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CASE REPORT

AIDS cholangiopathy: A case report and review of relevant literature

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Abstract
AIDS cholangiopathy is a syndrome that occurs in HIV/AIDS with advanced immunosuppression. It is characterized by obstruction of the biliary tree by opportunistic infection and may have complications including hepatic failure. Patients with this condition may have increased risk of poor outcome from opportunistic infection. Antiretroviral therapy is key to preventing this condition. Due to the paucity of literature on childhood AIDS cholangiopathy with the advent of antiretroviral therapy, a case of AIDS cholangiopathy is described and relevant literature is reviewed.

Background

Hepatobiliary disease in HIV infection is common, occurring in more than half of patients with HIV infection.[1,2] This may occur due to direct effects of HIV itself, opportunistic infection in immunosuppressed persons, co-infection with hepatitis B or C, HIV-related malignancies, antiretroviral medications or medications used to treat associated opportunistic infection. One pathology observed in patients with advanced immunosuppression is AIDS cholangiopathy. This is a syndrome characterized by biliary tree obstruction and associated liver injury. In the pre-antiretroviral therapy era, this was present in about 26-46% of patients with AIDS.[1] Many cases have been reported in adults since the first published case in 1983,[3] but remarkably less literature exists for paediatric cases. This condition follows biliary tree infection and inflammation from opportunistic infection, mostly *Cryptosporidium parvum*, *Cytomegalovirus* (CMV), *Histoplasma capsulatum, Microsporidia* and in some cases *Mycobacterium*

avium complex.[1,4] Chronic inflammation from these agents may lead to biliary tract strictures followed by cholestasis. CMV may also lead to vascular injury causing ischaemia of the biliary tree.

Typical symptoms on presentation are right upper quadrant pain, fever and diarrhoea. Less common signs and symptoms include jaundice and vomiting. This typically presents in patients with an absolute CD4 count <100 cells/uL.[5,6] The signs and symptoms may overlap with those of multiple pathologies in advanced HIV/AIDS.

With the advent of antiretroviral therapy, the occurrence of AIDS cholangiopathy has decreased.[5,7] Most of the literature on this pathology is in adults, hence there is a dearth in knowledge of this syndrome for children with HIV infection. In this report a paediatric case is described and relevant literature reviewed.

Case report

An eight-year-old boy was hospitalized at a tertiary hospital in Malawi with a five-day history of right upper quadrant abdominal pain, vomiting, diarrhoea and fever. There was no haematemesis. A fortnight prior to this he had been discharged from hospital where he was hospitalized with diagnoses of severe malaria and presumed sepsis. On this prior hospitalization he was identified as a patient with HIV infection who had defaulted antiretroviral therapy (ART) and treatment for possible tuberculosis (TB) two years prior. On discharge from hospital, TB treatment and ART were recommenced.

Physical examination on rehospitalization revealed jaundice, fever, right upper quadrant abdominal tenderness and hepatosplenomegaly. There were no signs of increased effort of breathing or any features of respiratory failure. Due to concerns of drug induced hepatitis from ART and TB treatment, these medications were halted. Abdominal ultrasound revealed hepatosplenomegaly, mild ascites and thickened common bile duct and gall bladder wall with gall sludge but no dilatation of extrahepatic or intrahepatic ducts. Broad spectrum antibiotics were administered due to differential diagnosis of sepsis and possible cholangitis.

The full blood count showed a haemoglobin of 4.4g/dL, MCV 77.9 fL (71-95), a white cell count of 14,300 cells/uL and a platelet count of 95,000 cells/uL. A blood transfusion was administered for the anaemia. Hepatitis B and Hepatitis C serological tests were negative. The liver function chemistry tests are reported in Table 1. The trend of initial and follow up liver function tests is shown in table 1, with a trend reflecting cholestatic liver disease. Serum renal function chemistry tests were normal on hospitalization.

Table 1. Liver function tests results

Date (DD/MM)	15/09	20/09	26/09
ALP (normal age range: 42-98 u/L)	215.7	460	495
GGT (normal age range: 8-78 u/L)	41.7	233	291.5
TB (normal age range: <2.0 mg/dL)	4.8	22.5	25.7
DB (normal age-range: 0.2-0.5 mg/dL)	3.7	-	16.3
AST (normal age range: ≤ 35 u/L)	122.4	-	24.1
ALT (normal age range: ≤ 45 u/L)	23	-	7.8
Albumin (normal age range: 3.9-5.0 mg/dL)	1.9	1.6	1.8

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; DB, direct bilirubin; GGT, gamma-glutamyl transferase; TB, total bilirubin

With an assessment of obstructed jaundice, a repeat abdominal ultrasound was performed with reported findings similar to the initial scan. In the second week of hospitalization, he developed increased effort of breathing requiring administration of oxygen via nasal prongs to maintain optimal peripheral oxyhaemoglobin saturation. The patient had a clinical course of progressive signs and symptoms of jaundice, right upper quadrant pain, fever and development of oedema. In week two of hospitalization, with increasing features of cholestatic liver disease and having previously defaulted ART, AIDS cholangiopathy was suggested as a diagnosis.

Due to the worsening abdominal pain, non-steroidal anti-inflammatory medications were commenced. Clinically the jaundice abdominal pain and oedema continued to worsen accompanied by the development of acute renal failure (Urea 234 mg/dL (20-40). A clinical diagnosis of hepatorenal syndrome was made. The patient eventually died following the development of respiratory failure, confusion and progressive depression in level of consciousness. At the time of death neither TB treatment nor ART had been recommenced. The patient died within week two of hospital stay prior to performing microbiological tests for common causes of AIDS cholangiopathy. An autopsy was not performed, and the patient died within two days of the clinical diagnosis of AIDS cholangiopathy.

Discussion

Hepatobiliary disease is common in HIV/AIDS.[2] One such
disease is AIDS cholangiopathy. This occurs in cases of advanced HIV/AIDS immunosuppression and is associated with opportunistic infections of the gastrointestinal tract,[1] most notably *Cryptosporidium parvum* and CMV.[5,7] Chronic inflammation, epithelial apoptosis, opportunistic infection related dysfunction of the sphincter of oddi and ischaemic injury results in biliary tree strictures in turn leading to biliary obstruction and cholestatic liver damage and failure.[1,5] Long-term biliary epithelial inflammation may lead to dysplastic changes. AIDS cholangiopathy patients have increased risk of morbidity and mortality due to associated opportunistic infections and liver failure.

A diagnostic approach towards AIDS cholangiopathy is based on clinical suspicion, deranged serum liver function tests reflecting cholestatic liver disease chemistry tests and imaging.[1,5] Imaging modalities to reflect features of this pathology include ultrasonography, computerized tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP). These imaging investigations may reveal patterns of multifocal strictures and segmental dilatation of the biliary tree with patterns that may further be categorized into papillary stenosis, intrahepatic and/or extrahepatic sclerosing cholangitis or common bile duct stricture.[5] The spectrum of AIDS cholangiopathy ranges from asymptomatic to symptomatic cases. The symptoms of severe abdominal pain are typically associated with papillary necrosis whilst mild to moderate abdominal pain occurs with sclerosing cholangitis.[5,8]

Our case patient had clinical features of right upper quadrant abdominal pains, fever and vomiting in the context of advanced HIV/AIDS secondary to defaulting ART. In the advent of ART, cases of AIDS cholangiopathy are seen in cases of poor ART adherence, ART resistance or ART naïve patients.[1] Laboratory investigations reflected cholestatic disease, whilst abdominal ultrasound imaging did not reveal the typical features of this pathology. Ultrasound is typically recommended as the first line imaging modality to identify any abnormalities. CT abdomen was not possible for this patient due to CT equipment failure at that time. MRCP and ERCP imaging of the biliary tree is not available at the facility where the patient was hospitalized hence this was a limitation in the assessment of this patient. However the clinical and laboratory test results were suggestive of AIDS cholangiopathy.

AIDS cholangiopathy has limited therapeutic success with medical therapy. Treatment for *Cryptosporidium parvum*, CMV or other opportunistic aetiological agents has limited to no effect on this condition.[5] Surgical interventions such as endoscopic sphincterotomy have been reported to decrease pain and reduce biliary dilatation. Unfortunately, such surgical interventions are seldomly available in low income and medium income countries which simultaneously have high HIV infection rates. Ursodeoxycholic acid is recommended for improving symptoms and liver function test derangements in cases with intrahepatic cholestasis.[1] The key medications demonstrated to prevent and

reduce the clinical picture of AIDS cholangiopathy is ART. Despite reducing clinical and laboratory features of disease, ART does not reverse sclerosing cholangitis that has already developed.

AIDS cholangiopathy is associated with high mortality.[1] This may be due to cholestatic liver failure or the co-existence of opportunistic infections in advanced HIV/AIDS. With biliary obstruction superimposed bacterial cholangitis may develop.[9] In this patient, sepsis or other opportunistic infections possibly led to the decompensation and demise. Possible sepsis and/or the administration non-steroidal anti-inflammatory medications may have contributed to the in hospital development of hepatorenal syndrome, a challenging complication with high morbidity and mortality rates which may be triggered by intravascular volume contraction, sepsis and nephrotoxic medications.[10]

AIDS cholangiopathy is challenging pathology developing in advanced HIV/AIDS immunosuppression secondary to opportunistic infection in the hepatobiliary tree. Recognition of this condition in ART naïve or poorly ART adherent HIV infected patients is prudent. With limited chance of improving outcome of this by treating associated opportunistic infections, early ART commencement and adherence remain key in preventing morbidity and mortality in patients with AIDS cholangiopathy and other hepatobiliary diseases in HIV/AIDS.

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