Author's response to reviews

Title: A case report of misdiagnosed Murine typhus infected patient presented with multiple cerebral infarctions and hemorrhage

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Author's response to reviews: see over
Dear Editors:

Thank you giving us a chance to revise our research article entitled “A case report of misdiagnosed rickettsia infected patient presented with multiple cerebral infarctions and hemorrhage” for consideration of publication at your prestigious journal.

This article had been revised after full consideration of the comments of two experienced reviewers. The responses are follows.

Responses to Reviewer 1

1) According to the serology and molecular study, this is a case of Murine typhus also called Endemic typhus. Therefore, I recommend to change the title of this case report to “Rickettsial Infection by Murine typhus”. The reason for change of title is that rickettsial infection is a general term used when rickettsia was not identified.

Title have been changed according to the reviewer’s suggestion. See line 1 to 2.

2) Change the term “moseri” to “Rickettsia typhi” in all the texts. The term “moseri” is an old appellation for rickettsia.

All Rickettsia mooseri have been revised to Rickettsia typhi. (See line 59, 98,105,124,144)

3) Change “Rickettsial infection” to “endemic or murine typhus” in Keywords.

We do the change in the paper. (see line 41)

4) Need to identify or specify which technique was used to do serology, and if other rickettsia antibodies were tested. In general there is a cross reaction between many rickettsia spp.
Reviewer is right, there is a cross reaction between Typhus and tsutsugamushi.

Technique was provided in the paper (see line 90 to 93)

5) For genetic sequencing, need to specify which technique and sample was used (peripheral blood, or CSF or skin biopsy), and in which laboratory this exam was conducted.

Peripheral blood was used for genetic sequencing in laboratory information was provided in the paper. (See line 95 to 99)

6) In Line 92, change “rickettsial disease” to “murine typhus”.

We do the change in the paper. See line 99.

7) In Line 97, change the term conclusion to discussion.

We do the change in the paper. See line 104

8) In Line 117, change “Rickettsia typhus” to “Rickettsia typhi”.

We do the change in the paper. See line 124.

9) In Line 136, change the statement “This older male farmer patient was bitten by murine typhus” to “This older male farmer patient presented murine typhus with…” since patient cannot be bitten by a disease!!

We do the change in the paper. See line 142 to 143.

10) In Line 137, change the statement “murine typhus involved endothelial and vascular smooth muscle cells resulting” to “Rickettsia typhi involved endothelial and vascular smooth muscle cells resulting…”.

We do the change in the paper. See line 144.
Responses to Reviewer 2

1. It is possible that the patient indeed suffered from a rickettsial disease as determined by seroconversion; however, the details of this etiological diagnosis are missing and should be included in the manuscript. In particular, the authors need to describe what diagnostic test was used and what antigen(s) were used, and on what days after onset of symptoms, the serum samples were collected for testing.

We have revised the etiological diagnosis in the paper. The time and diagnostic test, antibody, test time the serum were provided in the paper. (see line 89 to 94)

2. Presence of an eschar is not typical for endemic typhus and suggests instead a spotted fever group rickettsiosis. Since the authors claimed that the presence of R. mooseri (sic R. typhi) DNA was confirmed by sequencing, the source of DNA, timing of sample collection and method of detection (including specific primers used) should be reported in the manuscript. Nucleotide sequence of the fragment detected should be submitted to GeneBank and the accession number included in the manuscript.

The peripheral blood was used for genetic sequencing and the accession number has been included in the manuscript. (see line 95 to 99)

3. Specify the location of possible exposure of the patient – is it somewhere in Hangzhou Province or elsewhere? Specify the time of year when the patient became ill.
The older male patient came from Tonglu County in Zhejiang province China and became ill at April 2014, we do the change in the paper.(see line 64 to 66)

4. Term “R. mooseri” is an archaic name for Rickettsia typhi and is not used in modern literature. Please, replace.

We do the change in the paper.(also stated above).

5. Update information regarding the current knowledge of rickettsial diseases in China; the sources cited were published in 1987 and 1987, and are badly outdated.

We do the change in the paper for adding new epidemic data with reference.(see line 161-162)

6. Last but not least, the article needs to be edited by someone who speaks English as their first language.

The manuscript was edited by native English speaker.

Sincerely yours

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