Reviewer's report

Title: Obesity and progressive dementia associated with Tropheryma whipplei

Version: 2 Date: 27 July 2010

Reviewer: A von Herbay

Reviewer's report:

1. Major Compulsory Revisions

1.1. PCR testing was in the centre of this study, but the manuscript provides hardly any information to the reader about the PCR assay. While the authors feel this is stuff published elsewhere previously, essential information on methods must be included in the manuscript in sufficient details.

It appears unlikely that there should not have been changes in PCR testing over the years (2001-2009). If so, those changes should be made transparent accordingly.

1.2. Data about the success of DNA extraction from CSF samples, and from control PCR are lacking. This needs to be given in the results section.

1.3. It appears inappropriate to ban data about inconclusive findings in many patients to a supplementary table (#2). These conflicting data must be presented in the results section.

Given the absence of PAS positive particles and negative IHC, any positive PCR should be interpreted cautiously. Some readers might consider the author’s diagnosis in theirs cases #1 and #5 as “not certain”.

1.4. It is difficult to understand why in all patients with positive PCR results, cultures consistently failed to cultivate Tropheryma. This issue needs to be commented in the results section.

1.5. The author’s criteria how to define “certain” and “possible” WD, and how to exclude WD among published cases, needs to be reconsidered. How is it justified to restrict “certain” cases to those with PCR+, but to designate patients with electron microscopy as “possible”?

1.6. It is difficult to appreciate the reportedly low prevalence (0.7%) of positive PCR findings among the many CSF samples tested, as long as no information is provided about the patients under study.

To comply with standards of good practice, the authors must provide at least basic clinical data about their patients´ age and gender. In addition, they should provide information about the status of antibiotic treatment prior to CSF sampling, as this might explain some negative PCR results.
1.7. The report raises the question whether PCR testing of CSF in neurological patients is clinically reasonable, and whether a positive PCR result is sufficient to reach a diagnosis. This issue should be covered in the discussion section.

1.8. From a clinical perspective, the antibiotic regimen used to treat symptomatic cerebral Whipple’s disease is of interest. Unfortunately, this topic is not considered in the discussion section. This should be added in a revised manuscript.

2. Minor Essential Revisions

2.1. Information given on the index patient and the other four patients is out of proportion. A more balanced presentation of the five patients should be attempted.

2.2. The authors do not make use of the common designation “cerebral Whipple’s disease” for patients without intestinal Whipple’s disease. They prefer to designate their patients as “T.w. encephalitis”. They may have a point to do so, but they should outline this in more detail, and also why they consider a diagnosis of encephalitis, rather than cerebral infection.

3. Discretionary Revisions

3.1. The title should be reconsidered. The present title sounds a bit like a single case report.

3.2. The introduction section (about Whipple’s disease) is somewhat biased, and all references point toward the authors’ own publications.

3.3. The authors do not give reference to other’s experience with PCR tests applied to CSF samples in patients without intestinal Whipple’s disease. This should be added.

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 declare that I have no competing interests.