Reviewer’s report

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

Version: 0 Date: 25 Jun 2018

Reviewer: Reviewer 2

Reviewer’s report:

"PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: The Authors report a case of complicated hand, foot and mouth disease (HFMD) in a 16-year-old male, concurrent with the detection of enterovirous 71 (EV71) in the patient's CSF, serum and feces. Progression of deficits, culminating in neurologic compromise, led the Authors to implicate EV71 as the cause of HFMD with severe neurologic compromise.

Overall impression: The case is well-written and interesting with the potential to inform clinical practice in a meaningful way.

What have the Authors done well: The Authors have done a good job of highlighting the unique / rare aspects of this case, and the importance of considering EV71 in the differential diagnosis of older children / adults presenting with HFMD and neurologic compromise in the future.

In what ways does it not meet best practice: As the Author's articulate, symptomatic EV71 infection is extremely rare in older adolescents and teenagers. However, alternate explanations for EV71 detection and/or the clinical presentation have not (yet) been sufficiently explored or communicated (""Execution"" issue--see grading below).

REQUESTED REVISIONS:

Execution:

It is important to clarify the rate of asymptomatic infection in this age-group. Additionally, the Authors must stipulate what other etiologies were considered in this patient (e.g., HSV, West Nile, VZV, EBV?). This information is critical to support the assertion that EV71 may associate with HFMD in teenagers with potentially severe neurologic involvement.

Interpretation:
The current statement that "EV71 infection may cause HFMD…" is too strong a statement for the level of evidence (single case) presented.

Provided that the reader can be sufficiently convinced that other reasonable entities were excluded, this report will advance the care patients with HFMD with neurologic sequelae, informing diagnostic evaluation and treatment.

ADDITIONAL REQUESTS/SUGGESTIONS:

I offer the following specific comments to improve the utility and clarity of this case report.

Case Description:

- Reference to "some medicines for cold" is vague and non-informative. Please state the medicines that were provided to the patient prior to admission.

- If photographs of lesions were obtained at the time of admission these should be included as an informative figure.

- A more thorough description of neurological examination findings is required to ensure that readers fully appreciate the deficits. In addition, please specify the pattern of left-sided facial paralysis (upper and lower face? Upper only?). Note—due to the location of the facial nerve nucleus within the brainstem (very near to the abducens nerve nucleus), and the close proximity of the nerve root to other cranial nerves, it is highly unlikely that unilateral facial nerve palsy would be the only sequelae of brainstem encephalitis. Isolated facial nerve palsy would be more typical of distal CNVII compromise (i.e., "Bell's palsy").

- Was the patient chemically- / medically-sedated at the time of the EEG?

- Please include further details concerning "anisocoria". Were both pupils unresponsive to light?

- Dates of admission and testing are irrelevant to the reader. Please reference all testing to admission (i.e., CT brain was completed 5 days following admission), or symptom onset (i.e., CT brain was completed 8 days following symptom onset).

- Findings should be reported in the order that they were received / discovered. It is unlikely that EV71 results returned on day one of admission (prior to patient decline).

- This patient's presentation is very concerning for HSV encephalitis. Was empiric acyclovir provided?
The term "paroxysmal hypertonia" is unfamiliar to me. Please describe in greater detail. Are you implying dystonia? Posturing?

Discussion

- Symptoms and signs supporting the diagnosis of "brainstem encephalitis" should be explicitly stated in paragraph 2.

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

Yes

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.

No

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

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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