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RESEARCH ARTICLE

A brief review of current HIV infection and hepatopancreaticobiliary pathology

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Potent antiretroviral therapy (ART) has been associated with a significant reduction in morbidity and mortality among patients with human immunodeficiency virus (HIV). However, individuals with advanced immunosuppression are still at risk for hepatobiliary complications, such as acalculous cholecystitis and acquired immunodeficiency syndrome (AIDS)-related cholangiopathy.[1]

Additionally, patients on ART may experience adverse events related to the treatment, such as lactic acidosis, hepatic steatosis, and drug-induced hepatotoxicity. Many of these patients are also co-infected with hepatitis B or C viruses due to shared transmission routes.

As HIV patients live longer, the incidence of HIV-related malignancies has increased relative to the general population. Cancer-related deaths now account for a growing proportion of overall deaths among individuals with HIV, including a notable rise in hepatocellular carcinoma associated with viral hepatitis.[2]

The initial evaluation of HIV patients presenting with symptoms or signs of hepatobiliary disease should focus on determining the presence of intrahepatic and/or extrahepatic disease. The clinical presentation will guide the selection of appropriate laboratory tests and radiographic studies.

Right upper quadrant pain, with or without jaundice, can indicate various conditions, including HIV cholangiopathy, papillary stenosis, acalculous cholecystitis, cholelithiasis/choledocholithiasis, or drug-induced liver injury. While choledocholithiasis may present similarly, it usually results in a less pronounced elevation in alkaline phosphatase levels and greater aminotransferase levels.

Non-alcoholic fatty liver disease

Similar to the general population, the prevalence of non-alcoholic fatty liver disease (NAFLD) has risen significantly among HIV patients, with studies indicating incidence rates exceeding 30%. NAFLD is now the most common form of liver disease in this group. HIV patients may be at a higher risk for hepatic steatosis compared to those without HIV.[3,4] Furthermore, patients with HIV may experience liver injury induced by antiretroviral drugs or medications used to manage related conditions. Studies have demonstrated that HIV patients with chronic viral hepatitis and baseline elevations in aminotransferases are at a higher risk of ART-induced hepatotoxicity compared to those with HIV who do not have hepatitis B or C.[5]

Gallstone disease

Symptoms of gallbladder stones typically appear three to four years after starting an antiretroviral drug, with a range from one to 90 months. Complications associated with gallbladder stones include cholecystitis in 11 patients, cholangitis in one patient, and acute pancreatitis in four patients. Gallstone disease in sub-Saharan African populations is rarely investigated. Collectively, some studies suggest that HIV patients on ART exhibit altered hepatic regulation of cholesterol-metabolizing genes, leading to reduced cholesterol scavenging and increased cholesterol efflux.[6] Atazanavir has been associated with complicated cholelithiasis. In a study including 14 HIV patients on an atazanavir-based antiretroviral regimen, eight individuals had significant concentrations of atazanavir detected in their biliary stones.[7]

The incidence of metabolic disorders in settings with a high prevalence of HIV is a significant burden in developing countries. HIV infection and ART can alter cholesterol and fat metabolism, potentially leading to complications such as cholelithiasis. Among black South African women living with HIV, the age at onset of gallstone disease was significantly lower, and fewer women were obese compared to HIV-uninfected women with gallstone disease. These findings differ from gallstone risk factors observed in other populations and HIV-uninfected black South African women. This discrepancy may be attributed to the metabolic changes induced by HIV itself or the long-term use of ART. Larger cohort studies are needed to understand better the role of HIV and ART in the development of cholestatic diseases.[8]

Cholangiopathy

HIV cholangiopathy is a condition marked by biliary obstruction due to infection-associated strictures of the biliary tract. It is typically observed in patients with a CD4 count below 100 cells/µL. Before the introduction of effective ART, HIV cholangiopathy was found in a quarter of AIDS patients. The incidence of this condition has decreased with improved HIV treatment, but the current rate remains uncertain.

Liver cirrhosis

HIV infection accelerates the progression of hepatitis C virus (HCV)-related liver fibrosis, with lower CD4 counts being

associated with a faster rate of fibrosis progression. It has also been reported that hepatocellular carcinoma (HCC) tends to develop at a younger age and after a shorter duration of HCV infection in patients co-infected with HIV and HCV compared to those with HCV infection alone. This suggests that HIV infection may accelerate liver fibrosis and carcinogenesis, particularly in co-infected patients with CD4 counts below 200 cells/mm^3.[9]

High prevalence rates of liver cirrhosis and periportal fibrosis have been observed among adults co-infected with HIV and hepatitis B virus (HBV). In one of the first HCC screening initiatives in sub-Saharan Africa, 2% of patients co-infected with HIV and HBV had significant liver lesions. Additionally, one-quarter of the screened patients showed findings suggestive of schistosomiasis-induced liver damage.[10]

Chronic pancreatitis

HIV-infected patients with chronic pancreatitis, compared to non-infected patients with the same condition, tend to be significantly younger, even though they share similar risk factors. This suggests that HIV infection may contribute to an earlier onset of chronic pancreatitis in the presence of established risk factors. Chronic pancreatitis should be considered in the differential diagnosis for patients with persistent non-infective diarrhoea or steatorrhoea. Notably, fewer HIV-infected patients with chronic pancreatitis had diabetes mellitus, despite the duration of chronic pancreatitis being similar between the two groups. This difference might indicate a distinct pathological process affecting the islet cells in HIV-infected patients compared to non-infected individuals.[11]

Conclusion

HIV-endemic populations exhibit a higher incidence of metabolic disorders, as both HIV and its treatment are associated with altered lipid and cholesterol metabolism. Patients with HIV and severe immunosuppression are at risk for HIV cholangiopathy and opportunistic infections, which can lead to significant hepatobiliary diseases. Additionally, due to shared routes of transmission, individuals with HIV are also at increased risk for hepatitis B and C infections. These infections are significant causes of morbidity and mortality, often leading to complications such as decompensated cirrhosis and hepatocellular carcinoma.

Patients with HIV, chronic viral hepatitis, and baseline elevations in aminotransferases are at a higher risk of developing ART-induced hepatotoxicity compared to those with HIV without hepatitis B or C. Moreover, HIV infection appears to accelerate liver fibrosis and carcinogenesis, resulting in hepatocellular carcinoma developing at a younger age and after a shorter duration of HCV infection in patients co-infected with HIV and HCV compared to those with HCV alone.

HIV and ART increase the risk for many hepatobiliary and pancreatic pathologies, such as acalculous cholecystitis, cholelithiasis, choledocholithiasis, HIV cholangiopathy, papillary strictures, chronic pancreatitis, drug-induced liver injury, and malignancies. While ART has extended the lifespan of patients with HIV, it has also led to a higher prevalence of morbidity and mortality due to HIV-related malignancies compared to those who are not infected with HIV.

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