Vanishing bile duct syndrome in HIV infected patients: a case series

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Background

Vanishing bile duct syndrome (VBDS) is a rare acquired disorder associated with progressive destruction and disappearance of intrahepatic bile ducts and ultimately cholestasis. The diagnosis is made on histology.

''Ductopenia'' refers to the absence of interlobular bile ducts from within the portal and exists when there is loss of interlobular bile ducts in more than 50% of portal tracts.

Multiple aetiologies have been identified including infections, neoplastic disorders, autoimmune conditions and drugs. In HIV negative patients the commonest causes of VBDS in published case reports are drugs and Hodgkin lymphoma.

The condition is rare in HIV with only 4 published case reports by the end of 2012, with 3 further case reports this year. The case reports attributed VBDS to:

•Drugs (3) – 2 cases[1,2] there was a temporal relation to starting HAART with the development of symptoms and 1 case[3] a combination of HAART, antibiotics and NSAIDs were implicated.

•Cytomegalovirus infection (2) – all cases[4,5] presentation was with jaundice and abdominal pain. Both were immune suppressed (CD4 count < 200 cells/uL) with evidence of CMV infection

•Malignancy (2) – 1 case[6] initially thought to be related to ART toxicity, autopsy confirmed Hodgkin lymphoma. 1 case[6] presumed lymphoma based on histology

6 of the 7 cases the outcome was death within weeks of presentation.

We report the first case series of VBDS in HIV-1 infected patients

Methods

Case notes and electronic patient records were reviewed of patients known to have a histological diagnosis of VBDS

Results

Five patients were identified, all male. All presented with symptoms of cholestatic jaundice. There was no evidence of cholangiopathy on magnetic resonance imaging. Biopsy of their livers demonstrated cholestasis with severe ductopaenia (figures 1 & 2).

•The initial liver biopsy in patient A demonstrated features of VBDS; a second biopsy was done 15 months later as his symptoms did not improve which revealed Hodgkin lymphoma.

•Patient B presented with jaundice, weight loss and cervical lymphadenopathy. A lymph node biopsy revealed Hodgkin lymphoma. He was initially managed with chemotherapy (ABVD). He was referred to King's as he had persistently raised bilirubin. He went on to have a liver transplant with resolution of symptoms.

•Patient C had poor adherence with uncontrolled HIV viraemia. Histology revealed features of early VBDS (figure 2). He has been lost to follow up.

•In patient D the initial aetiology for VBDS was Darunavir toxicity. He has subsequently developed features suggestive of lymphoma and is awaiting a lymph node biopsy.

•Patient E the aetiology for VBDS is unknown.

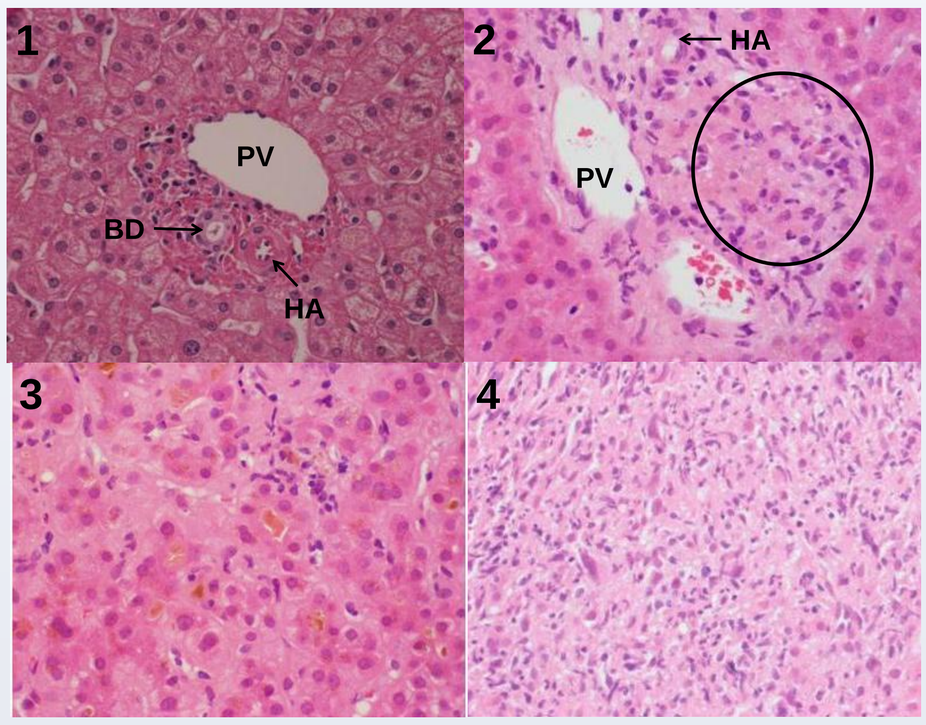
•All patients with the exception of patient E had chronic HIV infection with features of immune suppression with or without detectable HIV viraemia.

•Compared to the literature in HIV more of our cases were unrelated to drug exposure.

Conclusion

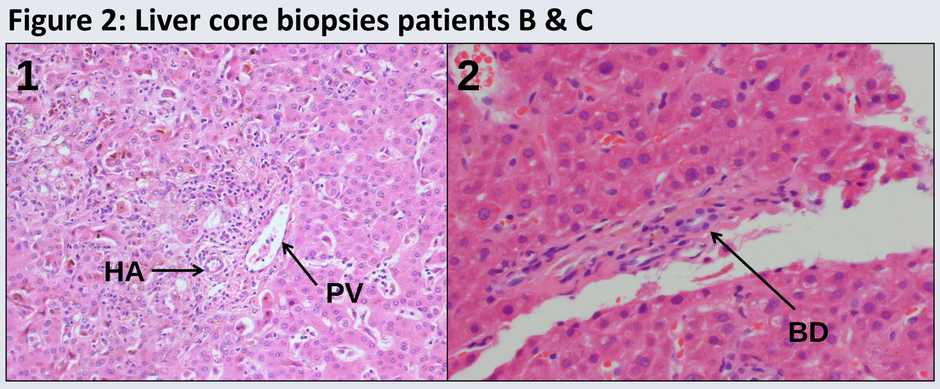
In HIV-1 infected patients who present with cholestasis and normal intrahepatic bile ducts on imaging, a diagnosis of VBDS should be considered. Early biopsy needs to be performed to establish a diagnosis. Lymphoproliferative malignancy and drugs are the commonest associations in our series.

Figure 1: Liver core biopsies normal (1) & patient A (2,3,4)



1- Portal tract from normal liver for comparison; 2- Chronic inflammation and absence of bile ducts as circled; 3- Cholestasis; 4- focal infiltration by crushed large lymphoid cells, consistent with Hodgkin lymphoma.
(HA- hepatic artery; PV- portal vein; BD- bile duct)

Figure 2: Liver core biopsies patients B & C



1- Explant liver of patient B demonstrating an absence of bile ducts. 2- Severe lobular cholestasis with bile duct damage and neutrophilic inflammation, early VBDS in patient C

Table 1: Characteristics of patients with VBDS

	A	B	C	D	E
Age	49	45	28	51	42
Ethnicity	Black	White	Black	Black	Black
Nadir CD4	75	Unknown	7	171	Unknown
Duration of HIV prior to presentation/ years	4	2	7	2	<1
CD4 at presentation	210	106	13	585	570
VL at presentation	<40	<40	67169	<40	6735
HAART regimen prior to presentation	Atripla / 4 years	Atripla / 3 years	Atripla / 3 years	Darunavir / <1 year	Naive
Adherence	Good	Good	Poor	Good	Poor
Evidence of Ebstein Barr virus viraemia	Yes	Yes	Yes	Yes	Not done
Aetiology	Hodgkin Lymphoma	Hodgkin Lymphoma	EBV driven process	?Lymphoma	Unknown
Management	Interruption and change of HAART	Chemotherapy, liver transplant	Steroids	Interruption and change of HAART	Started HAART
Outcome	Liver failure and death	Alive, normal liver function tests	Alive, abnormal liver function tests	Symptomatic improvement, abnormal liver function tests	Alive, improvement, abnormal liver function tests

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