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Case report

Disseminated paracoccidioidomycosis associated with lymph node tuberculosis in a non immunocompromised child

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ABSTRACT

The association of paracoccidioidomycosis (PCM) and tuberculosis (TB) produces an uncommon hyperinflammatory syndrome, causing multiorgan dysfunction. TB associated PCM is a rare condition, but it is fatal if not treated. Herein, we present a immunocompetent child who is admitted for fever and painful lymphadenopathy, with evidence of acid-alcohol-resistant bacillus (AARB) in cervical lymph node biopsy, antituberculous treatment was started with partial clinical improvement and is given discharge from hospital. At 3 weeks, he was readmitted by fever, weight loss, dyspnea and a greater number of adenopathies, in the new biopsy multiple yeasts were found compatible with PCM, our patient responded well to the combination of antituberculosis therapy(ATT), corticosteroid, and amphotericin B deoxycholate, presenting clinical improvement and subsequently continued with itraconazole.

Introduction

Paracoccidioidomycosis (PCM) is an infectious disease caused by dimorphic fungi such as Paracoccidoides brasilensis and Paracoccidioides lutzii [1], It has a geographic distribution limited to certain regions South America, Nearly 10 million persons are infected in Latin America by this fungus, although only 2% will eventually develop any clinical form [2]. Incidence rates range from 9 to 40 cases /100.000 inhabitants per year in hyperendemic areas, such as the Amazon region and tropical areas of Peru [3], however, this disease is increasingly reported in non-endemic areas due to migration [4], PCM very rarely affects the child population are characterized by fever, weight loss, lymphadenopathy, hepatosplenomegaly, anemia, and eosinophilia [5]. The growth of this fungus in microbiological cultures is slow (approximately 25 days) and its isolation is difficult. Given this delay, histological studies help to identify this fungus [6].

Tuberculosis (TB) is another infectious disease and is the most frequent worldwide, which causes more than one headache for treating physicians to the multiple clinical manifestations caused by this bacterium, even more so when microbiological culture methods are slow or suspected coinfection. by another infectious agent.

The clinical forms of PCM and TB are similar, mainly if there is systemic dissemination of both agents, which usually occurs in patients with some type of immunosuppression such as leukemia or lymphoma. So it is common to think of these pathologies as a differential diagnosis or perhaps co-infection. The objective of this article is to report the case of an immunocompetent child who.

The aim of this study is to report a case of an immunocompetent child diagnosed with disseminated paracoccidioidomycosis and later lymph node tuberculosis, successfully treated with amphotericin b deoxycholate.

Case report

A 7-year-old child patient, from the central Andes of Peru, with a history of multiple trips to the tropical region in the last 4 years, without other significant medical history presented to the emergency department with 3-month illness characterized by general malaise, weight loss,

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and in the last month, respiratory distress was added to physical effort, difficulty walking, sensation of unquantified thermal rise and presence of diffuse adenopathy throughout the lymphatic tract.

His physical examination was remarkable decrease in subcutaneous cellular tissue, generalized joint pain that intensifies on movement, the presence of multiple lymphadenopathy in the cervical, axillary, thoracic, and inguinal region of different diameters of indurated consistency and painful on mobilization, presence of crackless in the base of both lungs and respiratory distress, distended abdomen painful on deep palpation, the patient is in an uncooperative state of alert and responds adequately to questioning.

Laboratory tests showed; white blood cell count 8.67 × 103 / uL, eosinophils 1.75 × 103/uL (17.1%), hemoglobin 10.2 g/dL(Table 1). Ultrasound showed markedly enlarged liver and spleen with presence of multiple mesenteric nodes and 180 mL free fluid in the peritoneal cavity; Chest tomography showed lung consolidation at the bases and bilateral pleural effusion of 130 mL. The patient underwent a cervical lymphadenopathy biopsy showing multinucleated giant cells and the presence of positive acid fast bacilli in the Zielh Nielsen stain (Fig. 1), for which he began anti-tuberculosis treatment with rifampicin, isoniazid, ethambutol and pyrazinamide with clinical improvement and a decrease in fever for which he was discharged from the hospital.

Three weeks after starting treatment for tuberculosis, the patient returned with generalized lymphadenopathy, fever, abdominal distensión, lethargy, poor oral intake, cough with whitish sputum and dyspnea at rest, was noted to be tachycardic (heart rate of 119 beats per minute), tachypnoeic (respiratory rate of 28 breaths per minute) (Fig. 2), and had an oxygen saturation of 88% under room air. Arterial blood gas taken under room air revealed type 1 respiratory failure (pH 7.45, PO2 69 mmHg, PCO2 32 mmHg, HCO3 27 mmol/L). The patient was screened for HIV, HTLV1–2, with results negatives; and serologies were negative for antinuclear antibodies, antidouble-stranded DNA and anticardiolipin antibodies. Outpatient HIV testing was repeated five days later, this time including an HIV RNA, with results negatives.

Auscultation of lungs revealed reduced air entry over the lower area on both sides and chest radiograph of patient on admission revealed nodular and air space opacities bilaterally, no cavity, or pleural effusion was seen. Sputum smear examination showed multi-gemant yeasts and was negative for acid fast bacilli. Biopsy of the right cervical lymph node and of the thoracic region was performed, the histological study revealed presence of yeasts with multiple budding in ship's rudder compatible with paracoccidioidomycosis in both lymph node tissues (Fig. 2), therefore, the patient was treated as a case of disseminated CPM with secondary TB.

Amphotericin b deoxycholate and hydrocortisone were administered as per local Disseminated paracoccidioidomycosis treatment guidelines.

Table 1
Laboratory tests on admission and at discharge. Values of laboratory tests on admission and around discharge. For some tests with variable results, a range of values is reported.

Laboratory test (units; reference range)	Admission	Discharge
Creatinine (mg/dL; 0.7–1.2)	1.3	0.8
Glucose (mg/dL; 74–100)	116	105
Aspartate aminotransferase (U/L; ≤34)	162	43
Alanine aminotransferase (U/L; ≤55)	64	39
Alkaline phosphatase (U/L; 40–150)	155	131
White blood cell count (K/cmm; 4–11)	8.67	8.27
Lymphocytes (K/cmm;1–4.8)	1.76	2.34
Eosinophils (K/cmm; <500)	1.75	0.42
Eosinophils (%; 1–4)	17.1	3.7
Hemoglobin (g/dL; 13.5–17.9)	10.2	12.7
Mean corpuscular volume (fL;80–100)	92.3	94.1
Mean corpuscular hemoglobin (mg/dl; 34 ± 2)	31.3	30.6
Hematocrit (%; 41–54)	37.3	39.5
Platelet count (K/cmm; 150–400)	335	309
C-reactive protein (mg/L; ≤5)	107.8	12.4

He received amphotericin b deoxycholate 1 mg per kg of weight for 14 days through a central vein, with daily corrections of serum potassium for hypokalaemia, the patient presented clinical improvement from day 7 of receiving the medication.

The patient stayed in the hospital for almost two months. Upon discharge, her laboratory results are shown in Table 1. He showed significant improvement on the itraconazole regimen 200 mg daily and treatment for tuberculosis without any significant adverse effects. He has not had a recurrence of symptoms since.

Discussion

Paracoccidioidomycosis (PCM) and tuberculosis (TB) are infections that produce chronic inflammation of the granulomatous type that is acquired by inhalation of their infectious forms, conidia and mycobacteria, respectively, mainly affecting the lungs in more than 80% of cases, these characteristics are also common. in these pathologies, however, simultaneous involvement can also be seen in multiple organs [7].

In many cases of PCM and TB coinfection there is a previous TB diagnosis that does not improve with anti TB treatment or the improvement is minimal, likewise, baseline microbiological examinations with positive smear microscopy rarely show the presence of PCM yeasts. which in subsequent biopsies become evident, as in the case described.

Although the association between PCM and TB is reported in the literature, this infectious combination should be considered mainly in tropical and PCM endemic areas where about 8% of patients with pulmonary PCM presented coinfection with pulmonary TB with a positive sputum result [8], mainly when there is failure of the initial treatment of any of them or when the presentations cause invasion of multiple organs such as bone marrow, kidney, brain, skin and other organs with great systemic involvement [9,10] and in patients with immunosuppression such as infection due to HIV [11] or diabetes mellitus [12] the clinical picture is very aggressive or the clinical presentation can mimic neoplastic diseases [13] and in some cases as added comorbidities in patients with lymphoma.

Due to the delay in the growth of PCM and TB cell cultures, the histological examination of the biopsy is important for the diagnosis of both pathologies [14], likewise, the tissue culture should also be considered to identify the resistance to tuberculosis drugs [15].

We think that tuberculosis may contribute to the unmasking of PCM in cases of co-infection, since the association of both diseases and its severe presentation may be associated with the deficiency of some proteins responsible for the immune response such as myloperoxidase, an enzyme present in the lysosomes of monocytes and neutrophils that catalyzes the conversion of hydrogen peroxide and chloride ion into hypochlorous acid and thus destroy these pathogens during the process of phagocytosis by neutrophils and is considered an important defense against countless bacteria [16].

The treatment of choice for severe PCM infections continues to be amphotericin b, and in patients with tuberculosis infection, joint treatment with first-line anti-tuberculosis drugs (rifampin, isoniazid, ethambutol and pyrazinamide) are the recommended treatment, with no evidence of adverse clinical manifestations due to the interaction of these antituberculous drugs with amphotericin, some drugs are recently being studied for the joint treatment of both pathologies (TB and MCP), such as 4-methoxynaphthalene-N-acylhydrazones as a potential treatment for paracoccidioidomycosis and tuberculosis [17]. Additionally, although there is interaction between rifampicin and itraconazole, this was not evidenced in the patient, he presented clinical improvement, favorable response and no evidence of adverse effects for these drugs.

Conclusions

TB might rarely be complicated by PCM, physicians should consider PCM as an important aggregate diagnosis in TB patients with

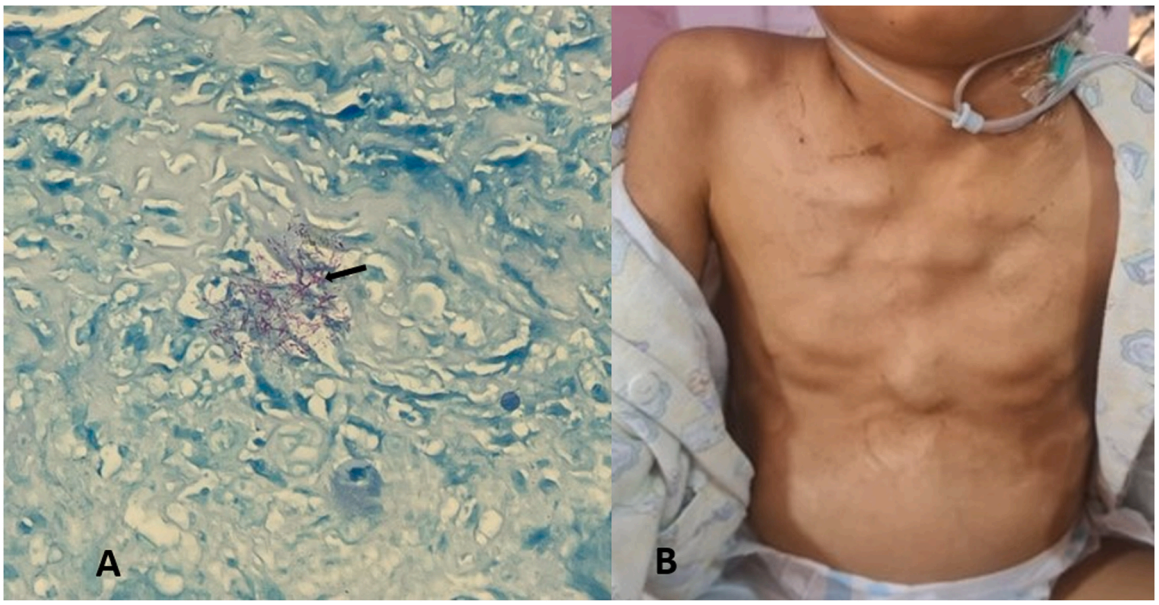

Fig. 1. Presence of acid-alcohol-fast bacilli in the lymph node, Zielh Nielsen staining, 40X (A). Child's chest showing multiple lymphadenopathy in the cervical and thoracic region, also cachexia and use of accessory muscles for breathing (B).

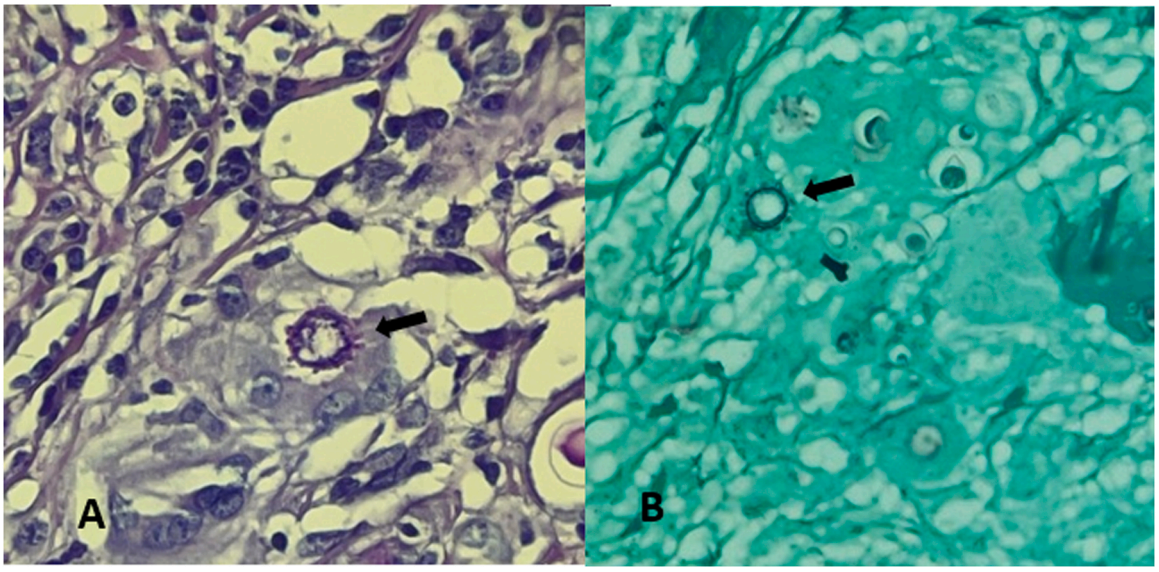

Fig. 2. Presence of yeasts with multiple budding on the ship's rudder, Periodic Acid-Schiff staining - PAS - 40X, (A). Presence of multiple budding yeasts, Gomori Grocott stain - 40X (B).

lymphadenomegaly, liver and respiratory system dysfunction, and underlines the importance of the histopathological diagnosis that helped to identify both pathogenic agents, the child presented a good clinical response to the administration of amphotericin b deoxycholate, antituberculous medication and corticosteroids. Any delay in definitive therapy will lead to increased morbidity and mortality.

Ethical approval

Ethical approval was obtained from the Institutional Ethical Committee of the Daniel Alcides Carrion Hospital, Huancayo, Peru.

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None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images and their confidentiality was also guaranteed. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions statement

RM, AD, JM, MP, MM and ET designed and conducted the research. RM provided the data. MM and ET had primary responsibility for the final content. All authors have read and approved the final manuscript.

Conflicts of interest statement

The authors declare that they do not have a conflict of interest.

Code availability

Not applicable.

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