Author’s response to reviews

Title: A case report of a teenager with severe hand, foot, and mouth disease with brainstem encephalitis caused by Enterovirus 71

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Editor Comments:

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Reviewer reports:

Reviewer 2 (Reviewer 2): "REVISION ASSESSMENT FROM THE ACADEMIC PEER REVIEWER:

Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? No

Reviewer comments: Thank you for responding to my comments, and for the opportunity to re-review. The introduction and discussion remain the most compelling components of this manuscript and are very well-written.

The responses to queries pertaining to the Case Presentation are appreciated, although frequently incomplete, raising additional questions that the authors may wish to consider. These instances are detailed below. Provided that case details could be appropriately clarified (and efficiently
communicated), I would confidently assert that the work represented "a technically sound contribution".

1. Description of neurological examination. As articulated in my earlier comment, more detailed description of the neurological examination is required. At a minimum, you should clearly state that lower and upper left face were involved. What pattern of weakness was observed in the left limb (pyramidal weakness? proximal > distal)?

Response:

The left nasolabial fold was flat and there was drooping of the mouth to the left side. The muscle strength of the left upper and lower limbs was grade III-IV; the right muscle strength was normal. The above information has been added in the revised manuscript.

2. The inclusion of detailed CSF findings strongly support the authors' assertion of an underlying inflammatory / process.

Thank you for the comment.

3. Clearly state where your clinical laboratory is located. E.g., "All testing was performed within the clinical laboratory at X Hospital (City, Province)."

All tests were performed in the clinical laboratory at the Children's Hospital of Chongqing Medical University, Chongqing, P. R. China. We have added this information in the revised manuscript.

4. Details are still missing when describing neurologic decompensation. It would be useful to present the neurological examination in a traditional format. E.g., Mental status ("the patient was somnolent and non-verbal"), cranial nerves ("Pupils were sluggishly responsive to light, with mild anisocoria (OD=3mm, OS=4mm) in light and dark. Comment on extra-ocular movements, facial symmetry / movement, palatal elevation and tongue protrusion), motor exam (including reflexes). These details are important to support your assertion of "brainstem encephalitis" (which two Reviewers have had reason to question).

Many thanks for the suggestion. The below details have been included in the revised manuscript.

The patient was drowsy and non-verbal, but was responding to painful stimuli. He showed left-sided facial paralysis. The left nasolabial fold was flat and there was drooping of the mouth to the left side. The pupils were equal in size (diameter: 4 mm) and the pupillary light reflex was bilaterally symmetrical. Neck resistance was normal. The left upper and lower limbs showed reduced muscle strength (grade III–IV). The muscle strength in right limb was normal. Abdominal reflex and cremasteric reflex were normal. Pathological reflexes (e.g., Babinski,
Chaddock, Oppenheim, Gordon) were negative. The rest of the physical findings were unremarkable.

Eight hours after admission, the patient showed progressive loss of consciousness and was transferred to the paediatric intensive care unit (PICU). He was in a coma and exhibited shallow breathing (30–40 breaths per minute). Pupils were sluggishly responsive to light with mild anisocoria (OD=3 mm and OS=4 mm). The patient showed no response to painful stimuli, and thus the muscle strength was not detected. The status of abdominal, cremasteric, and pathological reflexes was identical to that at the time of hospital admission.

Minor Points

- In P1 of Case Presentation--state which hospital the patient was admitted to and location (e.g., "Department of Infectious Diseases [Hospital X, City, Province]").

We have included the name and location of the hospital in the revised manuscript.

- In P1 it would be sufficient to simply state "He reported recent contact with a HFMD. Medications were limited to recent use of over-the-counter analgesics."

The suggested change has been incorporated in the revised manuscript.