Reviewer's report

Title: Positivity to p-ANCA in patients with status epilepticus.

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Reviewer: Meriem Bensalem-Owen

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I read the manuscript by Ferlazzo, Gambardella, Bellavia et al. with great interest. There are very few cases in the literature reporting the association of very frequent refractory seizures or status epilepticus with ANCA-associated-vasculitides. I would like to congratulate the authors for writing up and sharing their cases.

Please find below my recommendations for revisions, comments and suggestions.

Major Compulsory Revisions

1-Based on the description of the seizures and EEG findings, the third case represents in my opinion a case of very frequent seizures (occurring every 3-10 minutes on the EEG) rather than status epilepticus. Please clarify as this may have several implications on the title and the body of the manuscript (the title should then be changed to “POSITIVITY TO P-ANCA IN PATIENTS WITH STATUS EPILEPTICUS AND VERY FREQUENT SEIZURES”).

2-In the Abstract, in the section Case Presentation: Please provide more details regarding the demographics for each patient. For instance: “The first patient is a 48 year-old man who shortly after being diagnosed with AAV presented with convulsive status epilepticus. His course was catastrophic and he died 5 months after disease onset.”

3-In the Case Presentation, Patient 1, sentence 17, please clarify the use of “Polygraphic”. Asterixis is a clinical diagnosis while triphasic waves are an electroencephalographic (EEG) finding. Also, was video used concomitantly with the EEG?

4-Case Presentation, Patient 2, 3rd sentence: Please clarify if there was alteration of awareness with the patient’s left hemibody clonic jerks? Please precise if the periodic discharges were time locked with the patient’s hemibody clonic jerks?

5-Case Presentation, Patient 2, 9th sentence, was microalbuminuria found in the urinalysis (U.A.)? Please clarify as this is not clear from the wording as shortly thereafter it is mentioned that the U.A. was normal.

6-Case Presentation, Patient 3, first sentence, please detail the patient’s episodes of vision changes: How long were these lasting? Their duration may
have implications on determining if she was truly experiencing status epilepticus at onset of the disease. Did the patient experience any alteration of awareness with the visual changes?

Minor Essential Revisions

I would like to recommend the following changes be considered by the authors:

1. In the Abstract, section Background and in the main Background (1st sentence) please consider changing “several internal” to “several medical”.
2. In the section Conclusion of the Abstract: Please consider changing “ANCA dosage” to “ANCA assay” or “ANCA titers”
3. In the Background, please consider changing the 5th sentence to: “AVV may involve several organ systems, commonly upper and lower respiratory tracts, kidneys and skin.”
4. In the last sentence of the Background please add “with” and “and” so the sentence will read: “…3 patients (2 patients, upon clarification of the 3rd case) presenting with SE of unclear origin and whose sera were…”
5. In the Case Presentation, Patient 1, 1st sentence, please add “was diagnosed with AAV”.
6. In the Case Presentation, Patient 1, 3rd sentence: I would like to suggest to use “with” instead of “because”. The sentence will then read “Two months later he was admitted with generalized convulsive SE which was treated with intravenous (IV) lorazepam.”
7. In the Case presentation, Patient 1, sentence 7: Please consider changing the sentence to “Abnormal results included an elevated creatinine of 7.82 mg/dl (close to the patient’s baseline), ESR….”
8. In the Case presentation, Patient 1, sentence 7: Please add “and” before microhaematuria.
9. In the Case Presentation, Patient 1, last sentence: Please add the article “The” and correct the typo “for” to “from”. The sentence will then read “The patient died from…”
10. Case Presentation, Patient 2, first sentence: Please change “coeliac man” to “man with coeliac disease”. Please also consider ending the sentence immediately after “unknown origin” before starting a new sentence “He was treated with oral prednisone”. For the next sentence, I suggest to change “In the same epoch…” to “Around the same time (or period) he started experiencing weekly ….aura associated with diaphoresis for which he was prescribed levetiracetam”.
11. Case Presentation, Patient 2, 3rd sentence: Please change “i.v.” to “IV lorazepam and phenytoin”.
12. Please consider starting the 6th sentence with “His EEG showed…” and please substitute “epileptic activity” with “epileptiform discharges”.
13. Case Presentation, Patient 2, 9th sentence: Please add “and” immediately
before positivity to p-ANCA.

14. Case Presentation, Patient 2, 10th sentence: Please correct “urinalyses” to “urinalysis”.

15. Case Presentation, Patient 2, last sentence: Please change “A control MRI” to “A repeat MRI”.

16. Case Presentation, Patient 3, 6th sentence: Please change the sentence to “Topiramate was initiated and she remained seizures free for over 2 years”.

17. Case Presentation, Patient 3, 10th sentence: Please change “SE stopped after…” to “The seizures subsided after IV diazepam was administered”. It is still not clear that the patient has SE (but rather frequent focal seizures).

18. Case Presentation, Patient 3, 14th sentence: In order to help with consistency, please give either the values for the C-reactive protein and erythrocyte sedimentation rate or remove the values provided for the previous two patients.

19. Case Presentation, Patient 3, 19th sentence: Please consider substituting “She was given” to “She was treated with”.

20. Case Presentation, Patient 3, 20th sentence and on, please consider changing to “In the following 14 months, the patient had two similar episodes of very frequent occipital seizures (or occipital seizure clusters) associated with transient MRI abnormalities. These resolved with appropriate antiepileptic therapy. After her last episode of seizure cluster, a repeat brain MRI revealed…. Due to persistent positive p-ANCA titers and ANA, she was given in addition to an optimized dose of carbamazepine, oral prednisone for one month, followed by azathioprine. The patient remained seizure-free at her 30-month follow up visit. The right temporo-parietal-occipital atrophy remained unchanged in a repeat MRI”.

21. For the Conclusions, I suggest for the first sentence the following change: “In our short series, SE or very frequent seizures represented the main or first neurological manifestation of what appeared to be p-ANCA related vasculitides”.

22. In the Conclusions, 3rd sentence, please add “such” after “other conditions” to read “such as malignancy…” and please add “and” after sarcoidosis to read “…and secondary vasculitis”.

23. In the Conclusions, 4th sentence, please change “Patient #1” to “The first patient…” or to “Patient 1”.

24. In the Conclusions, for the 6th sentence, please change the beginning of the sentence to “His MRI findings could have suggested posterior…”

25. In the Conclusions, for the 10th sentence, may I suggest to substitute “suggested” with “entertained”?

26. In the Conclusions, in the last sentence of the 3rd paragraph, may I suggest to change “in our patient #3” to “in the third patient” or “in patient 3”?

27. For the last paragraph of the Conclusions, I would like to suggest to add the following “physicians and in particular neurologists should consider ANCA assays
in patients with an otherwise unexplained …”

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I received grants for sponsored clinical research as principal or sub-investigator from:

UCB, Eisai, Sunovion and Lundbeck.