

Manuscript ID:74640

Title: Mills' syndrome is a unique entity of upper motor neuron disease with N-shaped progression:
Three case reports

Journal: World Journal of Clinical Cases

Dear Dr Wang:

Thank you very much for your letter and advice. We would also like to express our sincere thanks to the reviewers for their constructive and positive comments. We have revised the manuscript according to the reviewers' comments, and the corrections are presented in red font in the revised manuscript. The point-by-point responses to the comments are given after this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal. I look forward to hearing from you.

Sincerely,

Corresponding author:

Jiajia Fang

Response to Reviewer 1

1.The introduction is short, it is preferred to add some information about the epidemiology, pathophysiology of the disease.

Response: Thank you very much for your suggestion. We have added the epidemiology and pathophysiology in the Introduction (page 3, line 3-20)

2.The references are mostly old, it will be better if references are updated.

Response: As advised, we have updated some of the references with those published in the last 5 years.

3. The relationships between grey matter and white matter are not described. I think that if ratios are reported, this may give better understanding of the syndrome.

Response: This suggestion has been taken seriously. We have discussed the relationship between white matter and gray matter from line 25 on page 9 to line 4 on page 10.

Response to Reviewer 2

1. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Please add a small paragraph.

Response: Thank you for your suggestion. We have added the method to the revised version. (page 4, line 4-10)

2.Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends?

Response: Thank you for your review. We have re-checked the table contents and think it can effectively illustrate the content of the discussion.

3.References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references?

Responses: Thank you. We have updated the references and marked the revised text in red. We appropriately cite current and important references.

4.Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Please add an Ethis statements. This may be done in the Methods Sections

Response: Thank you very much for your suggestion. We have added the ethics statements in the methods section (page 4, line 1-6) and submitted the related formal ethics documents on the website.

5. Further comments: -Case 1: please comment the MRI finding of atrophy of the right occipital lobe.

Response: Thank you very much for your suggestion. We added a small paragraph to the discussion. (line 25 on page 9 to line 4 on page 10)

6. Discussion: I suggest to expand the discussion by addressing the issue of pTDP pathology and spreading through the CNS related to the N shaped progression displayed by the patients

Response: We accept your suggestion. We have added this discussion to the revised version. (please see the fifth paragraph in discussion section, page 3)

Response to Reviewer 3

At first you have to clear how you have differentiated the Mill's Syndrome to theater neurological syndromes. Therefore you have to perform a structured review of the literature. I suggest to introduce a figure to clear the neurological pathway involved in the disease.

Response: Thank you. We used Table 2 to show the different progression modes and identification points of Mills' syndrome from ALS and PLS. It is difficult for us to add a figure to clarify the neurological pathway involved in the disease.

Response to Editorial Office's comments

Science editor:

1. Please add information on epidemiology, disease pathophysiology in the Introduction section;

We have added the epidemiology and pathophysiology in the Introduction (page 3, line 3-20)

2. Please comment on the MRI findings of right occipital lobe atrophy in case 1;

We have added the discussion about right occipital lobe atrophy in case 1 from line 25 on page 9 to line 4 on page 10.

3. The references are outdated, please cite recently published literature;

We have updated some of the references with those published in the last 5 years.

4. Please add a figure to clear the neurological pathway involved in the disease.

We used Table 2 to show the different progression modes and identification points of Mills' syndrome from ALS and PLS. It is difficult for us to add a figure to clarify the neurological pathway involved in the disease.

Company editor-in-chief:

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to

the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

We have checked the table format as requested.

2. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

We have submitted the relevant approval documents.

Response to language polishing

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

We have had our revised manuscript edited and proofread by a professional English language editing company. Please find the new certificate attached along with the manuscript.