

Dear Editor

Thank you very much for your decision letter and advice on our manuscript (Manuscript ID 81216) entitled “Epidemic Japanese B encephalitis combined with CASPR-2 antibody-positive autoimmune encephalitis-The world first case report”. We also thank the reviewers for the insightful comments and suggestions. Accordingly, we have revised the manuscript. All amendments are highlighted in red in the revised manuscript. In addition, point-by-point responses to the comments are listed below this letter.

We hope that the revision is acceptable for the publication in your journal.

Look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Dr. Pan huang

We would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1 comments:

1. This paper is a case report of CASPR-2 antibody-positive autoimmune encephalitis. It is an interesting paper.

**Response:** We thank the reviewer for the positive comments.

2. How was Epidemic Japanese B encephalitis diagnosed?

**Response:** We thank the reviewer for the positive comments. I have added the basis for the diagnosis of Japanese B encephalitis in the second paragraph of the discussion (highlighted in red). The diagnosis of Japanese B encephalitis in this case was based on the following: the patient's onset of illness was in the summer, the favourable season for Japanese B encephalitis, with the typical clinical presentation of high fever, impaired consciousness, convulsions and, most importantly, a PCR test of the patient's cerebrospinal fluid by the Centre for Disease Control that found positive for Japanese B encephalitis virus.

3. The relationship between Epidemic Japanese B encephalitis and CASPR-2 antibody-positive autoimmune encephalitis is not discussed in detail.

**Response:** We thank the reviewer for the positive comments (highlighted in red). In the third paragraph of the discussion we provide a brief description of the relationship between Japanese B encephalitis and CASPR-2 encephalitis. As we have not seen any further reports in the literature, the exact relationship between the two is not yet fully established, and more molecular mechanisms may be investigated by our group in the future. We speculate that it is possible that the patient first contracted Japanese B encephalitis and subsequently activated the autoimmune system to induce CASPR-2 autoimmune encephalitis. A review of the relevant literature revealed that viral encephalitis often tends to trigger autoimmune encephalitis, possibly through two pathways: The first is a molecular simulation mechanism, that is, the JE virus protein that infects the central nervous system has the same or similar antigen structure cluster as CASPR-2. The second is that after infection of the central nervous system JE virus leads to destruction of brain tissue, a large number of CASPR-2 antigen structure clusters are exposed, thereby inducing the body to produce autoantibodies against CASPR-2 and secondary autoimmune reactions.

4. Abstract No correction is necessary.

**Response:** We thank the reviewer for the positive comments.

5. Introduction Please cite references in each sentence.

**Response:** We thank the reviewer for the insightful suggestion. I have adjusted the references in line with your comments.

We do not know if our revised manuscript is enough to satisfy the reviewer. If our revised manuscript has some problems, please let us know.