Reviewer's report

Title: High frequency of Human Cytomegalovirus DNA in the Liver of Infants with Extrahepatic Neonatal Cholestasis.

Version: 1 Date: 2 June 2005

Reviewer: GIOVANNI NIGRO

Reviewer's report:

General
The subject of the study performed by the authors is interesting, since little is known concerning the relationship between biliary atresia and CMV infection. However, the data are scarce and poorly presented.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
• It is necessary to include a Table showing the time at which bioptic and serum samples were taken from infants with positive CMV DNA in the liver. In fact, the median infants' age at enrolment was ranging between 25 and 239 days. This implies that CMV infection could have acquired perinatally or postnatally. To correlate CMV infection with the development of biliary atresia, it is essential to demonstrate that CMV was acquired prenatally (diagnosis within 3 weeks from birth) or to evidence findings supporting a possible prenatal activity of CMV in the liver like typical histologic changes, high CMV IgG avidity, increasing or persistent IgG titres, decreasing IgM levels.
• Were bioptic and serum samples obtained at the same time or sera were drawn later? If the sera were obtained after the age of 3 months, this could explain the low prevalence of CMV-IgG antibodies, which are highly frequent in Brazilian mothers.
• Were sensitivity and specificity of PCR and serological assays tested? Specificity is essential both for PCR, since 3 infants had hepatic DNA but negative CMV IgG, and for the immunoassay, since 14 infants had CMV IgM. The specificity of the ELISA capture systems is generally suitable, and false positive IgM antibodies are rarely detected. However, checking confirmatory tests should be done.
• Controls are few. In particular, an adequate number of age-matched controls is needed to establish the significance of CMV seropositivity in the infants with biliary atresia.
• The conclusions should be changed: although CMV inclusions were not found in the liver, Table 2 shows that infants with DNA had some histologic findings which may be consequent to prenatal CMV infection of the liver (i.e. fibrosis, giant cells, inflammation). To this regard, a comparative Table on the histologic findings between DNA-positive and DNA-negative infants could be helpful.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
• Abstract: results should be clarified (i.e. the number of infants with positive DNA is not mentioned, while the percentage is indicated); the conclusions should be changed according to the previous observations.
• Serological investigations: ELISA systems were commercial (manufacturer should be indicated) or non-commercial?
• Conclusions: a possible use of antiviral therapy in the infants with CMV infection, and consequent improvement of the outcome, should be mentioned.
Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No

Declaration of competing interests:
'I declare that I have no competing interests'