Reviewer's report

Title: Progressive dementia associated to ataxia and obesity in patients with Tropheryma whipplei encephalitis

Version: 3 Date: 31 January 2011

Reviewer: Allan Tunkel

Reviewer's report:

I have a number of comments regarding this manuscript, as follows:

1. In the title and in the body of the manuscript, the authors make the point of the presence of obesity in their patients. I have a concern with this being considered a major factor. They only describe the presence of obesity in 2 of their 5 patients (only 2 of the total of 20 patients). In fact, in one of the patients, he only developed weight gain when he relapsed, not with the original infection. Given these low numbers, how can they consider this to be so important?

2. On line 224 and in Table 2, the dose of trimethoprim-sulfamethoxazole indicated is 320/3200. I need clarification here, as the usual dose of tablets is a 1:5 ratio, not 1:10. A single strength tablet has a 40 mg of trimethoprim and 320 mg of sulfamethoxazole.

3. Line 250, should be central nervous system.

4. First paragraph of the discussion indicates that this is a disease of middle age men. However, the age range of the patients was 33-72 years, with 6 of the patients less than or equal to 40 years of age, and 40% of the patients were women (8 of 20). Therefore, I don't understand their characterization. In that paragraph, they also indicate their patients would certainly have died without treatment - how do they state this with certainty when there have been only 3 patients reported in the literature who have died?

5. Lines 353 and 354, I don't like the terms "spectacular" effect.

6. In the final paragraph of the discussion, the authors suggest that patients with unexplained progressive dementia, generally associated with ataxia or recent obesity, should get a trial of antibiotic therapy. I find this to be a very surprising conclusion - that is, to suggest that a patient be put on an empiric trial of 15-18 months of therapy with no diagnosis. Are they serious about this recommendation?

7. Page 17, which lists the legends. Table 1 is not a summary of patients with T. whipplei chronic encephalitis - that is Table 2. The legend for Table 2 is really the one for Table 3. I am not sure of the purpose of Figure 1 - that is, to show histopathology of someone without T. whipplei encephalitis.

8. Table 1. I do not understand how 3 patients with positive PAS staining can be
excluded as having the diagnosis when PCR testing was not performed. Are the authors also saying that a negative PCR absolutely excludes the diagnosis of T. whipplei encephalitis? Did these patients all have encephalitis?

9. Table 2, patient #7 was in 2 references - are they the same patient in two different publications?

10. Table 3, the heading of the last column should be Patients with certain or possible T. whipplei encephalitis. In that column with data taken from Table 2, 12/20 patients were male. For the cases reported from the literature, was there enough information to get definitive information as to whether all of the patients had arthritis, arthralgias, chronic diarrhea, and weight gain. In other words, were these reported as being present or absent in ALL cases?

11. Table 4 needs a little more explanation for me. In the second column on Whipple’s disease with neurologic manifestations, I would assume that many of these patients had encephalitis, especially since 72% had cognitive impairment. This is being compared to their 20 patients with Whipple’s encephalitis, so I am not that surprised there were some statistical differences, given the likely expectation that many of the 74 patients with neurologic Whipple’s had other neurologic conditions and not encephalitis. Were some of their 20 patients also part of the 74 previously reported in the literature.

12. Spelling issues throughout the text: trimethoprim-sulfamethoxazole and myorhythmia.

Level of Interest: An article of interest in its field.

Quality of written English: Acceptable, but will need some editorial review.

Statistical review: Not needed.

Declaration of competing interests: I declare that I have no competing interests.

Level of interest: An article of importance in its field

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 declare that I have no competing interests