Paracoccidioidomycosis
A report of two cases in Peru

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Abstract

Introduction: also known as South American blastomycosis, paracocccidioidomycosis is a progressive systemic disease that usually affects Latin American males involved in agricultural activities, especially in Brazil, Argentina, Peru, Colombia and Venezuela (1, 2). It is one of the most prevalent deep mycoses. It is mainly found in the lungs, as the respiratory tract is its usual port of entry. However, extrapulmonary lesions are very common, including skin, mucosal, reticuloendothelial tissue and adrenal gland lesions, among others.

Method: a medical chart review of two patients with paracoccidioidomycosis.

Results: we report the cases of two male patients diagnosed with paracoccidioidomycosis: a 17-year-old and a 65-year-old, with skin and mucosal presentations with and without respiratory involvement, respectively.

Conclusion: paracoccidioidomycosis is a prevalent fungal infection with accessible treatment, which underscores the need for early and prompt detection. **(Acta Med Colomb 2025; 50. DOI: https://doi.org/10.36104/amc.2025.4162).**

Keywords: *paracoccidioidomycosis, deep mycosis, itraconazole*.

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Introduction

Fungi from the genus *Paracoccidioides* are the etiological agents of paracoccidioidomycosis, one of the most prevalent systemic fungal infections in Latin America, which affect working age people and can cause disability, sequelae and even death. Paracoccidioidomycosis, also known as South American blastomycosis, is a deep mycosis with a higher prevalence in countries like Brazil, Argentina, Colombia, Peru and Venezuela (1, 2). It affects mostly males, in approximately 95% of cases, and is caused by the dimorphic fungus *Paracoccidioides brasiliensis*, which was thought to be the only etiological microorganism for this disease.

The clinical presentation differs from patient to patient, depending on their comorbidities. Cases of skin lesions have been reported in patients with AIDS, as well as other cases associated with gastrointestinal and renal neoplasms (3, 4). Transcutaneous infection is less common, although it seems that cellular immunity disorders increase the risk of infection via this mechanism. More than 95% of the cases occur in males; involvement of the external genitalia is rare, and adrenal involvement has also been reported.

Given the side effects associated with most antifungals, itraconazole appears to be a good alternative to amphotericin B for treating skin lesions without significant systemic involvement (5). Its limitation is that its fungistatic effect increases the risk of relapses once treatment is stopped.

Methods

During the first quarter of 2020, data was collected on patients admitted to the internal medicine service with a diagnosis of paracoccidioidomycosis within the previous two years. Two patients were selected for their clinical relevance and successful follow-up.

Results

Case 1

A male patient in his teens from the city of Bagua, Amazonas, presented to the outpatient department complaining of the insidious onset of a "nodule" in the right submaxillary region approximately three years prior, which grew over the course of a few months and drained spontaneously. Since tuberculosis was suspected, the patient received specific treatment for six months.

One year prior to admission, he once again developed a right submaxillary nodule with a similar progression to the previous episode. There were no associated symptoms like pain or fever. Similar lesions appeared progressively on his face, neck, trunk, and upper and lower extremities, and he was therefore restarted on specific treatment five months before, with no response. Most of the lesions ulcerated and scabbed over, while others took on a rubbery appearance.

On exam, the patient was awake, cooperative and hemodynamically stable. He had multiple enlarged cervical, axillary and inguinal lymph nodes, along with ulcerated, scabby and rubbery lesions distributed over almost his entire body (Figure 1).

Laboratory tests showed no relevant findings. Tests for HIV and syphilis were nonreactive. His chest x-ray was normal. The skin lesions were biopsied, confirming *Paracoccidioides brasiliensis* infection.

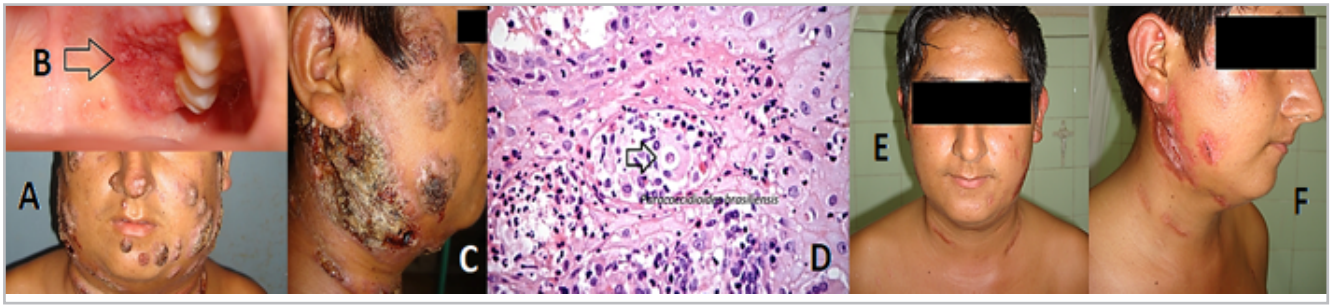

Figure 1. *A and C: multiple nodular, ulcerated lesions distributed over the face and neck, as well as enlarged lymph nodes in these areas. B: Granulomatous lesions on the palate. D: pathological anatomy showing P. brasiliensis. E and F: the patient after four weeks of itraconazole treatment.*

The patient was treated with itraconazole and showed clinical improvement after four weeks, as seen in Figure 1.

Case 2

This was a patient in his 60s, from the city of Rioja, San Martín, who had worked in agriculture since the age of 18. He denied significant comorbidities and reported a four-year period of illness during which he would develop mucocutaneous lesions in the mouth and nose, accompanied by swelling and perilesional erythema, which would partially resolve two months after their appearance. He mentioned self-medicating with anti-inflammatory drugs, whose names he did not recall.

One year prior to admission he developed hoarseness which intensified over time until he developed dysphagia and therefore presented to the emergency room and was subsequently hospitalized for testing.

On exam, he was hemodynamically stable, awake, and cooperative. He had painless, erythematous, enlarged lesions on the oral and nasal mucosa, with no evidence of discharge around them. He also had granulomatous lesions on his tongue, palate and cheeks.

An esophagoscopy revealed granulomatous lesions that partially occluded the proximal esophageal lumen, with no sign of lesions in the rest of the digestive tract. A chest x-ray showed bibasilar pulmonary fibrosis, predominantly on the right side, with no consolidations. A biopsy of the described lesions revealed a histological picture compatible with paracoccidioidomycosis (Figure 2).

The patient was given itraconazole, with positive progression and remission of the dysphagia and dysphonia six weeks after beginning treatment.

Discussion

Paracoccidioidomycosis (PCM) has a wide spectrum of clinical presentations. According to the most frequently used classification today, agreed upon in the III International Colloquium on Paracoccidioidomycosis in Medellín (3), it is classified as: 1. paracoccidioidomycosis infection; 2. PCM disease: 2a: acute/subacute form (juvenile), both moderate and severe; 2b: chronic form (adult), mild, moderate and severe; and 3. residual form (sequelae). The main etiological agent is *Paracoccidioides brasiliensis*, a thermodimorphic and saprophytic fungus, with infection mainly acquired through inhaling conidia.

The two reported cases perfectly describe the chronic form (2b). On the one hand, the patient in the first case started with a subacute presentation, with nodular lesions that worsened and improved over time, and in the second case, an older adult had significant mucocutaneous lesions, but with evident pulmonary involvement. The chronic form is the most common, found mainly in adult males whose work involves contact with the soil. Its clinical presentation is similar to tuberculosis: patients present with a cough, dyspnea, fever and hemoptysis. Lesions on the oral mucosa, lymph nodes and skin are common (6). These data match our patients´ profile: a history of contact with the soil due to agricultural activities and even having been treated

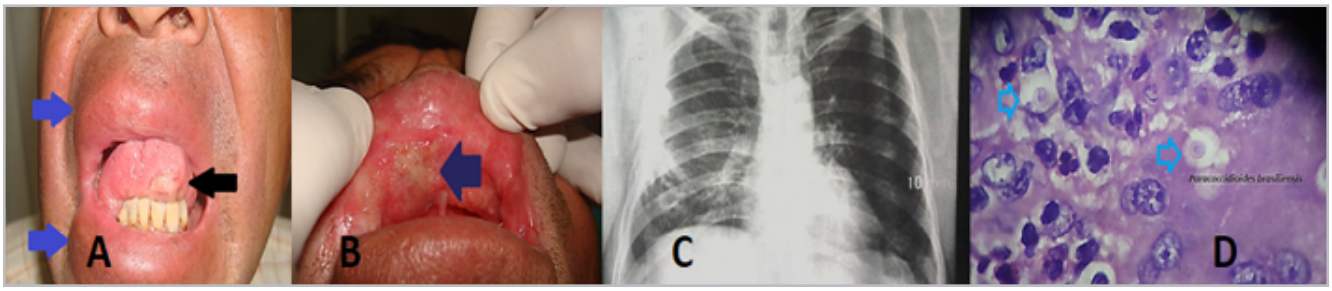

Figure 2. *A and B: granulomatous lesions localized to the oral and lingual mucosa. C: an x-ray showing interstitial involvement, predominantly in the lower 2/3 of the right lung. D: anatomy showing the presence of P. brasiliensis, establishing the diagnosis.*

for tuberculosis for long periods of time without clinical improvement.

The chronic form mainly affects the lungs, causing significant damage, and, in many cases, progressing to pulmonary fibrosis (7-9), as occurred with our second patient. *Paracoccidioides brasiliensis* enters through the respiratory tract, causing significant alveolar inflammation with interleukin (IL-6 and IL-8) production that activates fungal tissue adhesion mechanisms (laminin, fibronectin, fibrinogen, plasminogen) (1, 9). These inflammatory processes facilitate hematogenous dissemination of the fungus and would explain the mucocutaneous lesions as well as those in the reticuloendothelial tissue, adrenal glands, etc. (1, 2, 9).

Some reports suggest that tobacco and alcohol consumption are risk factors for developing the disease, speculating that the lung structure changes caused by smoking could be responsible for the higher prevalence of paracoccidioidomycosis in smokers, since smoking is a risk factor for other infectious respiratory diseases (8).

In the first case, lung involvement was not clinically evident, which is related to the residual capacity of young patients with any type of local inflammation. However, the three years of illness would explain the hematogenous dissemination and installation of the fungus, causing disease and inflammatory skin and mucosal lesions with a tendency toward chronicity, as occurred in our patient, without necessarily having a history of smoking, which the patient denied.

We should also keep in mind that the inflammatory response varies with age and comorbidities, with more intense production of caseous or necrotic material, which would explain the spontaneously draining nodular lesions.

In the second case, the clinical presentation of mucocutaneous lesions could suggest acute disease. However, the pulmonary involvement seen on the chest x-ray would suggest a progressive chronic disease, and that the acute lesions represent disease activation in response to an acute event that significantly compromised the patient´s cellular immunity (2, 9).

The diagnosis is made through direct visualization of the fungus using a direct exam of sputum or bronchoalveolar lavage samples, pathological anatomy of tissue biopsies (as occurred with both patients) and, finally, fungal culture, considered the gold standard for diagnosis. *Paracoccidioides* spp. occurs in its parasitic form in biological samples and cultures at 37 °C as a multiple budding yeast with a double wall and prominent intracytoplasmic lipid globules (5, 8). However, cultures are not very cost-effective (2, 6, 9).

The differential diagnosis should include chronic infectious diseases that produce a granulomatous reaction, like tuberculosis and histoplasmosis, among others. The pulmonary lesions are characterized by interstitial involvement, generally in the lower right lung (1-4, 9).

As far as treatment, which lasts for a minimum of one year in all cases, *Paracoccidioides* spp. is sensitive to most antifungals, like amphotericin B and the azoles (ketoconazole, fluconazole, itraconazole, voriconazole and posaconazole), terbinafine, and even sulfonamides (6, 8, 9). Of these, itraconazole has been most used, due to its high response rates, good tolerance, few side effects compared to other treatments, and easy outpatient monitoring (10, 11). Its most frequent side effects are hepatotoxicity, hypokalemia, palpebral edema, and, less frequently, heart failure.

In both reported cases, itraconazole was administered at a dose of 200 mg per day, with significant improvement seen in the first case, in which almost 80% of the lesions resolved after three weeks of treatment. Despite the previous recommendations, there is little information available regarding specific treatment schemes, which makes it important to report cases like these, to generate data that can be used in future studies.

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