Reviewer’s report

Title: Hepatotoxicity induced by horse ATG and reversed by rabbit ATG: A case report

Version: 2 Date: 29 May 2007

Reviewer: Phillip Scheinberg

I am familiar with the literature and believe that this case meets one of the 7 criteria for evaluation in the journal: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: No

Is the case report authentic?: No

Is this case worth reporting?: No

Is the case report persuasive?: No

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

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

Comments to authors:

Al-Anazi et al report on a case of a 23-year old female with Fanconi anemia who after receiving horse ATG as part of the conditioning regimen developed an increase in the LFTs which was managed by substituting the horse ATG for the rabbit formulation of ATG. The LFTs decreased in subsequent days and the patient underwent a successful matched sibling hematopoietic stem cell transplantation. The authors report that the effects on the liver by horse ATG were “reversed” by the rabbit ATG which allowed for continuation of the transplant conditioning. Throughout the Discussion the authors point out some of the differences in tolerability and complications with horse and rabbit ATG.

Major concerns:

1) My main issue is that elevations of the LFTs almost always occur following initial horse ATG administration with no significant clinical consequence with continued administration of the drug. It is not infrequent for the ALT and AST to increase 10 or 20 times the upper limit of normal after the first dose which then decreases with subsequent dosing. It is therefore highly likely that the same effects would have been observed with continuation of the horse ATG. Patients with post hepatitis aplastic anemia, for example, are often treated with horse ATG and the liver enzymes almost always decrease after its administration (it is not infrequent to administer horse ATG when the ALT is in the thousands in these cases).

2) The authors suggest that the rabbit ATG “reverses” the liver effects of the horse ATG. Although the mechanism by which the elevation of the LFTs occur following horse ATG is not fully understood, it is very unlikely that the rabbit ATG would “reverse” the process as the 2 drugs have a very similar mechanism of action. The differences between horse and rabbit ATG are more related to the half-life of each drug, affinity for the human T cells and the degree of lymphocytotoxicity. Both drugs contain polyclonal antibodies with varying specificities to the T-cell.

Minor concerns:

3) When the authors refer to the use of ATG in aplastic anemia or in transplantation, the most significant studies should be cited instead of small pilot studies.

4) The authors could summarize the case presentation and discussion highlighting the hepatotoxicity during conditioning (in the case description) and drug effects of ATG in the liver (in the discussion). The authors
should focus on describing the allergic-type reactions in both sections.

5) The discussion of infectious complications following the different forms of ATG is not relevant to the case description.

6) Improvement in the grammar would help with the readability of the manuscript.

Revisions necessary for publication

**What next?:** Reject

**Quality of written English:** Needs some language corrections before being published