Author's response to reviews

Title: A case of meningococcal meningitis with multiple cerebellar microbleeds detected by susceptibility-weighted imaging

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Comments to the reviewers:

Thank you for reviewing our manuscript entitled “A case of meningococcal meningitis with multiple cerebellar microbleeds detected by susceptibility-weighted imaging.”

In accordance with both reviewers suggesting we should include the follow-up MRI to show the improvement of the cerebellum microbleeds, we included the follow-up imaging performed on day 42.

Reviewer 1:
1- Figure one should include a sagittal T1 image with contrast to confirm the diagnosis of pus in the major fissure ??,
2- Empyema should be in the sub-dural space not in subarachnoid space. Please review line 121 and 122. please review the MRI again to confirm this finding.

- In Figure 1, we included postcontrast T1 imaging to show the inflammatory changes in the cerebellum. The contrasted subarachnoid space in the cerebellum (Figure 1a) indicated inflammatory changes in the subarachnoid space. Along with the findings of DWI with high-intensity areas in the great horizontal fissure, we considered these observations indicated a collection of purulent exudate in the subarachnoid space. Although we described this as “empyema in the subarachnoid space” in the previous version of the manuscript, “a collection of purulent exudate” is a more suitable description (L133–135)*. Therefore, we revised the Discussion section in accordance with these considerations. We also removed reference #9 and added a new reference for the discussion of amyloid angiopathy (L146-148).

* Acquired Pyogenic Infections. In: Osborn GA, editor. Osborn’s Brain. Imaging,

3- Line 107, I think this is discussion not conclusions.
4- Line 127 Vergouwen et al, you should put reference immediately after et al.
    - We corrected these sentences according to your comments (L119 & L139).
5- Lines 134 and 135 Bacterial meningitis can induce microbleeds in brain tissue, which can 135 be identified only by SWI… SWI is one of the susceptibility imaging methods in addition to T2gradient sequences which can also detect microbleeds. Of course SWI is more sensitive but not he only sequence to detect microbleeds.
    - I agree that SWI is not the only method that can be used to detect microbleeds. We changed the sentence and simply stated “Meningococcal meningitis can induce microbleeds in the cerebellum that can be identified with SWI” (L156–157).

6- The discussion should refer to microbleeds detected by SWI in other types of non infectious vasculitis and arteriopathy which can support the hypothesis of infectious vasculitis induced by meningitis.
    - As far as I know, other pathophysiology that can cause low-intensity spotty areas is amyloid angiopathy and hypertensive vasculopathy. This case had no history indicating these conditions and both generally occur in the elderly population. We included a discussion of the differential diagnosis and added a new reference (#9, L146–148 & L 214).

7- The discussion should refer to the possibility of telangiectasia as a DD of microbleeds which give very similar appearance by SWI after irradiation, especially that this patient recovered completely without neurological or cerebellar manifestations.
    - We included postcontrast T1 imaging to exclude the possibility of telangiectasia. We also described this point (L110–113).
8- Line 134, I think a missing title conclusion should be included.
    - We checked and corrected the subheadings.
9- Why the authors did not include a follow up MRI with SWI that can help to differentiate microbleeds from reversible telangiectasia ??
    - We added the follow-up MRI performed on day 42 to Figure 1.

Reviewer 2:

Major compulsory revisions:
1) Was the spinal tap performed before the CT scan? Since this patient had a
reduced level of consciousness, imaging should - according to international guidelines - be performed before the spinal tap. Please specify the sequential examinations performed. Same holds for the timing of antibiotics and dexamethasone administration.

- A spinal tap was performed after the CT scan study. Dexamethasone was also administered just before the antibiotics were given (L94–95 & L96–98).

2) Only on day 8 the cerebrospinal fluid culture turned positive for N. meningitidis. Does this mean that the gram staining of CSF was negative?

- Since the Gram-staining study was poor, we administered VCM and MEPM according to the guidelines for bacterial meningitis (L97–99).

3) Empyema is a very uncommon complication of an infection with N. meningitidis (Rothbaum E et al. Cerebral abscess associated with meningococcal meningitis. Pediatr Infect Dis J. 2006) and when reported it seems to involve infants and not adults. Treatment is usually surgical with prolonged antibiotal treatment. I would suggest to the authors to discuss this uncommon complication and the chosen treatment more explicitly. Since no surgical intervention was performed, the radiologically suspected empyema was not confirmed. Have the authors considered a differential based on the radiological findings?

- We suggested that the high-intensity areas in DWI indicated empyema collection in the previous version of the manuscript. As we commented to reviewer 1, we revised this to “a collection of purulent exudate in the subarachnoid space” (L133–135).

4) The autopsy studies referred to by the authors, both report on pneumococcal meningitis. Microbleeds in meningococcal meningitis seems not to be observed previously bases on autopsy studies. This needs to be adressed.

-We addressed this point in the Discussion section (L143–145).

5) Discussion, last sentence: ‘the microbleeds improved spontaneously.’ Was there a control MRI performed? If yes, this should be mentioned and discussed in the ‘Case presentation’. From literature it is known that the majority of lesions appear to persist over serial scans. (Yates et al. Front Neurol 2013) If no control MRI was performed, where do the authors base this statement on?

- We added the follow-up MRI performed on day 42 to Figure 1.

Minor essential revisions:
1) Page 5, line 85: Please use the common order to report the Glasgow coma scale (E1M4V1).
   - As you pointed out, we described Glasgow coma scale in the order E-M-V (L98).

2) Case presentation: Please specify the number of inflammatory cells and the protein level in the spinal fluid.
   - We included the number of cells, protein level, and sugar level (L97–99).

3) I suggest to write meningococcal with double 'c' (meningococcal).
   - We corrected this spelling mistake.