

Reviewer's report

Title: Hashimoto's encephalopathy: clinical features and outcomes in Chinese patients

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Reviewer: Sarah L. Tsai

Reviewer's report:

General Comments:

The central idea for the paper is good. The authors are providing a case series of "Hashimoto's encephalopathy" patients in the Chinese patients, which has not been done before. They describe clinical features, treatment and outcome in 15 patients by retrospective review.

This study provides useful information that I believe would be worth publishing. There are some significant issues that must be addressed prior to publication. I will address these issues in the requested categories:

• Discretionary Revisions:

- o I believe that Table 1 would look better if patient #, age and sex were put into different columns, this would simply make it appear more readable.

- o The authors state in the introduction that "a direct causal relationship between thyroid antibodies and HE seems unlikely," so why are they causing it HE? Many authors call HE "CNS vasculitis with positive antithyroid antibodies," as they feel it is more appropriate given the lack of evidence for antibodies in the pathophysiology of the condition. (This is my opinion, some current articles still call it HE.)

• Minor Essential Revisions:

- o There are some minor grammatical issues (corrections italicized):

- # Paragraph 5 of discussion "Cognitive impairment and altered level of consciousness have been proposed (as) essential for the diagnosis of HE."

- # Paragraph 2 of discussion "Cognitive impairment and psychiatric symptoms are among the most common symptoms; however, the frequency of seizures and myoclonus showed a big difference."

- # I am not sure what is meant by "the frequency of seizures and myoclonus showed a big difference" – how? Please be more precise.

- # The results are a bit hard to follow – I suggest identifying which patient (by study number) had features of interest. For instance, as a clinician reading this paper, I would like to know which patient had positive anti-thyroid antibodies in CSF or which one had abnormal MRI findings and correlate to information in Table 1. Perhaps Table 1 can be expanded or reorganized to incorporate other points of clinical interest. Alternately, the patients could be identified more clearly

in the results section.

- Major Compulsory Revisions:

- o The most significant issue that I have with this paper is how and why patients are classified as having “Hashimoto’s encephalopathy.” Why are patients without encephalopathy included as cases? Although the 2005 paper by Passarella is quoted, I do not feel that this is adequate evidence to include these patients. In the vast majority of HE literature, cases are identified as actually having encephalopathy.

Patient 1 – has positive antithyroid antibodies with “cognitive impairment, psychiatric symptoms and insomnia.” Could this be a patient with a psychiatric illness and positive antibodies? Patients with psychiatric illness can have insomnia and cognitive impairment as part of their condition and 10% of the general population has positive antithyroid antibodies. The authors have not convinced me that this is a “Hashimoto’s encephalopathy” patient. Why not a psychiatric patient who happens to have positive antibodies?

Patients 2 and 9 – Can we be sure that they are not patients with epilepsy who happen to have positive antibodies? Why are they classified as “Hashimoto’s encephalopathy?” They both got better on anti-seizure medication alone. Again, based on the information that has been presented, I am uncomfortable with these patients being labeled as HE.

- o We cannot label any patient with positive antithyroid antibodies and any kind of psychiatric or neurological symptom as having HE. This is not appropriate; however, this is what it seems like the authors have done. They either need to provide more evidence as to why they labeled certain patients as HE or take out cases without encephalopathy. Alternately, they could provide more evidence as to why patients without encephalopathy are included – at this point what they have provided is insufficient.

- o “Cognitive impairment” needs to be more clearly defined – this term encompasses a very wide clinical spectrum. How and why were these patients classified as being cognitively impaired?

- o The criteria that they are using for HE must be clearly stated in the introduction and in the abstract. Although diagnostic criteria have not been defined absolutely, they have been suggested in a number of papers (including some of their references) – it would be appropriate to mention these in the introduction and describe how patients have been classified in previous studies.

- o In paragraph 1 of the introduction, they state “Anti-thyroid peroxidase antibody, present in almost all HE cases, can also be found in euthyroid individuals.” This seems to imply that patients with HE are not euthyroid; however, this is often not the case. Many patients with “HE” have positive antibodies and normal thyroid function (the majority in several studies - this must be clarified.) There is no correlation with thyroid function and the encephalopathic process – this must also be clarified.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.