

Unexplained Severe Portal Hypertension in HIV Patients: A New Clinical Entity?

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Background

- Cases of non-cirrhotic portal hypertension have been reported in HIV-negative patients as result from exposure to adenosine analogues (eg, azathioprine), bacterial infections, trace metals and chemicals, genetic coagulation disorders and/or autoimmune diseases
- More recently, reports of similar cases in HIV-positive individuals have attracted much attention

Severe Liver Disease Associated With Prolonged Exposure to Antiretroviral Drugs

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J Acquir Immune Defic Syndr 2006;42:177–182

Nodular regenerative hyperplasia is a new cause of chronic liver disease in HIV-infected patients

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Anaïs Vallet-Pichard^{a,b,e}, Hélène Fontaine^{b,e},
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Hepatoportal Sclerosis as a Cause of Noncirrhotic Portal Hypertension in Patients With HIV

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Methods

- Description of clinical and histologic findings of all consecutive cases of SPH of unknown etiology seen in HIV patients in 3 outpatient clinics in Spain and Italy

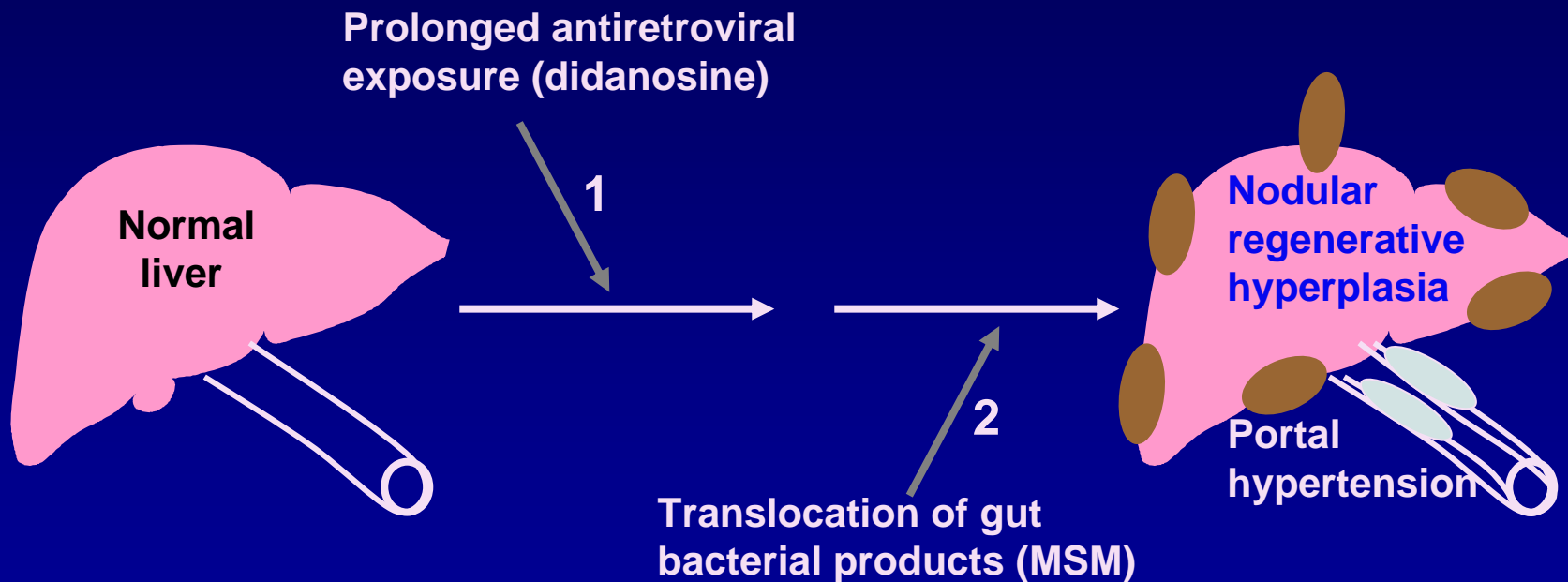
Results

- A total of 13 (31.7%) out of 41 HIV patients with unknown liver disease were diagnosed with SPH
- All had elevated ALT for >12 months and were followed for ≥ 4 years in 3 HIV outpatient clinics in Spain and Italy
- The majority (85%) were male and homosexuals (77%), with a median age of 50 years. The median time since HIV diagnosis was >7.5 years
- All but 1 were on antiretroviral therapy and had undetectable plasma HIV RNA. None had current CD4 counts < 200 cells/mm³, although 4 of them had CD4 nadir < 200 cells/mm³ any time in the past

Results (cont)

- Median time of exposure to antiretroviral drugs in the 12 individuals on HAART was 50.5 months for didanosine, 21 months for stavudine, and 18 months for nevirapine
- During follow-up, 8 patients (61%) experienced complications of SPH, including 6 with upper gastrointestinal bleeding from esophageal varices and 5 portal thrombosis
- A liver biopsy was performed in all subjects; none showed advanced hepatic fibrosis. Main features were as follows: nodular regenerative hyperplasia (31%), perisinusoidal fibrosis (8%), drug-induced hepatitis (8%), NASH (31%), and unspecific lesions (22%)

The “Two-hit” Model for Non-cirrhotic Portal Hypertension in HIV Patients



ddl-associated Liver Damage Overimposed to HCV-related Liver Disease

	Case 1	Case 2	Case 3
Age (years)	41	49	42
Gender	Male	Female	Male
Race	Caucasian	Caucasian	Caucasian
Risk group	IDU	IDU	IDU
HCV genotype	1	1	1
HCV-RNA (IU/mL)	1,380,000	989,000	17,200,000
Current antiretroviral Therapy	Tenofovir+Emtricitabine +Fosamprenavir/Ritonavir	Abacavir+Lamivudine +Atazanavir	Abacavir+Lamivudine +Atazanavir
Prior didanosine exposure (months)	64	30	44
CD4 count (cells/ μ L)	351	168	324
CD4 count nadir (cells/ μ L)	198	250	104
Plasma HIV-RNA (copies/mL)	<50	<50	<50
Liver fibrosis stage (Metavir estimate, KPa)	F2 (9)	F3 (11.5)	F4 (15)
Metabolic disorders	No	No	No

Conclusion

- A small subset of HIV patients may develop SPH in the absence of known predisposing conditions and advanced hepatic fibrosis
- These patients may eventually experience potentially fatal GI bleeding
- Exposure to didanosine seems to be involved in most cases
- A primary injury of the portal vessels by this adenosine analog may play a central pathogenic role in this condition