Reviewer’s report

Title: Bilateral granulomatous panuveitis in two patients with T-cell type of chronic active Epstein-Barr virus infection

Version: 0 Date: 31 Oct 2018

Reviewer: Praveen Balne

Reviewer’s report:

Reviewer's Comments to Authors:

The manuscript entitled "Bilateral granulomatous panuveitis in two patients with T-cell type of chronic active Epstein-Barr virus infection" done by Takahashi et al., reports two well-documented cases of steroid-resistant panuveitis in patients with a rare systemic disorder "Chronic active EBV infection (CAEBV)". The diagnosis of CAEBV was made by clinical presentation, serological, pathological, and molecular investigations. Though both cases were resistant to systemic chemotherapies, the clinical presentation was improved after hematopoietic stem cell transplantation. The article has an important clinical message, should be of great interest to the readers and be considered for publication. However, it needs minor corrections which include the addition of some more case details and grammar checking.

Minor comments:

Case 1:

1. Page 4, line 24: The lymphocytic fraction was isolated from the whole blood using antibody-conjugated magnetic beads. Please provide kit details.

2. Page 4, line 27: The EBV-DNA load was determined to be 1.2 x 10^5 copies of DNA/μg in the whole blood. It should be 1.2 x 10^5 copies/μg DNA in the whole blood. Was EBV-DNA load determined by commercial kit or in-house qPCR? Please provide the manufacturer's details or reference for the in-house qPCR.

3. Page 4, line 31: EBV-DNA was detected in the CD4-positive T-cells in the peripheral blood. Please correct the "positive" spelling and what was the viral load in CD4-positive T-cells?

4. Page 4, line 53: He was being treated with 0.1% betamethasone eye drops which was continued. Please mention the dose.

5. Page 5, line 1: Systemic immunochemotherapy consisting of steroids and cyclosporine was started for the CAEBV. Please provide complete details of the treatment. "Immunochemotherapy" is a single word. Please correct it.
6. Page 5, line 7: His BCVA was decreased to 20/32, and slit-lamp ophthalmoscopy showed mutton-fat keratic precipitates (KPs) and 2+ cells in the anterior chamber and the anterior vitreous of both eyes (Figs. 1A and 1B). Please correct the sentence. Multiple "and"s in one sentence. Please re-write the sentence. Use a comma (,) before any coordinating conjunction (and). In some places, it is missing.

7. Page 5, line 12: The optic disc, fovea, and all of the retinal vessels of the right eye were covered with white infiltrates (Fig. 1C), and several white nodules were seen along the retinal veins and arteries of the left eye (Fig. 1E). Please re-write the sentence.

8. Page 5, line 31: The right anterior chamber was tapped and processed for multiplex PCR with a search for the presence of specific genomic sequences of all 8 types of human herpes viruses. Is it a commercial kit or in-house PCR? If it is a commercial kit, please provide the manufacturer's details or if it is an in-house PCR, please provide the reference for the primers and methodology.

9. Page 5, line 46: Cytokine analysis by enzyme-linked immunosorbent assay (ELISA) revealed that the interleukin (IL)-6 concentration was over 1000 pg/ml, whereas that of IL-10 was below the detectable level. Please provide ELISA kit details.

10. Page 6, line 22: Although EBV-positive T-cells were not eradicated from the peripheral blood, the intraocular inflammation completely disappeared in 8 weeks. Please provide viral load details at 8 weeks.

11. Page 6, line 29: His last BCVA was 20/63 OD and 20/16 OS. Was it at 8 weeks after treatment? When was the last follow-up of this patient? At his last follow up, what was the viral load in AqH?

Case 2:

1. Page 7, line 12: EBV infection of the CD4-positive T-cells and their clonal proliferation were confirmed by the assays. Please mention the name of the assays and its references.

2. Please provide the details and/or references for PCR and ELISA.

3. Page 7, line 34: We treated the patients with 0.1% betamethasone eye drops… how many times a day and each time how many drops? Please provide complete treatment details.

4. Page 7, line 44: Although EBV-positive T-cells were not eradicated from the peripheral blood, the disease became inactive. Please provide the viral load details at last follow-up.

Discussion:
Page 9, line 5: there has been no study... Please correct it to "studies"

Please do crosscheck the manuscript for grammatical mistakes.

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

No

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

Yes

**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

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