Author’s response to reviews

Title: A case report of iatrogenic deterioration of yet undiagnosed Rhombencephalitis; always be careful with corticoids.

Authors:
Loes Mandigers (l.mandigers@erasmusmc.nl)
Jelle Epker (j.epker@erasmusmc.nl)

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Author’s response to reviews:

Dear editor,

We want to thank you and the reviewer for putting time and effort in the second review of our manuscript. The clear and constructive feedback was helpful for improvement of the manuscript. We added a point-to-point reply in the text listed below.

Yours sincerely,
Loes Mandigers and Jelle Epker

Editor Comments:

1. "Consent for publication is available on request." You need to make clear if you have obtained written consent from patients' lineal relatives to publish this case report? If yes, this sentence should be read as "Written informed consent was obtained from the patient's XXX for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.". Please also forward us a copy of signed written consent for check.

We included a copy of the signed written consent and added the next sentence to the ‘Consent for publication’: “Written informed consent was obtained from the patient's daughter for
publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.” Page 5, line 26-28.

2. Please revise your article and address the concerns from reviewer 1 properly.

We made changes to the manuscript according to the suggestions of reviewer 1, as is stated below.

3. The figures were cited as Picture 1, 2, ..., please keep consistent when citing figures in main text with figure legends part, better cite as Fig 1, 2, ...

We cited all figures as “Figure” and added the timeline as ‘Figure 1’.

4. "Availability of data and materials”, the statement should read as "All the data supporting the conclusions of this article is included in the present article."

We now stated: “All the data supporting the conclusions of this article is included in the present article.” At the section ‘Availability of data and materials’, page .. line..

5. Please delete CARE checklist from supplementary files.

We deleted the CARE checklist from the supplementary files.

6. Please cite the supplementary file Timeline properly in main text.

The Timeline is cited in the ‘Case presentation’, as “see timeline (Fig. 1)”, page 2, line 30.

7. Please provide us a clean final version without tracked changes.

We included the final version without tracked changes.
Reviewer reports:

Sing Sing Way (Reviewer 1): The revised paper is improved, however, I think the conclusions are still rather biased. Instead of avoiding corticosteroids, couldn't one just as easily make the argument that the progression of this patient's illness reflects delayed initiation of appropriate antibiotics and the need to take a thorough exposure history? Do the authors know that with early initiation of amino-penicillin antibiotics that corticosteroids are still contraindicated? I think the case is interested, but the conclusions and discussion SHOULD BE more balanced... not exclusively focused on the negative consequences of steroids, but also promoting the importance to early initiation of antibiotics that cover all the likely pathogens on the differential diagnosis.

Thank you for this comment. We tried to improve our paper by pointing out the severe course of the Listeriosis in case of late diagnosis and thereby late adequate antibiotic treatment. We highlighted the importance of treatment with antibiotics that covers the pathogens of the differential diagnosis. We made the following adjustments in the Abstract, Background, Discussion and Conclusion:

‘Abstract’: “Eventually the patient died of Listeria rhombencephalitis, most likely due to the late diagnosis and concomitant late initiation of antibiotics combined with badly timed and inappropriate corticosteroid prescription.

Conclusion: Early adequate antibiotic treatment is essential in Listeria rhombencephalitis and corticosteroid therapy should be avoided when Listeriosis is suspected.” Page 2, line 7-11.

‘Background’: “We report a case of a 67-year old immunocompetent women, who died of undiagnosed Listeria rhombencephalitis, that escalated probably due to the combination of late diagnosis, late adequate antibiotic treatment and inappropriately initiated corticosteroid therapy after 16 days of progressive neurological symptoms.” Page 2, line 22-25.

‘Discussion’: “Although at last the correct diagnosis was made and the appropriate antibiotics were administered, the patient unfortunately deteriorated and died. This emphasizes that early administration of the correct antibiotic treatment is crucial. In case of an unknown pathogen, initiation of antibiotics covering the most likely pathogens of the differential diagnosis could be life-saving. Therefore, it leaves no doubt that the marked delay in finding the correct diagnosis eventually has determined the disastrous course of events in this case. The administration of corticoids will only have contributed to the final stage of the lethal progression that already had taken its course.” Page 4, line 32-38.
‘Conclusion’: “Listerial rhombencephalitis is a challenge to diagnose, especially if cultures remain negative. Therefore a broad differential diagnosis combined with a thorough interview remains essential, because in the end what you will diagnose depends merely on what you are looking for. If Listerial infection is not considered or ruled out in infectious patients, late diagnosis and thereby late initiation of antibiotics will allow the disease to run its devastating natural course. The administration of corticosteroids will only catalyze progression of the disease.” Page 4, line 6-11.