# Vanishing bile duct syndrome secondary to anti-retroviral therapy in HIV

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Vanishing bile duct syndrome (VBDS) is an important cause of jaundice, and results from destruction of bile ducts in the liver. However, this syndrome is rare in patients with human immunodeficiency virus infection. Nevirapine, an anti-retroviral that is being increasingly used, was implicated as the cause of VBDS in a patient described in a recent report.

Vanishing bile duct syndrome (VBDS) refers to a group of disorders characterized by destruction and disappearance of intrahepatic (inside the liver) bile ducts. Multiple causes have been identified including infections, malignancies, autoimmune conditions and adverse effects of medications. The usual course of this condition is variable and many patients with VBDS respond to treatment of the underlying condition and/ or removal of the offending agent. However, others progress to cirrhosis and end stage liver disease requiring liver transplantation.

VBDS is rare in patients with HIV infection, and only one case has been reported in the literature, that of an HIV patient with advanced disease and cytomegalovirus infection. In addition, there are no reports of nevirapine, an anti-retroviral (anti-HIV) drug causing VBDS even though hepatotoxicity is an important side effect of the drug.

A case report to be published on July 14, 2010 in the World Journal of Gastroenterology describes VBDS secondary to nevirapine use in an HIV-positive, pregnant female. The patient received care at the University of Texas, Memorial Hermann Hospital and the Texas Liver Center in

Houston by Dr. Rajan Kochar and colleagues. A 28-yr-old African American female in the 3rd trimester of pregnancy presented to the emergency room with jaundice and itching for 3 days. She also complained of pruritus, light colored stools and dark urine. She was diagnosed with HIV infection in 2000 and had not been on highly active anti-retroviral therapy (HAART) since 2003, but recently started triple drug therapy to minimize risk of vertical transmission with zidovudine, lamivudine and nevirapine 4 wk prior to presentation. She had no history of any opportunistic infections and was not taking any prophylactic medications. Liver tests were abnormal and after liver biopsy was performed, a diagnosis of vanishing bile duct syndrome (VBDS) was made. Liver transplant evaluation was subsequently initiated for the patient.

The most likely cause of VBDS in this patient was drug-induced liver injury (DILI). Nevirapine, a non-nucleoside reverse transcriptase inhibitor, is being increasingly used in pregnant patients owing to its favorable side effect profile and lower teratogenicity compared to protease inhibitors. However, hepatotoxicity is the major adverse effect of nevirapine (5%) and most often manifests as a hypersensitivity reaction with fever, rash and elevated liver tests within the first few weeks of therapy. Late onset hepatotoxicity after several weeks of nevirapine use has also been described in several cases and may be an idiosyncratic reaction to the drug. Although several case reports have demonstrated a cholestatic pattern of nevirapine toxicity, VBDS has never been reported. Ms. B did not have fever and rash, but had evidence of cholestatic hepatitis and a temporal association between nevirapine use and development of biochemical abnormalities. Therefore, nevirapine toxicity was felt to be the most likely cause of cholestasis and VBDS.

To the best of the authors' knowledge, this is the first reported case of nevirapine induced cholestatic hepatitis in a patient with HIV leading to

severe ductopenia and VBDS. Therefore, VBDS should be considered in all HIV patients with chronic cholestasis, especially those with a history of nevirapine use. In addition, the possibility of this potentially irreversible adverse event should be kept in mind before making the decision to prescribe nevirapine.

**More information:** Kochar R, Nevah MI, Lukens FJ, Fallon MB, Machicao VI. Vanishing bile duct syndrome in human immunodeficiency virus: Nevirapine hepatotoxicity revisited. World J Gastroenterol 2010; 16(26): 3335-3338
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