• 45/M
• Homosexual
• Diagnosed to have AIDS since 1997
• Started on HARRT since 1999 with Lamivudine, Stavudine and Nelfinavir
• Changed to Lamivudine, Didanosine and Nevirapine since 2002 due to drug-related diarrhoea and lipoatrophy
In 2003, noted to have persistently elevated ALP (163 – 352 IU/L) and GGT (168 – 650 IU/L) levels

- ALT and Bilirubin normal
- No history of prior liver disease or excessive alcohol intake
- HBsAg, anti-HCV, HBV DNA, HCV RNA all negative
- Autoimmune markers (ANA, ASMA, AMA, Ig pattern) negative
- Serum ceruloplasmin, iron saturation and ferritin all negative
• Echocardiogram: no cardiac cause of liver cirrhosis
• Ultrasound showed mildly enlarged liver with coarsened echotexture, patent hepatic and portal veins, and mild splenomegaly measuring 13cm in length
• In 2006, Didanosine was stopped as patient developed drug-related acute pancreatitis
• HIV infection was then controlled with Lamivudine, Abacavir and Nevirapine
• In February 2011, patient developed fresh hematemesis
• OGD showed presence of grade III esophageal varices with stigmata of recent haemorrhage
• Variceal bleeding was controlled with repeated endoscopic band ligations
• ALP and GGT levels remained persistently elevated 5 years after stopping Didanosine
• Spleen was further enlarged to 16cm by ultrasound reassessment
• HIV RNA was undetectable
• CD4 count remained low (85/mm³) as a result of hypersplenism
• Transient elastography measured by Fibroscan showed a stiff liver with fibroscore 12.0 kPa
• Liver biopsy performed
• Characteristic dense fibrotic septa and nodules in liver cirrhosis were not seen
• Multiple densely fibrotic portal areas with small or absent portal venous branches were identified
• Herniations of portal vein branches into adjacent liver parenchyma
• Features of nodular regenerative hyperplasia, viral inclusion bodies or hepatic granuloma were not seen
DIDANOSINE-INDUCED LIVER INJURY LEADING TO DEVELOPMENT OF HEPATO-PORTAL SCLEROSIS AND NON CIRRHOTIC PORTAL HYPERTENSION
NON-CIRRHOTIC PORTAL HYPERTENSION
• Features of portal hypertension (clinical, radiological or endoscopic) in the absence of cirrhosis on liver biopsy
• Main pathological findings located in the portal venous system
• Hallmark histopathological features are portal fibrosis and nodular regenerative hyperplasia (NRH)
<table>
<thead>
<tr>
<th>Presinusoidal causes</th>
<th>Sinusoidal causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncirrhotic portal fibrosis</td>
<td>Alcoholic hepatitis</td>
</tr>
<tr>
<td>Idiopathic fibrosis</td>
<td>Hypervitaminosis A</td>
</tr>
<tr>
<td>Hepatoportal sclerosis</td>
<td>Incomplete septal fibrosis</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Nodular regenerative hyperplasia</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Methotrexate hepatotoxicity</td>
</tr>
<tr>
<td>Primary or secondary biliary cirrhosis</td>
<td>Syphilis</td>
</tr>
<tr>
<td>Sclerosing cholangitis</td>
<td>Postsinusoidal causes</td>
</tr>
<tr>
<td>Peliosis hepatis</td>
<td>Hepatic vein thrombosis</td>
</tr>
<tr>
<td>Hepatic arterioportal fistula</td>
<td>Veno-occlusive disease</td>
</tr>
<tr>
<td>Myelofibrosis</td>
<td></td>
</tr>
<tr>
<td>Toxic substances and drug hepatotoxicity (arsenic and azathioprine)</td>
<td></td>
</tr>
<tr>
<td>Partial nodular transformation</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from [22].
Chronic exposure to arsenic or vinyl chemicals may result in histological findings resembling hepatoportal sclerosis.

Vitamin A toxicity, methotrexate, 6-mercaptopurine and azathioprine may also result in a clinical picture of NCPH.
Autoimmunity theory

- Autoimmune diseases (especially connective tissue diseases) increases the prevalence of NCPH in certain patient groups
- Most important NCPH associated diseases are mixed connective tissue disease, systemic sclerosis and systemic lupus erythematosus
Proposed theory
1. Vasculitis of intrahepatic arteries leading to secondary portal venous obliteration and thrombosis of adjacent portal veins
2. Anti-phospholipid Ab may play a pathogenic veno-occlusive role in pathogenesis of NRH
Infection theory

- Chronic exposure to antigenemia of intestinal origin may result in mild portal inflammation.
- With repetitive antigenemia, these successive inflammatory reactions in portal tracts may trigger the pathological changes to eventually result in NCPH.
Repetitive micro-thrombosis theory

In the very early stage, clinically undetectable micro-thrombosis in the small intrahepatic branches of the portal vein eventually result in periportal fibrosis-like reconstruction.

Disease then become evident when portal hypertension develops, either as splenomegaly or variceal bleeding.

In the very late stage, overt portal vein thrombosis in major branches is observed.

Prevalence of thrombophilic factors is also found to be increased in NCPH population.
Genetic theory

• In 1987, Sarin et al found association of a high degree of HLA-DR3 aggregation in family members with NCPH.
• In 2005 and 2006, 2 case reports associated NCPH with a genetic syndrome called Adams-Oliver syndrome.
Figure 1  Our proposed theory about etiopathogenesis of idiopathic portal hypertension.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Examples</th>
<th>Mechanisms/other features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic/Connective tissue</td>
<td>Rheumatoid arthritis, Systemic lupus erythematosus, Systemic sclerosis,</td>
<td>Portal veins damaged as “bystander effect”, secondary to hepatic arteritis. Anti-phospholipid antibodies may predispose to small portal vein thrombosis.</td>
</tr>
<tr>
<td>tissue diseases</td>
<td>Polyarteritis nodosa, Wegener’s granulomatosis</td>
<td></td>
</tr>
<tr>
<td>Haematological diseases</td>
<td>Myeloproliferative and lymphoproliferative diseases</td>
<td>May reflect underlying thrombotic tendency. Also associated with Budd-Chiari syndrome. Anti-retroviral drugs may cause toxic endothelial injury. Protein S deficiency also occurs in HIV-positive patients. Some cases have progressed to liver transplantation.</td>
</tr>
<tr>
<td>Immunodeficiency syndromes</td>
<td>HIV/AIDS, Other (e.g. common variable immunodeficiency)</td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td>Azathioprine, Oxaliplatin, 6-Thioguanine, Other chemotherapeutic agents</td>
<td>Drug-induced endothelial injury. Overlap with “sinusoidal obstruction syndrome” and “veno-occlusive disease”.</td>
</tr>
<tr>
<td>Chronic biliary diseases (pre-cirrhotic)</td>
<td>Primary biliary cirrhosis, Primary sclerosing cholangitis, Biliary obstruction</td>
<td>Portal veins damaged as “bystander effect”, secondary to bile duct injury. In cases with combined features of chronic biliary disease and portal venous insufficiency, primary event may be difficult to determine. IgA anti-cardiolipin antibodies derived from damaged intestine in coeliac disease may predispose to small portal vein thrombosis. Possible mechanisms include previous rejection, drug toxicity, irregular regeneration in reduced-sized grafts. Common finding in late-post transplant biopsies. Frequently asymptomatic.</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>Coeliac disease, Ulcerative colitis</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Post-liver transplant</td>
<td></td>
</tr>
</tbody>
</table>
NON CIRRHOTIC PORTAL HYPERTENSION IN HIV
Liver disease in HIV

- Liver disease is a major cause of morbidity and mortality among HIV patients.
- Factors include co-infection with chronic hepatitis C, hepatitis B, alcohol abuse, drug-related toxicity and steatohepatitis.
- Recently, non-cirrhotic portal hypertension (NCPH) and its associated clinical manifestations have been described in HIV-infected patients without viral hepatitis.
- In most case series, it is found to be associated with didanosine (ddI) use.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year published</th>
<th>Study design</th>
<th>Setting</th>
<th>Number of participants</th>
<th>Primary results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saifee et al</td>
<td>2008</td>
<td>Case series</td>
<td>USA</td>
<td>11</td>
<td>Didanosine was the only medication taken by all patients. Eight patients with NCPH had at least one thrombophilic abnormality.</td>
</tr>
<tr>
<td>Maida et al</td>
<td>2008</td>
<td>Case series</td>
<td>Spain</td>
<td>32</td>
<td>HIV-infected patients with elevated ALT and/or significant fibrosis in the absence of any known cause of liver damage were followed Removal of didanosine in 27 patients was followed 12 months later by improvement in clinical and laboratory parameters in 13 (48%) patients</td>
</tr>
<tr>
<td>Kovari et al</td>
<td>2009</td>
<td>Nested case-control</td>
<td>Switzerland</td>
<td>90 (15 cases)</td>
<td>Strong association found between prolonged exposure to didanosine and the development of NCPH (OR 3.4; 95% CI 1.5-8.1)</td>
</tr>
<tr>
<td>Mendizabal et al</td>
<td>2009</td>
<td>Case series</td>
<td>USA, Argentina</td>
<td>6</td>
<td>Didanosine was the most common ART agent used in 4 patients with NCPH, and was the largest association found.</td>
</tr>
<tr>
<td>Vispo et al</td>
<td>2010</td>
<td>Case series</td>
<td>Spain</td>
<td>12</td>
<td>All patients had been treated with didanosine for long periods. This was the only large association found in the report Portal vein obliteration was the most distinctive histological finding in these patients.</td>
</tr>
</tbody>
</table>
Pathogenesis of NCPH in HIV

- NCPH in HIV may result from similar causes to general population
- Increased frequency of NCPH in HIV population supports several factors which tend to concur more frequently in HIV population

  - Exposure to chemotherapeutic agents, mainly purine analogues (e.g. azathioprine, 6-MP, abacavir and didanosine)

  - Thrombophilic abnormalities in HIV-infected individuals, including Protein S deficiency, deficient activity of Protein C, antithrombin III deficiency and factor V leiden mutations

  - Repeated episodes of endothelial portal vein infections, known as pylephlebitis, due to microbial translocation from gut
“Two-hit” model for unexplained NCPH in HIV infected patients

Thrombophilic state → Prolonged antiretroviral exposure (didanosine) → Obliterative portal venopathy

Genetic predisposition? → Translocation of gut bacterial products (MSM) → Portal hypertension
Proposed mechanism of hepatic vascular damage caused by Didanosine

Mitochondrial damage is another potential explanation.

Vascular damage due to Didanosine consumption could persist for a while or be only partially reversible after stopping the drug.

All have DDI or prior DDI exposure

Liver Biopsies revealed no cirrhosis. NRH was found in most cases

<table>
<thead>
<tr>
<th>Author, year of publication</th>
<th>Case definition</th>
<th>Study design</th>
<th>No. of patients</th>
<th>Liver biopsy findings</th>
<th>Proposed risk factors for NCPH or elevated liver enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maida et al, 2006 [5]</td>
<td>Elevated liver enzymes of unknown origin</td>
<td>Case-control (1:1; matched by age, sex, CD4 cell count)</td>
<td>17 with elevated liver enzymes, suspected NCPH in 9 of 17</td>
<td>Biopsy in only 5 of 17; microvesicular steatosis in 5 of 5, mild fibrosis in 3 of 5, cirrhosis in 2 of 5</td>
<td>Prolonged DDI exposure</td>
</tr>
<tr>
<td>Mallat et al, 2007 [6]</td>
<td></td>
<td></td>
<td></td>
<td>NRH in 7 of 8, sinusoidal dilation in 1 of 8</td>
<td>DDI exposure (DDI in 8 of 8)</td>
</tr>
<tr>
<td>Sandrine et al, 2007 [8] (letter)</td>
<td></td>
<td></td>
<td></td>
<td>NRH</td>
<td>Exposure to DDI and NVP</td>
</tr>
<tr>
<td>Garvey et al, 2007 [9] (letter)</td>
<td>Case series</td>
<td>6</td>
<td>NRH in 2 of 6, venous outflow obstruction in 3 of 6, normal in 1 of 6</td>
<td>DDI (in 5 of 6), coagulopathy (in 4 of 6)</td>
<td></td>
</tr>
<tr>
<td>Schiano et al, 2007 [10]</td>
<td></td>
<td></td>
<td></td>
<td>HPS in 4 of 4</td>
<td>NVP (current therapy in 3 of 4); ART history not described</td>
</tr>
<tr>
<td>Maida et al, 2008 [11]</td>
<td>Elevated liver enzymes of unknown origin</td>
<td>Case-control</td>
<td>Biopsy in only 12 of 32; unspecific liver fibrosis in 3 of 12, NRH in 2 of 12, periportal fibrosis in 3 of 12</td>
<td>Prolonged DDI exposure, homosexual transmission modus</td>
<td></td>
</tr>
<tr>
<td>Tateo et al, 2008 [12]</td>
<td>NCPH</td>
<td>Case series</td>
<td>11</td>
<td>NRH in 3 of 3</td>
<td>...</td>
</tr>
</tbody>
</table>

**NOTE.** ART, antiretroviral therapy; DDI, didanosine; HIV, human immunodeficiency virus; HPS, hepatoporal sclerosis; NRH, nodular regenerative hyperplasia; NVP, nevirapine; PH, portal hypertension.
Association of Noncirrhotic Portal Hypertension in HIV-Infected Persons and Antiretroviral Therapy with Didanosine: A Nested Case-Control Study

Helen Kovari,1 Bruno Ledergerber,1 Ulrich Peter,2 Markus Flepp,2 Josef Jost,2 Patrick Schmid,4 Alexandra Calmy,6 Nicolas J. Mueller,1 Beat Muellhaupt,2 Rainer Weber,1 and the Swiss HIV Cohort Study*

**Background.** Noncirrhotic portal hypertension (NCPH) is a newly described life-threatening liver disease of unknown cause in human immunodeficiency virus (HIV)-infected persons. Postulated pathogenesis includes prolonged exposure to antiretroviral therapy, particularly didanosine.

**Methods.** We performed a nested case-control study including 15 patients with NCPH and 75 matched control subjects of the Swiss HIV Cohort Study to investigate risk factors for the development of NCPH. Matching criteria were similar duration of HIV infection, absence of viral hepatitis, and follow-up to at least the date of NCPH diagnosis in the respective case.

**Results.** All 15 case patients had endoscopically documented esophageal varices and absence of liver cirrhosis on biopsies; 4 died because of hepatic complications. At NCPH diagnosis, case patients and control subjects were similar concerning sex; race; Centers for Disease Control and Prevention stage; HIV-RNA level; CD4 cell count nadir; and lipids and lipodystrophy. Differences were found in age (conditional logistic regression odds ratio [OR] for 10 years older, 2.9; 95% confidence interval [CI], 1.4–6.1); homosexuality (OR, 4.5; 95% CI, 1.2–17); current CD4 cell count <200 cells/μL (OR, 34.3; 95% CI, 4.3–277); diabetes mellitus (OR, 8.8; 95% CI, 1.6–49); alanine aminotransferase level higher than normal (OR, 13.0; 95% CI, 2.7–63); alkaline phosphatase higher than normal (OR, 18.3; 95% CI, 4.0–85); and platelets lower than normal (OR, 20.5; 95% CI, 2.4–178). Cumulative exposure to antiretroviral therapy (OR per year, 1.3; 95% CI, 1.0–1.6), nucleoside reverse-transcriptase inhibitor (OR, 1.3; 95% CI, 1.1–1.7), didanosine (OR, 3.4; 95% CI, 1.5–8.1), ritonavir (OR, 1.4; 95% CI, 1.0–1.9), and nelfinavir (OR, 1.4; 95% CI, 1.0–1.9) were longer in case patients. Exposure to nonnucleoside reverse-transcriptase inhibitor and other protease inhibitors were not different between groups. In bivariable models, only the association of NCPH with didanosine exposure was robust; other covariables were not independent risk factors.

**Conclusions.** We found a strong association between prolonged exposure to didanosine and the development of NCPH.
Risk factors for advanced liver fibrosis in HIV-infected individuals: role of antiretroviral drugs and insulin resistance

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SUMMARY. Liver damage may result from multiple factors in HIV-infected patients. The availability of reliable non-invasive tools to measure liver fibrosis has permitted the screening of large patient populations. **Cross-sectional study of all consecutive HIV outpatients who underwent examination by transient elastometry (FibroScan) at one HIV reference clinic during 2007.** Advanced liver fibrosis (ALF) was defined as hepatic stiffness >9.5 kilopascals, which corresponds to Metavir stages F3-F4 in the liver biopsy. A total of 681 consecutive HIV-infected patients (64% injecting drug users; mean age 43; 78% male; 98% on antiretroviral therapy) had at least one valid FibroScan evaluation. ALF was diagnosed in 215 (32%) of them. In the univariate analysis, ALF was significantly associated with older age, low CD4 counts, chronic hepatitis C, past alcohol abuse, elevated ALT, high triglycerides, low cholesterol, high homeostasis model assessment (HOMA) index and exposure to didanosine and/or stavudine. In a multivariate model (OR, 95% CI), chronic hepatitis C (2.83, 1.57–5.08), past alcohol abuse (2.26, 1.37–3.74), exposure to didanosine and/or stavudine (1.85, 1.14–3.01), high HOMA index (1.25, 1.04–1.51), older age (1.09, 1.05–1.14) and elevated ALT (1.04, 1.03–1.06) remained as independently associated with ALF. Therefore, in addition to chronic hepatitis C and alcohol abuse, insulin resistance and/or exposure to dideoxy-nucleosides may contribute to ALF in HIV-infected patients.

**Keywords:** antiretroviral drugs, hepatitis C, HIV, insulin resistance, liver fibrosis, transient elastometry.
FDA Drug Safety Communication: Serious liver disorder associated with the use of Videx/Videx EC (didanosine)

Safety Announcement

The U.S. Food and Drug Administration is alerting healthcare professionals and patient about a rare, but serious, complication in the liver known as non-cirrhotic portal fibrosis (didanosine). Didanosine, an antiviral medication, is used to treat HIV infection and AIDS. Videx EC is a delayed-release version of Videx (didanosine).
Data Summary
FDA's decision to revise the drug label for didanosine is based on post-marketing reports of patients developing non-cirrhotic portal hypertension while using didanosine. Other liver adverse events such as lactic acidosis, hepatomegaly with steatosis, and liver failure have been reported with the use of didanosine alone and in combination with other antiviral drugs.

Of the 42 post-marketing cases of non-cirrhotic portal hypertension in patients using didanosine:
- Twenty-six were males, 14 were females, and in two no gender was specified.
- The ages ranged from 10 years to 66 years.
- Duration of didanosine treatment ranged from months to years before development of non-cirrhotic portal hypertension.
- Definitive cases of non-cirrhotic portal hypertension were confirmed by biopsy and had no alternative etiology for the diagnosis.

Medical interventions described in the reported cases included:
- Banding/ligation of esophageal varices in 8 patients.
- Transjugular intrahepatic portosystemic shunt (TIPSS) procedure in three patients.
- Liver transplantation in 3 patients.

There were four deaths total in the 42 reported cases. The cause of death in the four patients was due to:
- Hemorrhage from esophageal varices in two patients.
- Progressive liver failure in one patient.
- A combination of multi-organ failure, cerebral hemorrhage, sepsis, and lactic acidosis in one patient.

The only patients who have been reported as fully recovered are the three non-cirrhotic portal hypertension patients who received a liver transplant.

A causal association is difficult to determine from postmarketing reports alone. However, based on the number of well-documented cases and exclusion of other causes of portal hypertension such as alcohol-related cirrhosis or hepatitis C, FDA concludes there is an association between use of didanosine and development of non-cirrhotic portal hypertension. Because of the potential severity of portal hypertension, including death from hemorrhaging esophageal varices, FDA has revised the Warning and Precautions section of the didanosine drug label to assure safe use of the medication.
Histopathology

- Most frequent macroscopic finding in HIV-infected patients with NCPH is Nodular Regenerative Hyperplasia (NRH), followed by hepatoportal sclerosis.
- Characteristic portal abnormalities are seen always; paucity of small portal veins being the most frequent findings.
- Lesion of small portal veins characterized by fibrous obliteration with marked thickening of small portal vein wall, along with partial or total occlusion of the lumen (sclerosing portal venopathy) are also seen.
- Focal dilatation of sinusoids and portal fibrosis also frequently reported.
Evolution of changes

Occlusion of small PV branches
(portal vein sclerosis/hepato-portal sclerosis)

- Atrophy of perivenular hepatocytes
- Formation of shunt vessels
  (portal vein ectasia)
- Collapse + passive septum formation
  (? due to superadded PV or HV thrombosis)
  (incomplete septal fibrosis)

- Hyperplasia of periportal hepatocytes
  (Nodular regenerative hyperplasia)
- Sinusoidal dilatation ± congestion
- Severe cases may develop progressive fibrosis/cirrhosis
Nodular Regenerative Hyperplasia (NRH)

- Central portion of nodules are made up of hypertrophied hepatocytes arranged in multi-layer plates
- Cells in periphery are atrophic and arranged in parallel sheets
- Characteristically no fibrosis is seen between nodules
- These findings are easily missed with routine staining and reticulin staining is needed
Hepatoportal sclerosis (HPS)

- Characterized by various degrees of fibrosis and sclerosis of portal vein branches
- May also see marked dilatation of sinusoids - Megasinusoids
- May see herniation of portal veins
Portal vein showing dense fibrous thickening of the wall, centered by central stenotic lumen
Herniation of portal vein branches into liver parenchyma
• The characteristic obstructive portal venopathy identified in HIV-infected patients may also appear superimposed on liver damage resulting from other conditions, such as chronic hepatitis C, fatty liver, alcohol abuse.

• NCPH should be suspected when clinical, laboratory and endoscopic signs of severe portal hypertension appear in patients in whom no or only mild liver parenchymal damage is evident.

• The features of NRH and HPS may appear inconspicuous in routinely processed needle biopsy specimen and findings can easily be overlooked if diagnosis has not been considered.
Clinical features

- Patients generally present with clear signs of portal hypertension and develop repeated episodes of **variceal bleeding** as the most frequent clinical manifestation.
- **Splenomegaly** and consequence of **hypersplenism** (thrombocytopenia) almost always recognizable.
- Development of ascites is almost always a finding of advanced cases.
- Jaundice and hepatic encephalopathy are only very late symptoms.
- Sarin et al. reported that 13.5% of patients had splenomegaly, 84.5% had history of upper GI bleeding, 92% had esophageal varices and 22.3% had gastric varices.
Laboratory features

• Most patients with NCPH had portal hypertension with reasonably well-preserved hepatic synthetic function with normal albumin, bilirubin and prothrombin levels
• Most have a mild elevation of serum ALT and a moderate increase in ALP
• Elevated ALP were identified in 25% of patients with NRH in one study
COMPLICATIONS AND TREATMENT
• No specific therapy for didanosine-related NCPH
• Prophylaxis and management of variceal bleeding and hypersplenism are key aspects in the management of NCPH in HIV-positive patients

• The esophageal varices formed during the course of NCPH have some distinctive features
• The walls are relatively thicker than those in cirrhosis and they rarely harbor red-spots
• The varices are simply dilated veins that rarely complicate, and are relatively easy to treat compared with cirrhosis
• Variceal band ligation, endoscopic sclerotherapy and non-selective β-blockers are effective methods to prevent acute bleeding
• Transjugular intrahepatic portal systemic shunts may be an alternative for patients with variceal bleeding that were refractory to medical and endoscopic treatment
• Liver transplant should only be reserved to those with repeated severe complications of portal hypertension
Is anti-coagulant therapy useful in NRH in HIV-infected patients?

- Treatment of NRH is directed towards elimination of the causative factors
- Long-term anti-coagulation treatment is usually indicated in thrombophilia cases
- As portal vein thrombosis is a frequent complication, benefit of anti-coagulation warrants further investigation
- One case report showed that in a HIV-infected patient with biopsy-proven NRH had a rapid improvement in liver condition and allowed to avoid liver transplant after anti-coagulant therapy with LMWH
- Major bleeding is a concern
Anticoagulant therapy for nodular regenerative hyperplasia in a HIV-infected patient

Florian Bihl¹*, Filip Janssens¹, Francoise Boehlen², Laura Rubbia-Brandt³, Antoine Hadengue¹, Laurent Spahr¹

Figure 2: Evolution of liver function, clinical parameters and selected parameters of haemostasis were shown. Please note the changes at the time of the switch from VKA to LMWH.
SUMMARY
NCPH in HIV patients is a rare (~0.5%) but potentially life-threatening condition. Patients usually present with esophageal varices and splenomegaly. Prolonged didanosine exposure seems to be involved. Inflammatory and thrombotic processes hypothetically triggered by this purine analogue in the hepatic microvasculature might result in this form of obliterative portal venopathy. A typical liver biopsy showed obliteration of portal veins. Physicians should be aware of the diagnosis in didanosine-exposed patients who have unexplained persistent elevation of ALP, splenomegaly or esophageal varices. Early recognition is crucial in preventing irreversible liver damage.
THANK YOU