Reviewer's report

Title: Cerebrospinal fluid CXCL13 in Lyme neuroborreliosis and asymptomatic HIV infection

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Reviewer: Tobias Rupprecht

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The manuscript "Cerebrospinal fluid CXCL13 in Lyme neuroborreliosis and asymptomatic HIV infection" describes the CXCL13 levels in two disease entities, patients with Lyme neuroborreliosis and those with asymptomatic HIV infection and in a control group without inflammatory disease. The results broaden our knowledge about CXCL13 as a biomarker for infectious CNS diseases, but they are not new. There are actually major compulsory revisions that should be definitively met before acceptance is possible:

1) the authors state, that CXCL13 CSF levels in patients with HIV have not been previously systematically examined. They should include the results of the study by van Burgel et al. in their introduction, as they have already tested seven patients with asymptomatic HIV infection and six patients with HIV meningitis.

2) the diagnostic criteria for LNB are not according to the EFNS criteria (Mygland et al, European Journal of Neurology 2010). The detection of activated plasma cells in the CSF can not be regarded equal to a positive AI for Borrelia-specific antibodies. Only the latter defines definite cases of neuroborreliosis. How many of the 25 LNB patients had an elevated Borrelia-specific AI? And what was the median CXCL13 level in these patients?

3) The median CXCL13 level in LNB patients in the cross-sectional part of this study (498pg/ml) is unusually low! The study of Tjernberg et al. (J Infection 2011) measured CXCL13 in a large collective of 142 LNB patients and over 90% were higher than 500pg/ml and therefore higher than the median in the actual study. It is also unclear, why they did not include the CSF samples of the longitudinal study (also 25 patients), where the median was much higher (3,727pg/ml). If they would have done so, the statement of this study would have been different...They should therefore include in their discussion, that the median of their cross-sectional study was unusually low and that this is a limit of this study. Regarding the CXCL13 values in LNB patients in the study by Tjernberg et al., the specificity of CXCL13 in the actual study would have been as high as >95%!

4) Taken these limitations together, the diction "For this reason, elevated CSF CXCL13 concentrations can no longer be regarded as specific for spirochetal CNS infections. This reduces the potential value of CSF CXCL13 in diagnosing LNB" should be attenuated. This comparably small study is not empowered to give such a conclusion. The same applies to the Conclusions in the abstract.

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

**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.