Reviewer's report

Title: Deep cerebral venous thrombosis mimicking influenza-associated acute necrotizing encephalopathy: a case report

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Reviewer: F Schuchardt

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The authors report the case of a woman with coincidental cerebral venous sinus thrombosis (CVST) and influenza B virus infection. They present clinical and radiological similarities of acute necrotizing encephalopathy (ANE) and CVST affecting the deep cerebral venous system.

This is an interesting case as it stresses the pitfalls of imaging findings in influenza compatible with ANE that might lead to unrecognized deep cerebral venous thrombosis. Imaging findings and the history of the presenting illness are well carved out. I have several minor comments that might further improve the presentation:

Introduction, first paragraph, second sentence: the authors might state the approximate no. of reported patients with ANE in viral infection in case reports and case series.

Line 64: Please specify that edema and/or hemorrhage as a complication of deep CVST result in lesions of the thalami.

Case presentation: please add the group (neuraminidase inhibitor) of Laninamivir and way of administration.

Line 86: Are there numbers about the frequency of positive D-dimer testing in case of influenza infection? Might D-dimer levels help to discriminate CVST from other infectious disease? If so, please add this aspect in the discussion section.

Line 92: How can CSF xanthochromia be explained (disturbed blood-brain-barrier? Venous stasis infarction?)?

Differential diagnosis: Did the treating physicians despite low CSF neutrophil count screen for other causes of infectious / viral encephalitis (PCR, serology)? The authors might discuss that
encephalitis due to influenza and tick-borne encephalitis were improbable given the CSF showed normal white cell count.

Line 114: Please state the rationale for treatment with osmotic agents, substances, dosage and route of administration. Might the dehydrating effects of the osmotic agents explain pulmonary embolism and deep venous thrombosis?

Line 122: For clarity, please add the reason for HLA-B51 typing. Screening for cancer using tumor markers is usually not recommended. As CT-screening was negative the additional information on tumor markers should be left.

Discussion: Although deep cerebral venous thrombosis (DCVT) and ANE are both relatively rare, DCVT seems to be far more frequent (see first comment regarding intro). ANE is an exclusion diagnosis and requires - among others - the exclusion of CVST. The current standard of CVST diagnosis is CT- or MR-venography. Implicit, this has not been performed initially. These aspects are not yet discussed and should be added.

The case report could be further improved by comparing (what do they have in common) and contrasting (how can they be differentiated) ANE and CVST in more detail, in addition to the presented information. I suggest adding one or two brief paragraphs in the discussion section adding a very brief description of histological changes due to ANE vs. CVST, clinical presentation concentrating on the symptoms of this reported patient, diagnostic strategies including imaging findings in both entities (please focus on MRI-sequences), and treatment. In my opinion naming differences of treatment is clinically especially relevant as corticoid treatment has pro-coagulatory effects and thus is not indicated in the treatment of CVST.

Fig 1D: the dilated deep cerebral veins could be emphasized e.g. by a box or arrows. It might be even more illustrative to add a magnification of this finding.

Fig 4: Please give the administration route of Peramivir. Typing errors in figure 4 (warfarin, GCS).

Language: some phrasing should be adapted.
Level of interest
Please indicate how interesting you found the manuscript:

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Quality of written English
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