LYMPHADENITIS BY PARACOCCIDIOIDOMYCOSIS MIMETIZING PANCREATIC HEAD CANCER

Matheus Puls¹, Flávio Barbieri¹, Henrique Carrascossi¹, Cibele Duch¹, Daniel Lopes¹,
Lídia Moura¹, Giulia Duarte¹, Mariane Montoro¹, and Matheus Perugini¹

¹Unira

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Abstract

Chronic paracoccidioidomycosis is an endemic fungal infection in Latin America and, although uncommon, the opening of the clinical condition can be an obstructive abdominal syndrome that can simulate a pancreatic head neoplasm. There are few cases like this reported in the literature.

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**AUTHORS: MATHEUS LOPES PULS; DANIEL PEDRO CASTELO BRANCO LOPES;
FLÁVIO AUGUSTO BARBIERI; CIBELE REPELE DUCH; HENRIQUE LUIZ CARRAS-
COSSI; MARIANE ARANJUES MONTORO; LÍDIA GOMES DE MOURA; GIULIA LIA
DUARTE; MATHEUS ROSSI LIMA PERUGINI.**

INTRODUCTION:

Paracoccidioidomycosis (PCM) is a potentially systemic fungal infection caused by the thermomorphous species *Paracoccidioides brasiliensis* (*P. brasiliensis*) and *Paracoccidioides lutzii* (*P. lutzii*) (1–3).

PCM is considered an endemic condition in Latin America, where 80% of the cases are concentrated in Brazilian territory, mainly in the states of São Paulo, Paraná, Rio Grande do Sul, Goiás and Rondônia (1,3). It is considered the eighth cause of mortality by chronic infectious and parasitic disease and, among systemic mycoses, the main reason for hospital admissions (1,2).

Among the main contamination risk factors, occupational areas related to agricultural activities and fungus contaminated soil handling are included, presenting high prevalence on rural workers (1,2). Smoking, alcoholism and immunodeficiency or immunosuppression states are also related factors (1).

The disease acute/subacute form, also called juvenile, is less frequent, occurring in 5–25% of the cases and generally associated to the disease endemic areas. The incidence on both genders is equal and occurs mainly within the first two decades of life, and after 40 years of age (1,4–8).

The chronic form is responsible for up to 96% of the cases, affecting mainly males (1,6,9,10). The lungs are affected in up to 90% of the cases, and mucous membranes and skin are other common foci (1).

The aim of this study is to present a PCM clinical case that simulated a pancreatic cancer with jaundice, cholestasis and significant weight loss.

CASE REPORT:

A 61-year-old male patient, born and residing in the state of São Paulo, a rural worker in a lemon plantation from childhood. The patient sought medical care at an external health service due to a complaint of jaundice that started 2 months before, with a weight loss of 20 kg during this period. He reported that the symptoms were presented in rapid progression, associated with fecal acolia, choluria, intense itching and sporadic pains in the right hypochondrium.

A smoking patient (43 packs/year), previously obese (BMI 33.95), with a previous inguinal right herniorrhaphy surgery. He reported allergy to dipyrone and penicillin and denied alcoholism, use of illicit drugs and other comorbidities. There was no history of relevant family or hereditary illnesses. The patient was not taking any continuous use medication.

On physical examination, the patient presented a regular general condition, ruddy, hydrated, jaundiced 2+/4+, acyanotic, eupneic in room air and afebrile to the touch. His cardiac auscultation had two rhythmic and hypophonetic sounds, with no audible murmurs, and a respiratory rate within the normal range. The abdomen was globose, flaccid, with present air-fluid noises, painless to superficial and deep palpation, without visceromegalies, without visceromegalies, palpable masses and signs of peritonitis. No further alterations were found.

In an external health service, an ultrasound study of the total abdomen was performed. The exam presented evidences of intra and extrahepatic bile duct dilatation without visualization of cholelithiasis, with a 1.0 cm diameter common bile duct, mild splenomegaly, diffuse periaortocaval lymph node enlargement and a nodular lesion of approximately 4 cm in the head of the pancreas.

A nuclear magnetic resonance with contrasted cholangiography visualized a solid nodular formation, peripancreatic, with extension to the duodenal papilla, measuring approximately 3.6 cm - suspicious for a primary neoplastic process with distally compression of the bile duct – and significant extra and intrahepatic bile duct upstream dilation associated with multiple heterogeneous lymph node enlargement in the retroperitoneum and mesentery, sometimes confluent, some with a necrotic center, compatible with secondary nodal involvement.

Due to the clinical condition and the results of the imaging exams, an endoscopic retrograde cholangiopancreatography (ERCP) was chosen for biliary decompression with an 8.5 FR prosthesis at an external health service.

The ERCP report showed an image of extensive stenosis in the middle and distal bile ducts, raising the suspicion of extrinsic compression due to pancreatic head neoplasm and dilated intrahepatic biliary tracts (Figure 1).

In view of the clinical and laboratory findings, the patient was referred to our institution for further investigation and treatment.

The laboratory exams on admission showed a normocytic normochromic anemia (hemoglobin 10,7 g/dL, hematocrit 35,60%, mean corpuscular hemoglobin 28,1 pg, mean cell volume 93,4 fl) with peripheral eosinophilia ($850/\text{mm}^3$) and thrombocytosis ($618000 \text{ platelets}/\text{mm}^3$) with a compatible picture of cholestasis, showing high levels of canalicular enzymes and transaminases (alkaline phosphatase 714 UI/L, gamma-glutamyl transferase 179 UI/L, oxaloacetic transaminases 60U/L, glutamic-pyruvic transaminase 71 U/L), as well direct hyperbilirubinemia (Total Bilirubin 6,1 mg/dL, direct bilirubin 5,8mg/dL, indirect bilirubin 0,4 mg/dL). His pancreatic enzymes were normal (amylase 27U/L). Tests for HIV, hepatitis B and C, and syphilis were non-reactive. His chest x ray hadn't signs of consolidation or diffuse infiltrates (Figure 2-A).

His electrocardiogram showed sinus rhythm with an electrical axis within normality. The contrast tomography (CT) of the abdomen and pelvis on admission, in turn, similar to the external examination, presented an image suggestive of heterogeneous expansive formation with cystic density (necrosis) adjacent to the head/unciform process of the pancreas, including the papilla, and with involvement of the bile duct, suspected for advanced-stage pancreatic neoplasm, with maintenance of intra and extrahepatic biliary tracts dilatation and signs of residual aerobilia upon biliary prosthesis implantation. It also showed multiple foci of pathological lymph node enlargement, some clustered and coalescents, notably periaortocavals, in the hepatic hilum and peripancreatic, the latter measuring up to 4.1 x 4.0 cm (Figure 2-B).

In view of the clinical suspicion and laboratory and imaging findings, exploratory laparotomy was performed. The procedure allowed the visualization of lymphonomegalies in the hepatic hilum, periaortic and peripancreatic regions and a lymph node biopsy was obtained. The anatomicopathological examination showed a chronic fungal granulomatous lymphadenitis suggestive of paracoccidioidomycosis with positive Grocott special staining in the fungal structures (Figure 3), with negative alcohol-acid-resistant bacilli research and no signs of malignancy. The patient was diagnosed with secondary jaundice to extrinsic compression of the fungal lymph node by PCM, and treatment with once a day oral 200 mg Itraconazole was initiated.

The control laboratory tests after three days of treatment showed a decrease in peripheral eosinophilia and thrombocytosis, in the levels of bilirubin and liver transaminases, until their normalization.

He was discharged stable, afebrile and asymptomatic with referral for follow-up.

DISCUSSION

Brazil is responsible for 80% of PCM cases in Latin America and has a heterogeneous distribution with endemic areas, being considered a neglected disease and a public health problem. (1,2,9).

The literature points to an increase in cases in non-endemic areas and countries in recent years, related to the contamination during visits to endemic regions (10,11).

Although isolated lymphadenopathy is more common in acute cases of the disease, our patient has epidemiological data on the chronic and most common form of the disease (74 to 96%) with slow and progressive clinical evolution pattern (1,3,9). The clinical condition is commonly associated with significant weight loss (72%), asthenia (65%), mucocutaneous pallor (62%), fever (51%), cough (50%), dysphonia, dysphagia, odynophagia, and in lower frequency, ulcerations in the mouth and throat (9). The main sites of involvement are the lungs (90%), the skin and mucous membranes, the lymph nodes, with lymph node enlargement (79%), and, less frequently, adrenals (50%), and digestive, bone (20%) and central nervous (25%) systems (1,2,9).

The chronic PCM lymph node involvement with its enlargement, may present itself with suppurative, and/or cancer-like features (9). Some lymph nodes may be superficial, with involvement of the cervical, submandibular, submental, supraclavicular, axillary and inguinal chains. The deep involvement of structures usually affects the intra-abdominal segment (9).

In the latter situation, the disease can present as a mass effect compressing a wide range of organs and structures, depending on its site.

Thus it can evolve with several clinical syndromes such as cholestasis, due to biliary tracts obstruction, pancreatitis, due to the pancreatic duct obstruction, chylous ascites, due to the thoracic duct compression, pyelonephritis and acute renal failure, due to the ureters compression, and malabsorption syndrome and acute abdomen, due to intestinal compression (4,9).

In the present case, Our patient presented a cholestatic syndrome resulting from extrinsic compression of the common bile duct by mesenteric lymph node enlargement in the hepatic hilum, peripancreatic and periaortic regions, evolving with cholestatic jaundice syndrome.

The performed imaging exams (US of the abdomen, MRI of the upper abdomen with cholangio-MRI, ERCP and CT of the abdomen and pelvis) showed evidence of extrinsic compression and suspicion of malignant neoplasm of the pancreas head with lymph node involvement. However, the neoplastic diagnosis was ruled after the laparoscopic biopsy findings of chronic fungal granulomatous lymphadenitis due to paracoccidioidomycosis.

The PCM gold standard diagnostic procedure is the fresh analysis of the sputum or other clinical sample and/or biopsy, with histopathological analysis of the affected organ, wich allows the visualization of fungal structures suggestive of *Paracoccidioides* spp. (1,2,7,10,12,13).

For the mild and moderate form of PCM, the first line of treatment is with daily 200 mg oral-Itraconazole (1,2,6,7,11,14,15). The length of treatment ranges from 6 to 12 months with periodic reassessments to verify the cure criteria that allow the withdrawal of the medication (1,7). After the treatment begins, the regression of symptoms differs according to the site of involvement, with lymphadenopathies regressing in two to three months and imaging exams becoming normal around six months (1).

The length of drug-treatment must be guided by the patient's healing criteria, which involves clinical, mycological, radiological and immunological criteria. The definitive cure is not viable due to the impossibility of eradicating *P. brasiliensis* and *P. lutzii* from the human body. Therefore, the main objective of the treatment is to allow an improvement in cellular immunity by reducing the fungal load to re-establish a balance between parasite and host. (1,12,15).

CONCLUSION

The description of PCM simulating a malignant pancreatic neoplasm with jaundice in an immunocompetent patient is extremely rare to find in the scientific literature. We presented a case of atypical presentation of a condition poorly diagnosed in clinical practice. PCM should be considered as a differential diagnosis of abdominal obstructive syndromes due to supposed tumoral events. The guided biopsy might be a valuable diagnostic procedure in such cases.

This case report demonstrate the importance of the comprehension of PMC on its various presentation forms. This knowledge allowed an early diagnosis, treatment and follow-up, ruling out the hypothesis of a gloomy prognosis neoplasm.

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CONFLICT OF INTERESTS:

The authors of this article declared that there is no conflict of interest in this case report.

AUTHORS' CONTRIBUTION:

Barbieri, F. A; Moura, L. G; Perugini M. R. L: Provided anatomopathological study and other materials to compose the report. **Lopes, D. P. C. B; Duarte, G. L; Montoro M. A:** Wrote, edited and adapted the article. **Puls, M. L; Duch, C. R; Carrascosi, H. L:** Revised and coordinated the writing process of this article.

ETHICAL APPROVAL:

Confirmed that the manuscript was read and approved by all authors mentioned here, and had the patient's consent. All precautions with identity confidentiality and personal protection were taken during the preparation of the article.

REFERENCES:

1. Shikanai-Yasuda MA, Mendes RP, Colombo AL, de Queiroz-Telles F, Kono ASG, Paniago AMM, et al. Brazilian guidelines for the clinical management of paracoccidioidomycosis. *Rev Soc Bras Med Trop.* 2017;50(5):715–40.
2. Hahn RC, Rodrigues AM, Terra PP Della, Nery AF, Hoffmann-Santos HD, Góis HM, et al. Clinical and epidemiological features of paracoccidioidomycosis due to *paracoccidioides lutzii*. *PLoS Negl Trop Dis.* 2019;13(6):1–13.
3. Batista M, Vermelho F, Correia AS, Suzart KK, Almeida LA, Khoury Z. Alterações abdominais da paracoccidioidomicose disseminada. 2015;48(2):81–5.
4. PARACOCCIDIOIDOMICOSE JUVENIL MIMETIZANDO SÍNDROME COLESTÁTICA - relato de caso. *Rev científica Fagoc Saúde.* 2017;II:87–90.
5. Marcio Nucci, MD, Arnaldo L Colombo M. Clinical manifestations and diagnosis of acute/subacute paracoccidioidomycosis. Uptodate. 2021;
6. Cavalcante R de S, Sylvestre TF, Levorato AD, de Carvalho LR, Mendes RP. Comparison between Itraconazole and Cotrimoxazole in the Treatment of Paracoccidioidomycosis. *PLoS Negl Trop Dis.* 2014;8(4).
7. Travassos LR, Taborda CP, Colombo AL. Treatment options for paracoccidioidomycosis and new strategies investigated. *Expert Rev Anti Infect Ther.* 2008;6(2):251–62.
8. Instituto de Infectologia Emílio Ribas. 2013;31.
9. Vasconcellos A, Ambrósio A, Camelo CCS, Barbosa CV, Tomazatti FG, Brazões FA de S, et al. Paracoccidioidomycosis disease (Lutz-Splendore-Almeida) - clinical manifestations. *Rev Médica Minas Gerais.* 2014;24(1):67–73.
10. Marcio Nucci, MD, Arnaldo L Colombo M. Clinical manifestations and diagnosis of chronic pulmonary paracoccidioidomycosis. Uptodate. 2021;
11. Queiroz-Telles F, Goldani LZ, Schlamm HT, Goodrich JM, Espinel-Ingroff A, Shikanai-Yasuda MA. An open-label comparative pilot study of oral voriconazole and itraconazole for long-term treatment of paracoccidioidomycosis. *Clin Infect Dis.* 2007;45(11):1462–9.
12. Ambrósio AVA, Camelo CCS, Barbosa CV, Tomazatti FG, Brazões FA de S, Veloso JM, et al. Paracoccidioidomycosis disease (Lutz-Splendore-Almeida disease): Additional workup, differential diagnosis, cure control. *Rev Médica Minas Gerais.* 2014;24(1):81–92.
13. Ferreira CMSD, Souza NG de O, Tostes FM, Moutinho BD, Segheto NN. Paracoccidioidomycose subaguda abdominal em paciente adulto imunocompetente: relato de caso. *Rev Soc Bras Clín Méd.* 2013;11(2):201–3.
14. Borges SRC, Da Silva GMS, Da Costa Chambela M, De Vasconcellos De CRO, Costa RLB, Wanke B, et al. Itraconazole vs. trimethoprim-sulfamethoxazole: A comparative cohort study of 200 patients with paracoccidioidomycosis. *Med Mycol.* 2014;52(3):303–10.
15. Marcio Nucci, MD, Arnaldo L Colombo M. Treatment of paracoccidioidomycosis. Uptodate. 2021;