Reviewer’s report

Title: Emerging (val)ganciclovir resistance during treatment of congenital CMV infection: a case report and review of the literature

Version: 0 Date: 25 Jan 2017

Reviewer: Gail J Harrison

Reviewer's report:

The authors provide a case report of single mutation ganciclovir resistance emerging in an apparently immunologically normal infant with congenital CMV disease who received treatment with oral valganciclovir. The case report provides important information to start the conversation about detection, significance if any, and management emergence of antiviral resistance during treatment for congenital CMV.

Comments for the authors

The statement that the patient was immunologically normal - how did the authors determine this? A general exam? Newborn TRECS screen? Full immunological evaluation of T cell and NK cell numbers and function? The negative CMV antibody responses may reflect natural nadir of maternal IgG antibody and increase in patient antibody, but usually the two overlap and the CMV IgG antibody does not decline to zero. Therefore, did the authors fully evaluate NK cell FUNCTION - as this reviewer has encountered patients with congenital CMV, persistence of viremia, and low to nil CMV gG antibody levels due to NK cell FUNCTION abnormalities that at times are maturational and not permanent. While a full immune evaluation of cellular function is not necessary for publication, it would be of great interest for the authors to complete and or at least comment on this if it was done or not done as supportive evidence of the statement about normal immune function.

State clearly the viral load was one BLOOD. It is assumed, but for clarity please state. If it was urine or saliva, please also site. If additional sights like saliva or urine were also sampled, could the authors also please include those, since CMV is known to compartmentalize.

Do the authors have an explanation for the low to nil ganciclovir levels shown on the Figure well into treatment? Was the valganciclovir oral solution fro the original manufacture or was it compounded? Did the infant have malabsorption? Can the authors comment on this?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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