American Journal of Case Reports

ISSN 1941-5923
© Am J Case Rep, 2017; 18: 1114-1117
DOI: 10.12659/AJCR.904520

Received: 2017.03.26
Accepted: 2017.04.28
Published: 2017.10.18

Hypereosinophilia Secondary to Disseminated Paracoccidioidomycosis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 28
Final Diagnosis: Disseminated paracoccidioidomycosis
Symptoms: Fever • rash
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Unusual clinical course

Background: Paracoccidioidomycosis is an endemic mycosis in Central and South America caused by the thermally dimorphic fungus *Paracoccidioides brasiliensis*. Despite its self-limited course and usually asymptomatic infection, some patients may present with a systemic illness mimicking multiple conditions and thus question the general state of their immune system.

Case Report: A 28-year-old male presented to the hospital with fever, dry cough, and non-pruritic rash with no characteristic distribution for the past 10 days. Past medical history revealed that the patient had worked as a farmer three years ago, had abused cocaine paste over the same period, and also had in the last month presented to the hospital for acute appendicitis. Initial laboratory tests revealed hypereosinophilia greater than 10,000 eosinophils/mL. Infection of *P. brasiliensis* was confirmed by lymph node, skin, and colonoscopy biopsies. After treatment with itraconazole, the patient's eosinophil count returned to normal and his symptoms resolved.

Conclusions: Paracoccidioidomycosis may present as a systemic illness with only marked eosinophilia on initial diagnostic tests. Furthermore, in our patient's case, the high degree of eosinophilia may have contributed towards the patient's appendicitis in the weeks preceding the subacute infection. It is possible that the patient's history of working at a farm and abusing cocaine paste may have contributed to the initial colonization by the fungus.

MeSH Keywords: Hypereosinophilic Syndrome • Immunocompetence • Paracoccidioides

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/904520

Background

Paracoccidioidomycosis, also known as South American blastomycosis, is an endemic mycosis caused by the fungus *Paracoccidioides brasiliensis*. It is endemic in Central and South America, being hyperendemic in Brazil, Colombia, Ecuador, and Venezuela [1–3].

The initial infection by *P. brasiliensis* generally does not cause symptoms and has a self-limited course [2,4]. In patients who become infected, the disease course can vary widely. It may cause an acute, subacute, or chronic illness, which may depend more on the host response than the fungus itself [2,5]. Progression to an acute episode is most often seen in young males who present with high fevers, generalized lymphadenopathy, hepatomegaly and/or splenomegaly, and in severe cases, bone marrow involvement [6].

Although the habitat of the fungus is not well understood, there have been reports of a correlation between infections and patients whose occupations include contact with soil, such as farmers and miners, and other agricultural environments [1,7].

Unlike other endemic mycoses, immunocompetent hosts may develop disseminated forms of the disease, and thus it should be considered among the many differential diagnoses when evaluating a patient with nonspecific constitutional symptoms. The symptoms of this mycosis may appear similar to other infections, such as tuberculosis or histoplasmosis, and therefore careful review of these patients is warranted. The diagnosis of paracoccidioidomycosis is made by culture or under direct microscopic visualization. Most cases can be treated with azoles; itraconazole is the treatment of choice, or amphotericin B IV for severe cases [2,4,8,9].

We present the case of a young immunocompetent patient who presented with severe hypereosinophilia and no risk factors for such disease.

Case Report

A 28-year-old male, with a history of a recent appendectomy performed one month before admission, was referred to the Internal Medicine Department of the CES Clinic in Medellín, Colombia. The patient´s chief complaint was a dry cough and a non-pruritic rash with no characteristic distribution for the past 10 days, as well as high-grade fever and night sweats that did not improve with paracetamol treatment. He denied any recent travel or contact with sick people.

He was found to be febrile, tachycardic, with normal blood pressure, normal oxygen saturation, and a Glasgow Coma Scale of 15/15. The only positive findings were non-tender anterior and posterior cervical lymphadenopathy of approximately less than 1 cm in diameter and the presence of erythematous vesicles and papules in the abdomen, chest, back, and extremities. The patient denied other cardiovascular, gastrointestinal, musculoskeletal, or nervous symptoms.

He was hospitalized and his initial work-up showed a leukocyte count of 16,630 cells/mL (5,987 eosinophils/mL). However, five days later the count grew to 38,570 cells/mL (13,885 eosinophils/mL), with no other hematologic abnormalities and normal liver and kidney function tests. A test for human immunodeficiency virus, three sputum smears for tuberculosis, and bacterial blood cultures were negative.

A thoracic CT scan revealed bilateral and diffuse lung micronodular infiltrates with axillary and mediastinal lymphadenopathy. The abdominal CT scan demonstrated an enlarged liver and spleen with retroperitoneal adenopathies and changes in the distal colon compatible with colitis.

Biopsies were taken: one from a cervical lymph node, one from the skin lesions, and a third one through colonoscopy. All biopsies were positive for *P. brasiliensis* (Figures 1, 2). The colonoscopy described multiple nodular lesions without hemorrhage.

The patient was initiated on amphotericin B deoxycholate to complete a 1,000 mg accumulated dose. Following the initiation of the amphotericin B, the patient showed significant improvement as evidenced by his clinical examination and on follow-up examinations. The improvement was tracked through temperature, rash, and hypereosinophilia, all of which resolved within the first week of treatment. Following the resolution of symptoms, the patient was discharged home and treatment was to be continued with itraconazole for six to nine months, total duration to be determined by the infectious disease specialists on follow-up visits.

The decision to order further testing for severe hypereosinophilia was considered, but after prompt resolution with antifungals, no further work-up was undertaken.

During the final two days of his hospital stay, the patient recalled that he had worked as a farmer three years before the symptoms began, and admitted having used cocaine paste during the same period for approximately three months. No other risk factors were found and during the past three years he had been living in the city without exposure to soil, farms, or such terrains. The patient presented four weeks earlier to the clinic with acute abdominal pain on the right lower quadrant with pain and tenderness to palpation. He did not present with fever and there were no palpable lymphatic chains in the abdomen or inguinal region. He was taken to the operating room with a preoperative clinical diagnosis of appendicitis. He

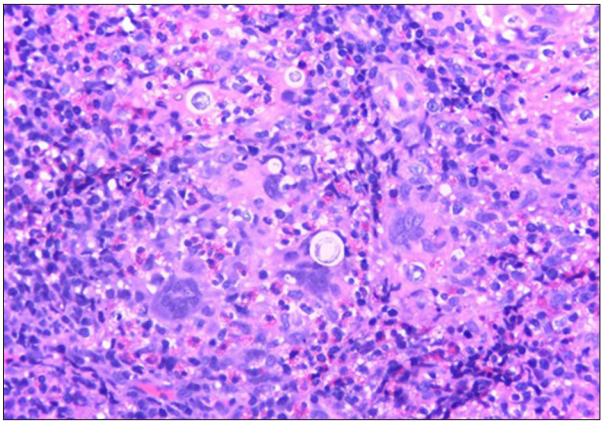

Figure 1. Hematoxylin and Eosin staining at 120× of an anterior cervical lymphatic node demonstrating round mycotic appearing structures compatible with yeast of *Paracoccidioides brasiliensis*.

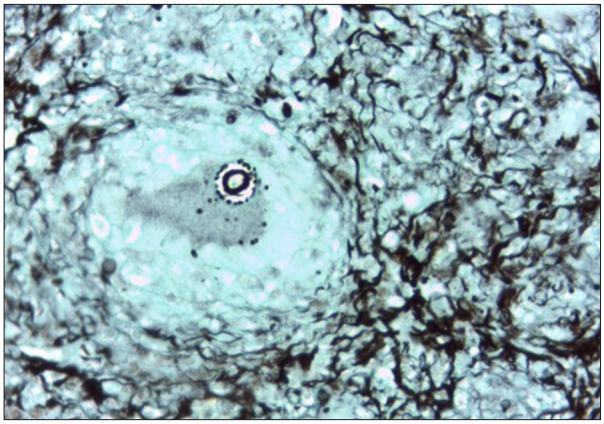

Figure 2. Special fungus stain demonstrating at 120× demonstrating granulomatous reaction with typical *Paracoccidioides brasiliensis* round appearance from a posterior cervical lymphatic node.

underwent an uncomplicated acute laparoscopic appendectomy and his symptoms resolved. He was discharged home without complications. During his inpatient stay for the presented symptoms, reexamination of the biopsy of the recent appendectomy was conducted. It did not reveal microorganisms.

Discussion

Infection by *P. brasiliensis* is a disease not frequently encountered by our Medical Department, although it is one of the most prevalent systemic mycoses in Latin America. This thermally dimorphic fungus is said to have its habitat in the soil of endemic areas. Risk factors for infection, such as living near a river or other water source, working in agriculture, age greater than 25 years, and contact with bats, have been described. Although risk factors have been observed, it is difficult to determine specifically the course of the disease, as the latency period between acquisition and infection might be in the magnitude of years, if not decades [3,4].

The disease presents more often in young males, and some reports have stated that the ratio of males to females to be as high as 70: 1. This odd distribution of the disease by gender has been a subject of various studied. Most recently Shankar et al. provided a thorough and detailed review of the relationship of hormonal status to fungi [10]. With regard to *P. brasiliensis*, it has been found that the Coccidioides species possess certain human-binding proteins. More specifically, estrogen has been found to promote endosporulation and the release of spores, and thus extrapolation of this disease stimulating effect can be thought of as a primary cause for the greater incidence of paracoccidioidomycosis in males [10]. Although no absolute relationships between *P. brasiliensis* and the host have been identified, most of the cases in the literature report that the patients lived or worked in an endemic area. Coinfection with tuberculosis is reported in 8% of cases, and coinfection with HIV is even less frequently, only approximately 1.2% of cases but symptoms are more severe accounting for a mortality rate as high as 53% [7,11].

The clinical manifestations have been classified as acute-subacute or juvenile, and chronic or adult paracoccidioidomycosis [2]. The former presents in younger patients, but only in less than 10% of those infected with the disease. The primary clinical presentation consists of infiltration to the reticuloendothelial system causing lymphadenopathy and hepatosplenomegaly [2]. The latter form is a chronic disease entity that progresses throughout the years and causes patients to have pulmonary involvement as well as mucosal membrane lesions [11].

Because of the major production of various immunoglobulins, hypereosinophilia may develop and, thus, exclusion of clonal cell proliferation as well as cancer may not be required if it resolves along with the treatment of the infection.

Few case reports of paracoccidioidomycosis and hypereosinophilia have been published; although mild to moderate eosinophilic reactions have been found in patients with diverse parasitic, fungal, and bacterial infections, which have been adequately described in disseminated paracoccidioidomycosis patients [12–14]. Hypereosinophilia in this disease has been attributed to high levels of cytokines (particularly IL-5), which are accompanied by Th2 cell immune response and disseminated injury [15,16]. The variability of the white cell count and eosinophilia was found to be evident during our review of the literature. Some patients have been described as having normal white cell counts and normal eosinophils but others have been reported to have only eosinophilia upon initial work-up [17,18].

The case we present here is that of a young immunocompetent patient who presented with a typical case of juvenile paracoccidioidomycosis with a history of having lived in a rural area three years before the symptoms began, and which was associated with severe hypereosinophilia. Our attention was brought to the fact that the patient presented four weeks earlier with a case of acute appendicitis. Although the biopsy of the appendix did not demonstrate fungi, we believe that congestion of the lymph nodes surrounding the appendix might have increased the patient's risk of appendicitis. To our knowledge, there is no report of *P. brasiliensis* infection presenting as acute appendicitis; therefore, we encourage the medical community to be aware of such a possible relationship.

Also, the fact that the patient consumed cocaine paste while living on the outskirts of the city, led us to think that this may have also been a possible way to inhale or ingest the fungus.

Conclusions

P. brasiliensis, an endemic fungus of Latin America, can present as an acute hypereosinophilic syndrome in young immunocompetent patients. Identification of risk factors for this fungus, together with a thoughtful past medical history, revealed that the patient in our case may have been carrying the pathologic entity for a number of years. Furthermore, the presentation of acute appendicitis near the course of the disseminated paracoccidioidomycosis may have been related to systemic hypereosinophilia, however, further studies are needed in order to prove causation.

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