Author’s response to reviews

Title: Guillain-Barre syndrome associated with hemorrhagic fever with renal syndrome in China: a case report

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Author’s response to reviews:

Dear Editor,

Point-by-point response to the comments are listed as follows,

Technical Comments:

Reviewer reports:

Lei Zhang, Ph.D. (Reviewer 1):

1. Line 68, change 'testsshowed' to 'tests showed'.

Checked.

2. Line 89 and 175, author dose not have to emphasis the patient’s daughter here. As CSF examination is not necessary for GBS diagnosis and author also stated in conclusion part that they for the first time classified GBS based on the electrophysiology characteristics, no CSF examination should not be limitation in this report.
Line 89 was depleted. Line 175 was still reserved since it could answer other review’s question and also emphasize the diagnostic ability of electrophysiology of GBS

3. Line 135 and 164, please leave space between two sentences.

Checked.

4. Line 148, change 'Krea' to 'Korea'.

Checked.

Rafdzah Ahmad Zaki, MBChB,MPH,DrPH (Reviewer 3):

1. This article need editing /proofreading. Few spelling and typing error e.g line 63 and 114 spacing, and line 103 spelling error.

Checked.

2. Inappropriate statement/conclusion:

* Line 186- "GBS might only accompanied with Hantavirus infection in Europe and Asia". I don't think based on current evidence that author can conclude this. No cases reported from other continents (either no case or underreporting), thus unable to make association.

We change the statement as “Until recent now, GBS was only reported in hemorrhagic fever patients in Europe and Asia, which termed as hemorrhagic fever with renal syndrome.” We also change the Abstract conclusion.

* Abstract- "Conclusions: We reported the world's sixth case of Guillain-Barre syndrome associated with hemorrhagic fever with renal syndrome." This statement also inappropriate. This may be the 6th cases reported in literature, but does not mean the world's sixth case.

We change the statement as “Our case was the 6th reported case of Guillain-Barre syndrome associated with hemorrhagic fever with renal syndrome”

Danielle Vuichard, M.D. (Reviewer 4):
Major issues:

1. The diagnosis of Hantavirus infection (HFRS) has been made by clinical presentation, laboratory changes and by serological detection of antiviral IgG (page 4, line 79). However, by the time a patient develops symptoms, antiviral antibodies of the IgM class are almost uniformly present indicating recent infection, and shortly later most patients have antibodies of the IgG class. Seroprevalence of Hantavirus IgG in the Chinese population is very high and, therefore, evidence of Hantavirus IgG could also represent past infection unless there was a documented fourfold rise in titers of anti-hantavirus IgG, which the authors cannot proof. Have the authors ruled out other differential diagnoses, e.g. Leptospirosis, Malaria or Dengue fever (outbreaks of Dengue fever in southern coastal area of China described by Xia Jin and colleagues, Emerging Microbes and Infections (2015)). Malaria and Dengue fever are also associated with neurological complications such as Guillain-Barré-Syndrome.

Dengue fever was ruled out by Dengue fever IgG and IgM detection, while Malaria was eliminated by blood smear. (Those statement was added in Line 83). Leptospirosis was eliminated since the symptoms and signs were not incompatible.

2. In this case report, the diagnosis of Guillain-Barré-Syndrome relies on electromyography (EMG) studies only. Unfortunately, the authors failed to obtain consent from the patients' daughter to perform a lumbar puncture to show evidence of cerebrospinal fluid albuminocytologic dissociation. Did the authors look for the presence of specific antibodies associated with acute motor sensory axonal neuropathy, e.g. Anti-GM1, anti-GM1b, and anti-GD1a IgG?

Could the authors graphically show the particular EMG changes?

Those antibodies were not determined. EMG results were attached in revised version.

3. Page 5, lines 98-102: the time relation of the sodium level increase is not exactly documented and at the first glance it is unclear why the authors mention it. At a second glance it becomes clear that they were looking for differential diagnosis for the flaccid paralysis. This section would need to be rephrased starting e.g. with "Since we noted a marked increase of the serum sodium level an MRI was performed but the suspected osmotic demyelination syndrome as a
potential differential diagnosis of...". The MRI showing no lesions is probably not important for the reader. Besides, the authors could mention that the syndrome of inappropriate antidiuretic hormone secretion (SIADH), can be a complication of GBS.

Checked. Statement was changed in Line 104. SIADH presented extremely hyponatremia which was opposite to our case and thus was not mentioned in our manuscript.

4. Overall the whole case report lacks a fundamental discussion of the potential underlying pathophysiology and mechanism why Hantavirus infection should trigger GBS.

Our case was the world’s 6th reported case of GBS triggered by Hantavirus, indicating that this disease context was not fully detected. Thus we didn’t mentioned potential underlying pathophysiology and mechanism why Hantavirus infection could trigger GBS in the manuscript because of lack of precise conclusion.

5. The report needs to be extensively re-edited because of typos and low quality of written English.

Checked.

Minor issues:

Abstract: the authors use abbreviations (e.g. AMSAN) that have not been introduced, instead GBS should be introduced at first mention. To the best of my knowledge the expression "dyskinesia" is not appropriately used in this context because it represents "involuntary repetitive movements" which is not a feature of GBS.

AMASN was deleted in abstract. Dyskinesia was changed into delayed paralysis.

Page 3, line 46: the syndrome of hantavirus infection found predominantly in North and South America is typically described as Hantavirus cardiopulmonary syndrome.

Checked.

Page 3, line 62: "intermittent fever" is a specific fever pattern usually associated with malaria, and, unless there were spiking temperatures every 24 hours, it is hard to catch an intermittent fever pattern within 4 days as described in this patient.
Page 5, lines 91-95: Abbreviations such as MCVN or SNAP are unnecessary since it does not occur in the text anymore.

Abbreviations were reserved for the non-native speaking English readers to better understand EMG.

Page 9, line 193: "AMSAN" is incorrectly spelled out: the word "sensory" is missing

Checked

Thank you very much for consideration!

Sincerely Yours,

Dr. Hu