Reviewer’s report

Title: Dideoxynucleoside HIV reverse transcriptase inhibitors and drug-related hepatotoxicity: a case report.

Version: 2 Date: 14 February 2007

Reviewer: Pablo M Barreiro

I am familiar with the literature and believe that this case meets one of the 7 criteria for evaluation in the journal: Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: No

Comments to authors:

General
Authors describe a patient under HAART that experiences two consecutive episodes of ALT/AST elevations, which seem to resolve upon treatment modification. The lack of data indicating acute or chronic liver infection, nor consumption of other drugs or toxics, allows interpreting it is a case of antiretroviral-related liver toxicity, probably linked to d4T use. The absence of clinical or laboratory data suggestive of lactic acidosis points at liver damage not related with mitochondrial impairment, the usual form of d4T hepatotoxicity.

The availability of liver histology is a strong point of this case. However, we would like to have more data on histologic findings. Foamy degeneration of hepatocytes is pretty unspecific, as it is found in alcoholic live disease, NAFLD and NASH; this issue should be discussed.

Other points to be commented in the Discussion:
- mitochondrial toxicity may not be absolutely discarded, even though lactate levels are not elevated: please provide pH and bicarbonate values; are there data regarding mitochondrial morphology at biopsy?
- so is the case for alcohol abuse (what was gGT value or indirect markers of alcohol abuse?)
- it is also important to know lab data that may indicate metabolic syndrome (cholesterol, triglycerides, glucose) underlying NAFLD. Did the patient have frank lipodistrophy?
- we agree that direct liver injury by stavudine may have happened

Revisions necessary for publication

Abstract. Line 5. Better describe main histologic findings rather than the interpretation of the biopsy.

Page 4. Line 7. Provide doses (mainly d4T and IDV/r)

Page 5. Line 3. Two different ALT elevations have been recorded along the follow-up. The first one seemed to partially resolve upon IDV/r discontinuation, although d4T was still on board. This observation should be commented and interpreted. In fact liver biopsy reflected this first episode of ALT elevation, rather than the second which seemed to resolve after d4T discontinuation.

Page 5. Line 13. Describe histologic findings, rather than the clinical interpretation, which should be left for the discussion. Are electron microscopy data available?

Conclusion: I am not sure that liver biopsy clarified the cause of ALT elevation

What next?: Revise and resubmit

Quality of written English: Acceptable