Jin et al compared the cytokine and chemokine levels from EV71 patients with varieties of illness severity, disease phrase, with treatment by IVIG and glucocorticoids and analyzed the correlation of the cytokines, inflammatory markers, and illness severity. Their data provide solid evidence that severe or critical illness with CNS symptoms in EV71 infection is correlated to inflammatory cytokines either in CNS or plasma. Although the findings are not of complete novelty, the analyses were complete and the conclusion is of value for both basic and clinical studies of EV71 infection.

Minor changes are suggested as following:

P2 Line21: Severe complications are NOT commonly associated with EV71 infections. Many patients are infected with no or mild symptoms. Pathogenesis of EV71 infection in the severe cases remained poorly understood.

P2 Lines 36-38: The second half of the conclusion may not be correct. Even though high cytokine levels in CSF correlate with severe cases, but not with critical cases, it doesn’t mean the cytokines in CSF play a less role in critical illness.

High cytokine levels in CSF may be transient, and their levels become lowered when the patient progresses to the critical illness stage.

It may have nothing to do with “changing battlefield” from CSF to plasma with disease progression.

On the other hand, neither CSF nor plasma may be the original site of induced inflammation. Cytokines/chemokines could be induced in some tissues/organs that are secreted into CSF and plasmas. Organs or tissues, in periphery or CNS, may be the true “battlefield”.

Remove or replace the word “battlefield”: it is too dramatic.

P3 Line 60: A vaccine has been in the market in China since 2014.

P4 Line 74-75: The sentence needs to be rephrased. Semicolons should be removed; neutrophils, lymphocytes, and monocytes are part of WBC.

Suggestion: Moreover, we also determined the correlations between cytokine
levels and markers of inflammation including temperature, white blood cell (WBC) counts or individual counts of neutrophils, lymphocytes, or monocytes.

P4 Line 78: Spelling: Enrollment

P5 Line 92, 93 & P7 Line 142 & thereafter: “generally” and “general” could be replaced by “mildly” and “mild”.

P5 Line 98: “examination” – wrong spelling?

P8 Line 153: “subjected to repeat lumbar puncture” > “subjected to repeated lumbar puncturing”

P9 Line 187: Remove the word “rather”.

P10 Lines 193-194: Comment: It’s unlikely that peripheral blood is a major site of inflammation. More likely, cytokines are produced in organs, which are secreted in the blood. And the organ(s) or tissue(s) is the site of inflammation. In another word, inflammatory cytokines/chemokines may not be produced much in both severe and mild patients, resulting in less or little being secreted into blood. By the same token, higher levels of cytokines in plasma may not be the cause of the critically illness. They could be the outcome of it.

P10 Line 197: “tested” should be replaced by “detected”.

P11 Line 210: “high quality” should be replaced by “solid”.

P11 Line 216-7: “development of a CNS inflammatory response was important in terms of induction of CNS disease in EV71-infected patients”.

Suggested change: “development of a CNS inflammatory response may be essential in induction of CNS complications in EV71-infected patients”.

P11 Line 218: Remove “However”

P11 Line 223: EV71 infection may be “prevented” only by vaccines, not by anti-inflammation therapy. Manage clinical cases? Yes.

P12 Line234# “Further work is needed and optimal therapeutic doses and timing of intervention require attention”

Suggested change: “Further study is needed to determine optimal therapeutic doses and timing of intervention clinically”.

P12 Line 243: Replace “agents” by “molecules”