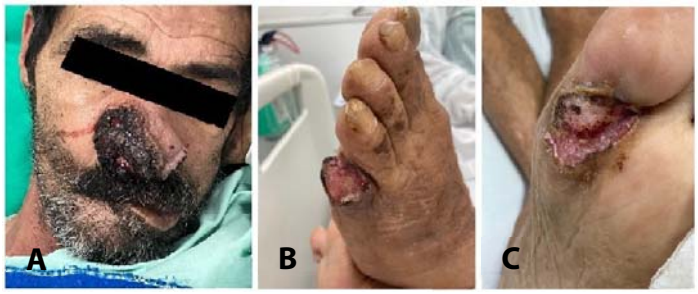

Figure 1. ***A)*** *Extensive and deforming necrotic vegetative lesion in the nose, extending to the oral mucosa, larynx and trachea.* ***B)*** *Flat ulceration with a clean surface on the fifth toe of the right foot. The lesion caused destruction of the nail and phalanx.* ***C)*** *Flat, delimited ulceration with a necrotic surface on the plantar region of the right foot.*

In September 2023 (five months later), dyspnea, persistent cough and progressive changes in consciousness appeared. Six months after the onset of symptoms, the patient presented to a university hospital, with weight loss, moderate respiratory failure, and disorientation. Brain computed tomography (CT) showed nodular lesions in the left capsular nucleus and midbrain. CT of the neck showed an expansive nodular supraglottic lesion with involvement of the vocal cords. Chest CT showed excavated lesions in the lower lobes and nodules in both lungs. Mucosal lesions were identified in the nose, oral cavity, and larynx. Histopathological examination of the skin of the nose showed chronic granulomatous inflammation and rounded fungal structures (**Figure 2**). Concomitant diagnosis of pulmonary tuberculosis was confirmed by positive acid-fast bacilli sputum smear. Tracheostomy and enteral tubes were necessary to ensure breathing and nutrition.

Paracoccidioidomycosis treatment was carried out with amphotericin B for 6 weeks, with moderate thrombocytopenia and anemia as an adverse reaction. The patient was stable and PCM treatment was continued with cotrimoxazole (sulfamethoxazole 800mg/trimethoprim 160mg, twice a day), scheduled for another year (however, it was interrupted after three months, owing to the patient's death). Tuberculosis treatment was started with rifampicin, isoniazid, pyrazinamide and ethambutol, expected to last six months. There was improvement in mucosal and cutaneous lesions, but mucosal scars produced permanent strictures in the larynx and pharynx (**Figure 3**). On January 23, 2023 (nine months after the onset of symptoms) the patient died as a result of severe respiratory failure.

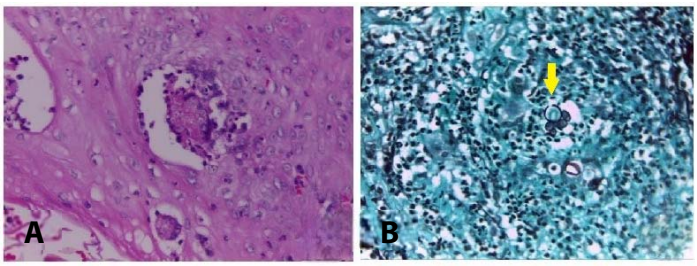

Figure 2. *Histopathology of a skin biopsy from the nose.* ***A)*** *Squamous epithelium showing two Langahans giant cells and neutrophils. H&E, 400×.* ***B)*** *Identification of fungal structure with sporulations (arrow). Grocott, 400×.*

Figure 3. ***A)*** *Nasal lesion healed after treatment with amphotericin B.* ***B)*** *Skin lesion on the foot healed, with sequelae of destruction of the toe.*

Case Discussion

Pulmonary PCM can present by X-ray with ground-glass attenuation, consolidation, nodules, cavitations, reversed halo sign, interlobular septal thickening, emphysema, and fibrosis [5]. The concomitance of these multiple pulmonary patterns in the same patient, initially restricted the diagnosis of pulmonary tuberculosis, but the mucocutaneous lesions raised a strong hypothesis that there could be an associated fungal infection. The radiological highlights of the chest CT in this case suggested an infectious granulomatous condition and the brain MRI showed an abscess with fungal characteristics, leading to strong suspicion of PCM with concomitant involvement of the central nervous system and lungs.

Cutaneous PCM can have variable lesion morphology, from erythematous papules and nodules to vegetative ulcers. An infiltrated cutaneous form with a lichenoid appearance has been described, with almost exclusively cutaneous involvement and has been referred to as sarcoidosis-like [6]. The patient had localized and limited skin lesions on the lower limbs, characterized by the presence of tuberculoid granulomas and fungal structures.

Paracoccidioidomycosis is the most prevalent chronic infection of the upper airway and digestive tract in Latin America [7]. Oral mucosal lesions are

most common in lips, gums, and oral mucosa and are associated with pain, difficulty chewing, and poor oral hygiene, predisposing to weight loss and impairment of general condition [8,9]. Laryngeal PCM occurs in 22 to 43% of cases in chronic form, which can lead to irreversible damage. Hoarseness is a very common initial symptom in laryngeal injuries. Dysphonia and dysphagia are the main functional sequelae [10]. In the case presented, there was severe involvement of the nasal, oral, and laryngeal mucosa, causing it to be impossible to swallow and breathe. The injuries produced serious sequelae, requiring tracheostomy and the use of enteral tubes.

Conclusion

Skin and mucosal lesions are very important for the diagnosis of chronic PCM in endemic regions, as isolated pulmonary involvement has a large diagnostic differential. The sequelae of PCM have a negative impact on quality of life, by permanently compromising swallowing and breathing activities. Treatment requires continued multidisciplinary actions to avoid early death.

Potential conflicts of interest

The authors declare no conflicts of interest.

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