Reviewer's report

Title: Cytokine responses and correlations thereof with clinical profiles in children with enterovirus 71 infections

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Reviewer: Zhi-Min Chen

Reviewer's report:

The manuscript of “cytokine responses and correlation thereof with clinical profiles in children with enterovirus 71 infection” by Jin et al. presents the cytokines changes and their correlation to the clinical variables in EV71-infected patients with different severity. To some extent, the manuscript is interesting since it tried to analyze the cytokine responses in HFMD patients with different severity following EV71 infection. But unfortunately, I think this paper is not good enough to be published at the present moment.

Major Compulsory Revisions

1. Although it seems to be an interesting report involving multiple parameters, the work has many missing links. Rationale for undertaking the work is not clear and thus need to be strengthened in introduction. For example, why cytokines including “IL-1#, IL-6, TNF-# et al.” were chosen for this study.

2. The English language should be improved.

3. Selection of patients is one of the essential components for any clinical study. Explain the inclusion and exclusion criteria clearly in the methodology section.

How many cases were confirmed by detection of EV71 nucleic acid and/or EV71-specific IgM-positivity?

What’s the indication of IVIG and/or glucocorticoid administration? Were all the severe or critical cases in present study given both IVIG and glucocorticoid?

How many severe and critical cases provided both plasma and CSF specimens? Please described in detail.

4. Fever is, of course, closely tied to cytokines. Why did the authors not include fever as a criterion by which to group the HFMD patients (e.g. no, low, high fever), to determine if the immune response pattern was related to the presence (or to the degree) of fever?

5. Authors should compare results obtained against data in published literature and discuss further in details.

In Discussion, second paragraph, author stated that “proinflammatory cytokines and chemokines may play both beneficial and harmful roles…”. Please elucidate in which status it may be beneficial and in which status it is harmful based on published literature and this study.

What’s the possible mechanism of IVIG and glucocorticoid in reducing
EV71-induced inflammation?

6. Between- and among-group comparisons should be performed by Man-Whitney rank-sum test and Kruskal-Wallis test.

Minor Essential Revisions:

1. Due to the limited experimental data, the author may add the “(data not shown)” to the “supplemental data”. It would help to provide an unbiased interpretation and better acceptability of the presented data.

2. The exact p values should be shown in Results, first paragraph, instead of fuzzy expression in Table 1(e.g. p<0.05).

3. Since the limited number of cases (16 generally, 25 severely and 12 critically ill cases), the conclusion “systemic inflammation, indicated by elevated plasma IL-6 and IL-8 levels and higher WBC counts, may by a good predictor of critical illness”(Conclusion, first paragraph) is overstated.

4. How about the prognosis of EV71-infected patients enrolled in present study? Any sequelae? (Discussion, last paragraph, last sentence).

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: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.