Reviewer's report

Title: Evidence for HSV-1-induced pneumonitis in patients under standard immunosuppressive therapy for rheumatic and vasculitic autoimmune disease

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Reviewer: Peter Coyle

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In this well written report, the central question, i.e. the potential for HSV to have a significantly pathogenic role in pulmonary infection in immunocompromised patients is clearly explained. The methods used in the paper are standard clinical investigative procedures and treatment protocols and are reported in a straightforward but comprehensive manner. In fact this is the essence of the paper i.e. to record and account for clinical findings where HSV is the sole or contributory infectious pathogen and then measure outcomes. The findings and their interpretation, and the potential clinical significance of their interpretation are well handled. The paper provides data that both supports the central and treatable role of HSV in respiratory infections in immunocompromised patients but also where treatment was not successful. In the later cases HSV was not the sole pathogen.

While there was no real possibility that this brief clinical case series could produce clear-cut findings, the report highlight the need to have this issue addressed in a more comprehensive manner and add to the evidence base suggestive of an acute role for HSV in pulmonary infection in immunocompromised patients. It also gave treatment schedules that individual physicians might wish to use in similar cases. The data is placed against a background of the conflicting body of literature that surrounds this area.

Some Points for the Authors to address.

1. A total of 4 HSV-1 cases were detected out of 1080 case reviews. How many of the 1080 had respiratory deterioration and how many had HSV tested for in total.

1. In Case 1 and 2, while HSV 1 was the only pathogen detected, only a small number of respiratory viruses were tested for in each case. Those relevant would depend on the time of year for some of these viruses e.g. influenza and RSV in winter; parainfluenza 3 in spring/summer; rhinoviruses all year round. It would therefore be useful to give the time of year that the cases presented. It would also be useful to outline the rationale of the test repertoire e.g. why were adenoviruses tested for but not rhinoviruses etc. In many cases there is little rationale for this selection but a mere reflection of laboratory practice. Where this is the case then it should be stated as this is quite educational in its own right.

3. Also the relatively insensitivity of culture based assays opens up the likelihood of missing some bacterial infections. In any given situation there are a lot of
confounding variable that can influence detection sensitivity e.g. prior antibiotic usage, assay sensitivity, assay availability etc. Some comments in the discussion, as for Point 2, would be useful.

4. Why was immunohistochemistry staining not available to confirm the inclusion disease as being HSV associated.

5. It is highly doubtful that the perianal ulcer in patient 2 was linked to HSV reactivation.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests