Author’s response to reviews

Title: Severe Skin Disease in Lupus associated with Hemophagocytic Lymphohistiocytosis: Case Reports and Review of the Literature

Authors:
Christina Thornton (christina.thornton@albertahealthservices.ca)
Parham Minoo (Parham.Minoo@cls.ab.ca)
Michelle Schneider (Michelle.Schneider@cls.ab.ca)
Aurore Fifi-Mah (Aurore.Fifi-Mah@albertahealthservices.ca)

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Author’s response to reviews:

Dear Reviewers,

Thank you for your kind and insightful comments. Please find attached a point form note of each comment.

Hector Chinoy, PhD FRCP (Reviewer 1): The case report is well written and of clinical interest. I note that a CARE checklist has been completed. The literature is also reviewed.

Are they any available photos of the patients’ rashes that could be used as part of the case report?
Thank you. Unfortunately, we do not have available photos of the patients’ rashes. This certainly would have added to the case but were not obtained during the patients’ admissions.

I would be interested to know what methodology used for serological testing.

Thank you. This has been included in the case report. Line 100 demarks the use of a bead-based immunoassay for the soluble IL-2r serology.
Overall, the novel component(s) of the cases is not clearly delineated - early communication of this in the paper will improve the paper.

Thank you. This has been changed, in particular lines 211-212 have been moved to the introduction of lines 66-69 to highlight clearly and early the novel component of the cases.

Specific points:

1- Line 65 - capital "S" on "systemic" is erroneous.

Thank you, this has been corrected.

2- The second presented patient did not have a clear objective diagnosis of HLH on biopsy, for example, in the way that the first patient did - this calls the diagnosis into question?

Thank you. To clarify, and as highlighted in Table 1, the patient meets criteria on the basis of 5/8. I have also added the fibrinogen into the document, line 132 to be more clear for criteria.

3- Lines 186-187 - this is an important sentence as it outlines the novel features of this paper - please re-write for clarity.

Thank you. This has been revised to highlight the H-score and the use of it in HLH.

4- Line 191 - no fullstop at the end of the sentence.

Thank you. This has been revised.

5- Lines 211-212 - a further important sentence - I think this should come much earlier in the paper to make the novel component clearer.

Thank you. This has been moved up into the introduction, lines 66-69 to make the novel component of the paper clear.
Shereen Oon (Reviewer 2): Worthwhile case descriptions and literature review highlighting a rare association of new onset severe cutaneous lupus with haemophagocytic lymphohistiocytosis.

Minor points

Define abbreviation HLH after first use in abstract.

Thank you, this has been done. HLH abbreviation has been added to line 32.

Where is Table 1? (Line 151)

Thank you, this has been included at the bottom of the text.

Might it be worth including a summary Table highlighting the manifestations and investigations that fit SLE vs HLH criteria, and treatment/outcome, of these two cases vs the other similar cases in the literature?

Thank you. Table 1 reflects part of this with regards to HLH criteria. Given the limited cases in the literature, we feel there would be less utility to have a summary table as currently the discussions with the text do highlight this rare and novel finding.

Should Line 190 read 'furthermore, HLH can present with skin manifestations but (in) the absence of antibodies can eliminate an associated autoimmune process’?

Thank you. This has been revised in line 190.