Reviewer's report

Title: Cerebrospinal Fluid HIV Infection and Pleocytosis: Relation to Systemic Infection and Antiretroviral Treatment

Version: 2 Date: 25 June 2005

Reviewer: Gabriele Arendt

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Spudich et al. present a paper on correlations between cerebrospinal fluid (CSF) viral load (VL), white blood cell count (WBC) in CSF, plasma viral load, CD4+ cell count, AIDS dementia complex (ADC) stage and a quantitative neurological performance Z-score = QNZP), i.e., they examine the relationship between CSF and systemic HIV-infection. They found a positive correlation of CSF white blood cell count and plasma VL, but no correlation with CD4+ cell count, ADC stage and QNZP. Furthermore, they present the follow-up of 28 subjects over years. The authors conclude that CSF infection is common across the stages of HIV infection, but that it is unclear, whether the correlation to CSF pleocytosis is a response to CSF infection or its contributing cause. They expose the hints in the literature for a transient and an autothone CNS infection with the latter only slowly reacting to highly active antiretroviral therapy (HAART). The authors underline also that there is a long-term response of CSF infection to HAART, even though therapy fails in systemic disease pointing to discordant pharmacological resistancies.

The authors clearly expose their questions and use appropriate methods to answer them. The results and conclusions are convincing.

However, the authors should work on the data presentation, i.e., present
1. the clinical cases in a table, which would shorten the paper considerably;
2. furthermore, they should improve the table on clinical data of the study subjects, i.e., provide information on the CDC stages and duration of HIV-1-positivity of the study subjects, because it would be interesting to know, whether the patients with CSF pleocytosis are a longer or shorter time known to be HIV-1-positive than those without;
3. also, more precise information on duration and history of HAART in the individuals is warranted (f.e. on page 10, roe 3, it is said, that a patient has taken ddC and delarvidine, which seems to be an unusual combination; HAART history would make clear, whether there are individuals with more or less drugs said to be able to penetrate into CSF).

This paper is important, because it makes the lack of knowledge on neurological HIV disease quite clear. As long as we dont integrate information on CSF infection into routine patient care, clinicians will never know, whether an individual patient is in danger of developing virus related CNS disease, although it is well understood, that conventionell CSF markers do not provide this information very precisely.

Thus, conventionell CSF analysis including VL, could help to differentiate subgroups of patients (f. ex. those with higher CSF than plasma VL) and researchers must look for better disease markers for the other patients.
the paper should be accepted with minor essential revisions.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.