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## CASE REPORT

### Paracoccidioidomycosis infection in an immunocompetent adolescent: a neglected disease

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#### Abstract

Acute Paracoccidioidomycosis (PCM) represents 5 to 10% of total PCM cases. The estimated incidence varies between 1-4 cases for 100.000 inhabitants in the endemic regions of Brazil. It is known that PCM can coexist with other systemic mycoses such as Histoplasmosis. We report a case of a 10-year-old adolescent from Barra Mansa, RJ, Brazil. He was hospitalized after recurrent visits to the emergency department for approximately one month, presenting with non-bloody diarrhea, weight-loss of 6kg in six weeks, dry cough and nocturnal fever (average temperature 38°C). Counterimmunoelectrophoresis and lymph node biopsy were positive for *Paracoccidioides brasiliensis*. The treatment consisted of Amphotericin B IV 0,6 mg/kg of body weight per day for 10 days and Itraconazole PO 200mg per day for 12 months. After 5 years, the patient remains asymptomatic. Reports of similar cases are scant in the literature and, the few encountered, are of immunocompromised children. The incidence and prevalence estimation of PCM might be inaccurate due to underdiagnosis and under-reporting.

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## INTRODUCTION

Pulmonary fungal infections are less frequent than those caused by bacteria. However, they have the same clinical relevance, with rapid evolution and difficulties in early diagnosis and adequate intervention<sup>1,2</sup>. They often affect the pediatric population and are frequently asymptomatic. Therefore, most cases go undiagnosed. The reports of these infections in the literature are scant and, when encountered, often describe cases of immunocompromised children<sup>1</sup>.

Acute paracoccidioidomycosis (PCM) is an infection caused by *Paracoccidioides brasiliensis* (*P. brasiliensis*) in childhood and may present with nonspecific extrapulmonary manifestations that can rapidly evolve and disseminate through lymphatic chains, mainly submandibular, clavicular, axillary and cervical (fistulizing or not). Other manifestations are fever, asthenia, anorexia, weight-loss, hepatosplenomegaly, gastrointestinal symptoms, cutaneous lesions and osteoarticular injury. The gold standard in the diagnosis of PCM is direct mycological examination<sup>2-6</sup>. The acute form represents 5-10% of total cases of PCM, with an estimated incidence between one and four cases for 100.000 inhabitants of Brazilian endemic regions. Reports from rural areas represent 45,8% of the national prevalence<sup>4,6</sup>.

There are barriers to the accurate estimation of incidence and prevalence of PCM, that involves underdiagnosed and under-reported cases, since there is no mandatory disease notification<sup>5-8</sup>. Therefore, this article aims to relate a case in an immunocompetent adolescent, contributing with epidemiology and literature regarding a neglected disease in Brazil.

## CASE REPORT

The patient is a 10-year-old male living in the urban area of Barra Mansa, state of Rio de Janeiro, Brazil. He reported several episodes of non-bloody diarrhea after meals, weight-loss (6kg in six weeks), dry cough and nocturnal fever (average temperature 38°C) for, approximately, one month. He had a history of exposure to an environment inhabited by hematophagous bats (probably *Daemys youngi*) while practicing capoeira at his school in the city of Barra Mansa.

In a previous visit to another emergency department he received a prescription of Ceftriaxone IM 1g per day for five days, due to a suspicion of sinusitis. The fever improved during the course of antibiotic, however, symptoms returned and his mother reported an increase in the size of lymph nodes in the cervical region. The patient went to an Ear, Nose and Throat specialist, who rejected the hypothesis of sinusitis.

After several visits to healthcare services, the patient went to the emergency department with a worsening of the general condition and was hospitalized for a diagnostic investigation.

During the physical examination, the patient presented with regular general condition, emaciated, pale, hydrated,

afebrile and eupneic. Pulmonary and cardiac auscultations were unremarkable. The palpation of the abdomen was difficult due to voluntary resistance. There was subtle hyperemia of the oropharynx. Ear and nose examination were unremarkable. Lymph nodes of several sizes were mobile and palpated in cervical, submandibular, axillary and inguinal regions (Figure 1).

Laboratory findings revealed microcytic and hypochromic anemia, with Red Blood Cells = 4,10 millions/mm<sup>3</sup>; hemoglobin = 8,2g/dL; hematocrit = 26%; mean corpuscular level = 63,4fL; mean corpuscular hemoglobin concentration = 20pg; reticulocyte count = 0,3%; ferritin = 411,14ng/mL and serum iron = 25mcg/dL. It also revealed 17.000 leukocytes/mm<sup>3</sup>; segmented neutrophils = 11.900/mm<sup>3</sup>; eosinophils = 1.360/mm<sup>3</sup>; 568.000 platelets/mm<sup>3</sup>; Erythrocyte Sedimentation Rate (ESR) = 127mm and C-reactive protein (CRP) = 130mg/L. Bilirrubine and transaminases were normal.

Serology for recent infections was negative for HIV, Syphilis, Herpes, Epstein-Barr, Toxoplasmosis, Cytomegalovirus and Rubella. Tuberculin skin test was negative. Chest x-ray and abdominal ultrasound were normal. Computed tomography of the chest demonstrated a few small nodules in the lung parenchyma in the lateral segment of the middle lobe, hepatomegaly and several enlarged lymph nodes in the retroperitoneum, with maximum diameter of 2,8cm, as well as a small amount of free fluid in the pelvis. Lymph nodal biopsy revealed chronic granulomatous inflammation with giant cells and absence of neoplasm. No mycobacteria were present, but structures compatible with *P. brasiliensis* in silver impregnation were found (Figure 2).

The treatment consisted of Amphotericin B IV 0,6mg/kg of body weight per day for 10 days and Itraconazole PO 200mg per day for 12 months, being suspended after clinical, radiological and serological cure. The patient was discharged from the hospital 24 hours after admission.

After 18 months from the beginning of the treatment, a counter immunoelectrophoresis for *P. brasiliensis* was reactive (title 1:4). A immunodiffusion serology for *H. capsulatum* was also done, showing a reactive

result. The immunodiffusion serology for *P. brasiliensis* was negative at the time.

After a five-year follow-up, he remains asymptomatic with normal laboratory exams.

## DISCUSSION

PCM is a systemic disease induced by thermophilic fungi, *P. brasiliensis* and *P. lutzii*. It is endemic in region that extends from Mexico to Argentina, with a higher incidence in Brazil, where it is mostly diagnosed in the state of São Paulo<sup>9</sup>.

More than 15,000 cases of PCM were reported between 1930 and 2012 in Latin America, a number that only partially represents the prevalence of the disease<sup>5,7,8</sup>. It is important to consider that 80% of these cases are from Brasil<sup>5</sup>. Recent data suggest that in endemic areas the incidence of PCM

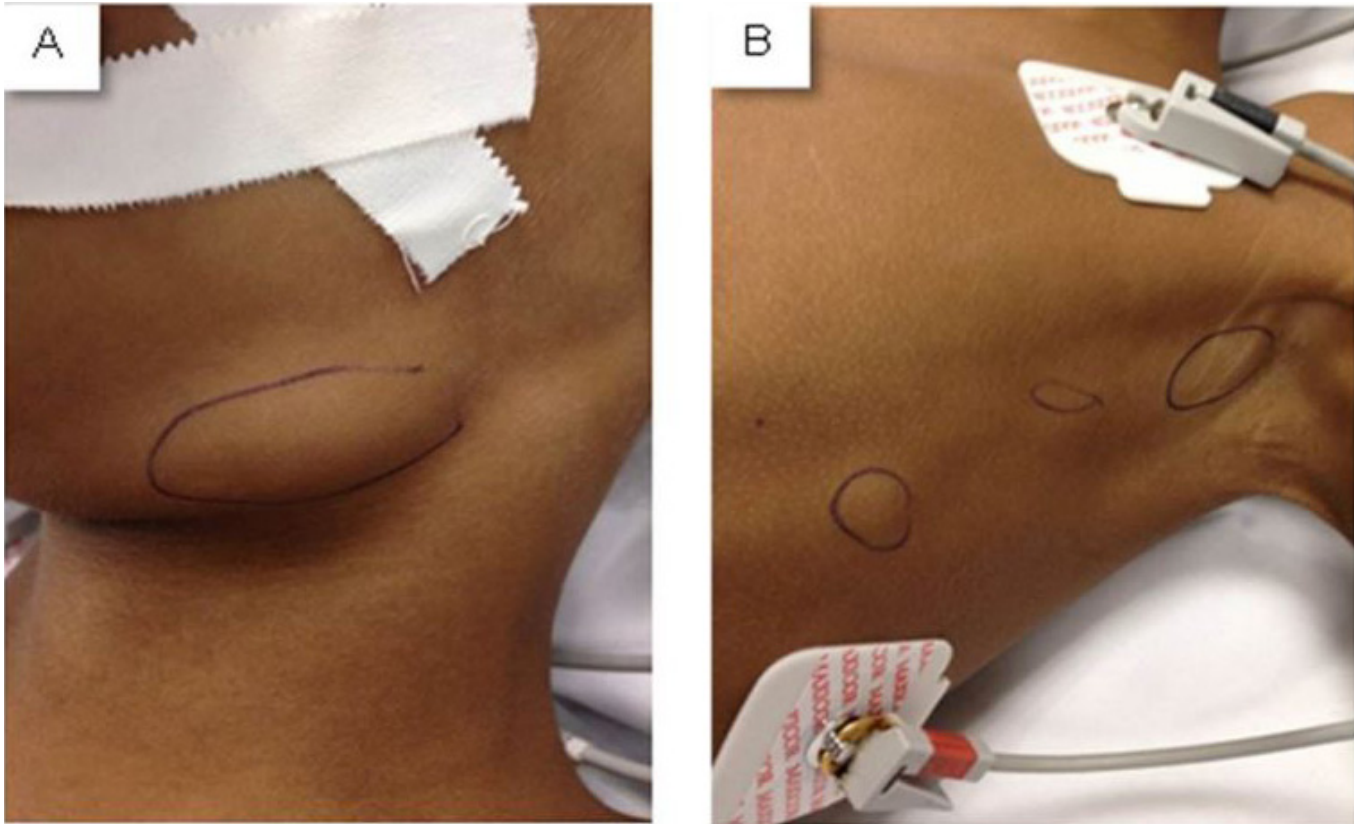


**Figure 1.** Submandibular (a) and axillary (B) visible lymph nodes on physical exam.

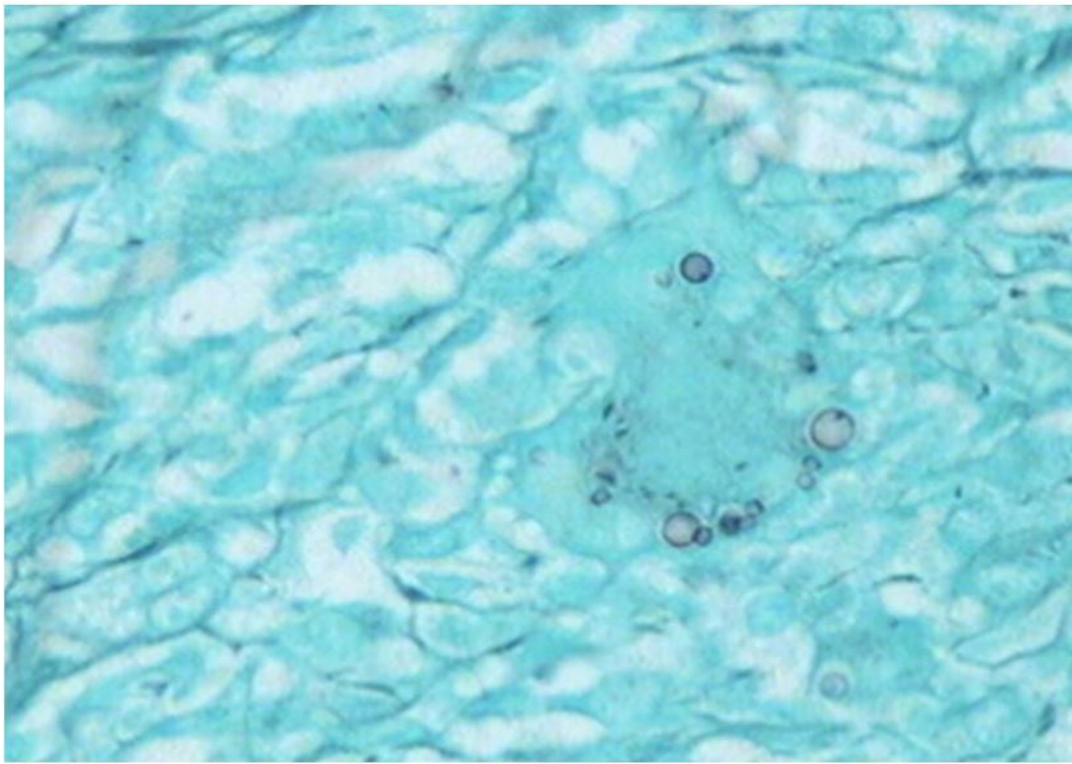


**Figure 2.** Direct microscopic exam by the Grocott methamine-silver stain, with material from lymph node biopsy, showing circular structures with accentuation of margins and budding, compatible with *P. brasiliensis* fungi.

varies from one to four cases for 100.000 inhabitants. However, in hyperendemic regions, such as the state of Rondônia, it can be nine to forty for 100.000 inhabitants<sup>6</sup>. This data is underestimated since the notification is not compulsory in Brazil and other Latin American countries. The disease is considered neglected by health policies<sup>5,7,8</sup>.

Gonçalves et al (1998)<sup>10</sup> found 36 cases of PCM in the state of Rio de Janeiro. Forty-four percent of these cases were from the cities of Volta Redonda and Barra Mansa. This is the only data available, to our knowledge, about the incidence of PCM in the region of where our patient is from. Moreover, within the state of Rio de Janeiro, the largest number of positive skin tests for PCM was found in Barra Mansa. It is believed that in this region there are favorable environmental and climatic conditions for the survival of *P. brasiliensis*, with an abundance of water and native vegetation<sup>11</sup>.

The main risk factor for PCM is the prolonged contact with rural areas<sup>6</sup>. However, eight cases of the juvenile form of PCM were found in the state of Rio de Janeiro after the construction of Arco Metropolitano, a highway that bypass the metropolitan area state area, between 2008 and 2014, when there was deforestation and an intense remotion of land during a period of abundant rain, showing that urbanization influenced in the process of infection<sup>11</sup>.

The acute form is the only variation that affects those below 15 years of age. The disease progresses with enlarged lymph nodes, gastrointestinal symptoms and oral involvement<sup>2,4,6,7</sup>. Case reports are few and usually related to immunocompromised children<sup>1</sup>.

Laboratory findings in our case showed hypochromic and microcytic anemia with reactional thrombocytosis, leukocytosis, neutrophilia and eosinophilia, that correspond to the findings in literature<sup>4,6</sup>. Another aspect that matches our researches is the increase of the inflammatory markers ESR and CRP, frequently found in PCM<sup>4</sup>. Iron deficiency anemia was excluded, suggesting the anemia was due to chronic infectious disease.

There is evidence of cross-reaction of *P. brasiliensis* and *H. capsulatum* in blood and skin tests<sup>2</sup>. Shumoto et al. (2019)<sup>12</sup> reported a case of serologic cross-reaction between these two fungi.

However, there is no scientific evidence that a coinfection occurred since the titration was not done before the treatment and there was not found the *H. capsulatum* in direct microscopy. Therefore, a cross-reaction or a previous Histoplasmosis infection might be considered to have occurred in this case, considering the patient's history of important exposure to *H. capsulatum* and its clinical presentation is most often asymptomatic or subclinical<sup>2</sup>.

## CONCLUSION

Even though the patient was immunocompetent, he presented with clinical features and epidemiology compatible with PCM. The *H. capsulatum* finding in immunodiffusion serology suggests a cross reaction with *P. brasiliensis*.

The accurate estimation of the incidence and prevalence of PCM remains a challenge. The absence of compulsory notification, the difficulty in early diagnosis and the deficient capacity of laboratory diagnosis in some areas are reasons for the underdiagnoses of this disease, which is also neglected by public health policies.

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