

Cryptosporidiosis of the biliary tract mimicking pancreatic cancer in an AIDS patient

Criptosporidiose do trato biliar simulando câncer do pâncreas em paciente com AIDS

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ABSTRACT

Diarrhea caused by Cryptosporidium sp is frequent in patients with AIDS, but involvement of other organs of the digestive tract is uncommon. We report a case of Cryptosporidium-associated obstruction of the biliary tract mimicking cancer of the head of the pancreas in a 43-year-old woman with AIDS.

Key-words: Cryptosporidiosis. AIDS. Biliary tract. Pancreatitis.

RESUMO

A diarreia causada pelo Cryptosporidium sp é muito freqüente em pacientes com aids, mas o envolvimento de outros órgãos do aparelho digestivo é incomum. Relata-se o caso de uma mulher de 43 anos, que tinha aids, que apresentava obstrução das vias biliares associada ao Cryptosporidium, simulando câncer da cabeça do pâncreas.

Palavras-chaves: Criptosporidiose. AIDS. Trato biliar. Pancreatite.

Cryptosporidiosis is one of the most common human enteric infections, mainly among children^{2,14}, which has been recognized after onset of the AIDS pandemic^{11,13}. The etiologic agent is *Cryptosporidium* sp, which was described in mice by Tyzzer in 1907²⁰. The first case of human cryptosporidiosis was reported only in 1976 in an immunocompetent patient with acute enterocolitis¹⁷.

The occurrence of asymptomatic intestinal infections caused by *Cryptosporidium* sp has been documented; these infections are rare in normal individuals but frequent in AIDS patients¹¹. Disease manifestations include self-limited acute, chronic and fulminating forms. Spreading of *Cryptosporidium* sp leads to hepatobiliary and respiratory infection, affecting the nasal and sinus mucosa^{5,9}. Pitlik et al¹⁸ reported the first case of gallbladder infection in an AIDS patient. There have been other reports of this complication of intestinal cryptosporidiosis in immunocompromised patients^{13,17}.

Despite being a frequent cause of morbidity, cryptosporidiosis is rarely the sole cause of death, even among AIDS patients. However, cryptosporidiosis may be the disease defining AIDS²¹, in these patients.

According to the AIDS Epidemiological Bulletin⁴, cryptosporidiosis is diagnosed in 2.8% of patients aged 13 or older and in 2.7% of individuals aged less than 13 years old. Prospective studies carried out in Brazil on patients with AIDS reported a prevalence of 12 to 20%^{6,8}. However, cryptosporidiosis of the biliary tract has not been described to date.

The objective of the present study was to present the case of a patient with AIDS and biliary tract cryptosporidiosis mimicking malignant neoplasia of the head of pancreas.

CASE REPORT

A 43-year-old white female patient was admitted to the Surgical Gastroenterology Ward with a three-month history of anorexia, weakness and a weight loss of 15kg. Forty days after the onset of symptoms, the patient presented jaundice, fecal acholia and choluria. One month later, she started to show lower limb edema (LLII), diarrhea (3-4 times/day) and abdominal pain, without any respiratory symptoms. Physical

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examination revealed regular to poor general condition, 40kg of weight, skin and mucosal jaundice, whitish lesions on the palate, LII edema, a tense abdomen with pain upon palpation in the right hypochondrium and epigastrium, and discrete hepatomegaly. Ultrasonography showed hepatomegaly with a discrete and diffuse increase in the echogenicity of the parenchyma, an enlarged head of pancreas, and dilatation of the intrahepatic bile ducts and of the common bile duct. Computed tomography (CT) of the abdomen, using oral contrast dye followed or not by intravenous injection of contrast dye, demonstrated hepatomegaly, dilatation of the intrahepatic bile ducts, common bile duct and pancreatic duct, an increased head of pancreas, discrete enlargement of the left suprarenal gland, and thickening of the rectal and sigmoid walls (Figures 1 to 4). These results suggested neoplasia of the head of pancreas and the patient was submitted to gastroduodenopancreatectomy. During surgery, a lymph node was removed from the head region of the pancreas and histological examination of a frozen biopsy revealed, rare granulomas surrounded by fibrotic scar tissue with *Paracoccidioides brasiliensis* yeasts. The patient was then transferred to the Tropical Disease Ward. Since she was a woman outside the expected age range for the juvenile form of paracoccidioidomycosis (PCM), with poor epidemiologic

history for this mycosis, and with intense impairment of general and nutritional status, and the presence of a history favoring the possibility of HIV infection, the patient was submitted to anti-HIV antibody detection by ELISA, with a positive result. However, no anti-*P. brasiliensis* antibody was detected. Histological examination of the surgical specimen revealed suppurative cholangitis associated with *Cryptosporidium* sp infection (Figure 5). Cryptosporidia were observed in the head of pancreas near the surface of the pancreatic duct epithelium close to the papilla. Enzymatic necrosis of the pancreatic parenchyma was absent. Although the patient did not have any respiratory complaints, a simple chest X-ray revealed discrete and diffuse linear and micronodular interstitial infiltration. The CD4⁺ T cell count showed 35 cells/mm³. Antiretroviral treatment with stavudine, lamivudine and indinavir was initiated. The patient

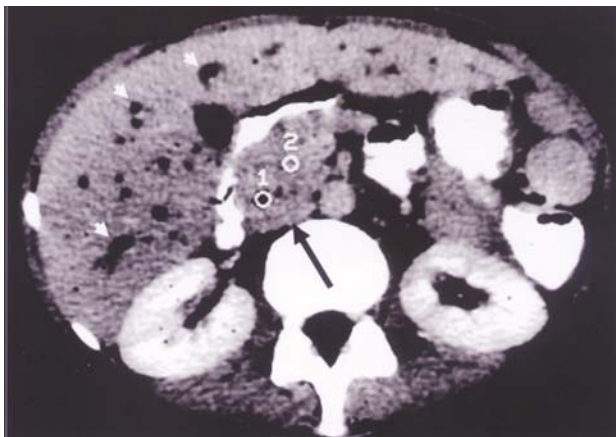


Figure 1 - Axial contrast-enhanced CT demonstrates enlargement of the pancreas head (→) and intrahepatic biliary tract dilatation (↔).



Figure 2 - Axial contrast-enhanced CT image demonstrates common bile duct, pancreatic canal and intrahepatic biliary dilatation (↔).



Figure 3 - Axial contrast-enhanced CT image demonstrates intrahepatic biliary tract dilatation (↔) and enlarged liver and spleen (☆).



Figure 4 - Axial contrast-enhanced CT image at the level of the pelvis demonstration thick walled colon and rectum (↔).

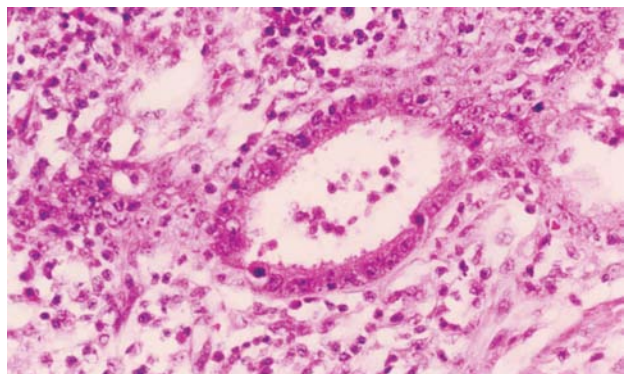


Figure 5 - Cryptosporidiosis in suppurative colangitis - Dot-like organisms on the surface epithelium (arrows) (HE 400x).

received intravenous clarithromycin (1g/day) and fluconazole for the treatment of cryptosporidiosis and oral candidiasis, respectively. The patient showed clinical improvement after two months and was discharged from the hospital. She did not return for outpatient follow-up and died at home two months later.

DISCUSSION

The present case demonstrates the difficulty in obtaining the diagnosis of pancreatic and bile duct diseases. The clinical signs and symptoms of the patient suggested neoplasia of the head of the pancreas. Although, this disease is more frequent in male patients (1.5:1) over 60 years of age, the present case was a 43-year-old woman.

The diagnosis of PCM was suggested, but this disease is much more frequent in men (10.7:1) and an age range below 30 years old is expected for the acute or subacute form¹⁵. The absence of rural working, abdominal and superficial adenomegaly, splenomegaly, and the histopathological findings of granulomas with latent yeast forms did not point to subacute PCM diagnosis. In addition, the confirmation of the diagnosis of pancreatic and biliary tract cryptosporidiosis, which is a disease defining AIDS, indicated the need for the determination of anti-HIV antibodies that confirmed this diagnosis.

Biliary cryptosporidiosis has been observed in 15% of the AIDS patients¹³. Such a localization favors the occurrence of relapses, with the biliary tract serving as a reservoir of this agent¹¹. These patients commonly present chronic disease, manifesting with diarrhea, weight loss and malabsorption of nutrients, water-soluble vitamins, D-xylose and fat^{11,17}. In the present study, the patient did not present chronic diarrhea as usually reported^{11,16}, but showed biliary tract involvement and intense weight loss.

Biliary involvement by *Cryptosporidium* seems to be related to a more advanced stage of the disease and a low CD4⁺ T lymphocyte count, especially when it falls below 50 cells/mm³, with a higher risk of death due to cryptosporidiosis²¹. Our patient had a CD4⁺ T lymphocyte count of 35 cells/mm³, a two-month hospital stay and died two months after discharge.

Clinical manifestations of cryptosporidiosis can be misdiagnosed, and in AIDS patients it can mimic sclerosing cholangitis, cholecystitis and pancreatitis¹⁶. In AIDS patients, stone-free cholecystitis and thickening of the gallbladder are mainly caused by *Cryptosporidium* sp and cytomegalovirus¹.

Imaging findings are nonspecific. Hashmey et al¹² performed 38 diagnostic imaging studies on 20 cryptosporidiosis patients. Ultrasonography detected thickening of the gallbladder wall in five out of 10 patients, biliary sludge in two, dilatation of the bile duct in two, and calculi in one. Computed tomography scan revealed dilatation of the bile ducts in 3 out of 4 patients. Endoscopic-retrograde cholangiopancreatography (ERCP) detected *Cryptosporidium* sp oocysts in material obtained by brushing and/or biopsy of the bile ducts in three patients. Narrowing of Vater's ampulla and alternating narrowing and dilatation of the intrahepatic bile ducts could also be observed by this method. These authors considered *Cryptosporidium* sp to be the primary cause of cholecystitis in AIDS patients.

In our case, abdominal CT scan and ultrasonography showed alterations suggestive of sclerosing cholangitis, such as dilatation of both common and intrahepatic bile ducts. Enlargement of the head of the pancreas was also observed, suggesting neoplasia.

Autopsy studies¹⁰ have shown the presence of *Cryptosporidium* sp inside the pancreatic duct, with evidence of periductal inflammation. In the present case, histological examination demonstrated *Cryptosporidium* sp near the surface of the pancreatic duct epithelium close to the papilla, in addition to lymphoplasmocytic inflammation, a fact that might explain the enlargement of the head of the pancreas as detected by ultrasonography, CT scan and during surgery. Goodwin¹⁰ reported the occurrence of pancreatic disease with periductal inflammation and interstitial edema in five cases, generally observed in the head region of the pancreas, without histopathological evidence of pancreatitis. Our patient did not present enzymatic necrosis of the pancreatic parenchyma, which is fundamental for the diagnosis of pancreatitis.

In the present study, a chest plain film showed mild and diffuse linear and micronodular interstitial infiltration of the lungs. Although some authors^{3,7} have suggested pulmonary involvement by *Cryptosporidium* sp, more frequent etiologies such as *Pneumocystis carinii* cannot be excluded.

Diagnostic confirmation of extraintestinal cryptosporidiosis is difficult. Vakil et al.²¹ established the diagnosis in 9 (38%) patients with biliary symptoms by demonstrating *Cryptosporidium* sp in the biliary tract through the analysis of biliary brushings obtained by endoscopy and histological examination of gallbladder material obtained by biopsy. In our study, the diagnosis of cryptosporidiosis was confirmed by histological examination of the surgical specimen.

Treatment of cryptosporidiosis is difficult, and variable degrees of efficacy were observed with macrolides, paromomycin and sulfonamides^{11,19,21}. Our patient showed an excellent response to clarithromycin maintained for 38 days.

Sphincterotomy has been reported to provide a rapid result and substantial relief of pain in the right hypochondrium in most AIDS patients with biliary cryptosporidiosis¹. Endoscopic papillotomy and cholecystectomy have also been used with favorable results²¹. In the present study, the probably overly extensive surgery, led to the removal of the distal obstacle of the common bile duct, with a similar effect to that obtained with papillotomy and sphincterotomy.

Our experience with the case presented herein leads us to consider the extraintestinal cryptosporidiosis in AIDS patients with biliary tract involvement.

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