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CASE REPORT

Cryptococcosis manifesting as isolated biliary infection: Case report and brief review of literature

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KEYWORDS
Cryptococci infection;
Biliary;
Eosinophilia;
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Summary
Background: Biliary cryptococci infection is rare, which is frequently diagnosed by exploratory laparotomy, preoperative diagnosis is difficult.
Case presentation: A 14-year-old girl presented with intermittent jaundice for 6 years. She had no pruritus, anorexia, nausea or vomiting, fever, abdominal pain, or clay stools. Laboratory tests showed obstructive jaundice, eosinophilia, and increased IgE levels. The patient was ultimately diagnosed as Cryptococcal infection by bone marrow culture. The patient responded to antifungal therapy.
Conclusion: Unnecessary surgical intervention was avoided by an early and accurate diagnosis. Cryptococcosis infection of bile duct should be highly suspected, when the children with obstructive jaundice have eosinophilia and increased IgE levels.

Abbreviations: ALP, alkaline phosphatase; INR, international normalized ratio; IgE, immunoglobulin E; MRCP, magnetic resonance cholangiopancreatography; CT, computed tomography.

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Introduction

Cryptococci disease is a potentially fatal fungal disease caused by *Cryptococcus neoformans*, which is common in immunocompromised hosts. The central nervous system, lung and skin are the common site of cryptococcal infections. Involvement of the biliary tract is rare. In review of the literature, only 11 cases of cryptococcal infection presenting with obstructive jaundice as initial manifestation were reported [1—11], however, most of which were diagnosed after exploratory laparotomy. Preoperative diagnosis for biliary cryptococcal infection is rare, here; we reported a case of cryptococcal infection with obstructive jaundice diagnosed by bone marrow culture.

Case description

A 14-year old girl was admitted to our hospital on January 20, 2016 with intermittent jaundice for six years. She had no pruritus, anorexia, nausea or vomiting, fever, abdominal pain, or clay stools. Her earlier medical history was not significant and she denied alcohol or drugs. The patient had no direct contact with pigeon or their excreta, nor had she travelled to tropical areas, and she was unlikely to have eaten food contaminated with Cryptococcus infection.

Few positive findings were noted on the physical examination except the patient was visibly icteric, poor development with a body weight of 33 kg (body mass index: 16.2 kg/m^2), and had anemic appearance and hepatosplenomegaly. No palpable lymph nodes were found and Murphy's sign was negative.

On admission, the laboratory investigation revealed abnormal liver function tests consistent with cholestatic jaundice (alanine aminotransferase [ALT] 121.6 U/L aspartate aminotransferase [AST] 213.5 U/L, alkaline phosphatase [ALP] 1025 U/L, g-glutamyltransferase [GGT] 365 U/L, total bilirubin [TBIL] 113.6 μmol/L, direct bilirubin [DBIL] 100.4 μmol/L and albumin 25.9 g/L). The white blood cell count, percentage of eosinophils and hemoglobin (Hb) level were abnormal (9.95×10^9/L, 11.4% and 82 g/L, respectively). The prothrombin time (PT) and international normalized ratio (INR) were normal. The immunoglobulin E (IgE) is above 6000 ng/mL. Anti-hepatitis viruses (A-E), anti-HIV and abnormal autoimmune antibodies were negative. The blood culture was negative.

The chest X-ray was negative. An abdominal contrast-enhanced computerized tomography (CT) scan and a magnetic resonance cholangiopancreatography (MRCP) revealed a dilated intrahepatic bile duct, thickened common duct wall, retro-peritoneal lymph node enlargement, enlarged liver, and huge spleen (Fig. 1). The patient was advised to do bone marrow biopsy or exploratory laparotomy to rule out lymphoma, special bacterial infection, or the other disease. Seven days later, Microscopic examination of bone marrow culture showed numerous encapsulated yeast-like organisms measuring 7—10 μm in diameter scattered in the culture medium. Gram staining (Fig. 2) and India ink staining (not shown) were all positive, and a diagnosis of Cryptococcosis was confirmed. So the exploratory laparotomy was not scheduled. The patient received Amphotericin B deoxycholate (0.7 mg/kg IV daily) plus flucytosine (25 mg/kg PO qid). The patient tolerated chemotherapy very well. After more than one month of antifungal drug therapy, the disease was effectively controlled. The liver enzyme and jaundice dropped to almost normal. The hemoglobin elevated to 101 g/L, and the percentage of eosinophils were 8.10%. The IgE decreased to 4093 ng/mL. The patient was discharged with fluconazole for six months. The latest follow-up on February 2nd, 2017, showed no evidence of recurrence. Her liver function and Hb is normal, ALP dropped to 162 U/L, percentage of eosinophils is 3.1%, the IgE was 641 ng/mL, and huge spleen has reduced below the left coastal margin.

Discussion

Cryptococcal infection presenting as obstructive jaundice as initial manifestation is extremely rare. In one review of the literature, only eleven reports were related with hepatobiliary cryptococcosis manifesting as obstructive jaundice [1—11]. Children patients under 14 years occupied three of cases [3,6,7]. There are two reports on isolated biliary cryptococcosis [1,3]. Biliary cryptococcosis was diagnosed by exploratory laparotomy in eight cases [1—3,6—11], by the culture of bile obtained by percutaneous transhepatic biliary drainage in one case [4], by the lymph node aspiration biopsy in one case [6], and by autopsy in one case [5]. None of them noticed the changes of eosinophils and IgE. All of cases have normal immune- competence, and there is no HIV infection. Nine cases recovered after antifungal therapy [1—4,6,9—11], three cases died [5,7,8].

Cryptococcosis manifested isolated biliary infection is difficult for preoperative diagnosis, Their MRCP or abdominal CT usually showed hepatosplenomagly, extra- and intrahepatic biliary dilatation, thickened bile duct wall, narrowed or occluded the bile channels, or enlarged lymph nodes founded in the hepatic portal. Preoperative diagnosis is usually bile duct cancer, biliary calculi, biliary ascariasis, or lymphoma. Except for obstructive jaundice, eosinophilia and increased IgE levels is also observed in the present case, and which relieved with the remission of the disease. Recently, Ji et al. [12] reported that Cryptococci infections in children patients often have the varying degree of increased eosinophil cells and IgE, and the increase of peripheral blood eosinophil cells may be the characteristics of the early or acute stage in *Cryptococcus neoformans* children patients or disseminated cryptococcosis immunocompetent host, and these can be used as improved cryptococcosis and repeated a hint. The exact mechanism of eosinophilia is not clear, it may be allergy caused by some specific cryptococcal capsular components, such as: capsular polysaccharide, glucose mannopyranose [13—15].

This patient has obviously jaundice, cachexia, poor development, severe anemia, huge spleen reaching pelvic cavity, and poor operation condition at admission. The life-threatening may occur, if correct diagnosis cannot bet gotten. So for low immunity or young patients with obstructive jaundice, eosinophilia and increased IgE levels, biliary cryptococcal infection should be suspected. *Cryptococcus neoformans* antigen, blood culture, bone marrow culture, and bile culture obtained by percutaneous transhepatic biliary drainage should be evaluated.

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