Reviewer's report

Title: Severe course of Lyme neuroborreliosis in an HIV-1 positive patient; case report and review of the literature.

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Reviewer: Raphael Stricker

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General Comments

The report by van Burgel and colleagues describes the fifth case of Lyme neuroborreliosis (LNB) in an HIV-infected patient. The manuscript is well written and the subject is important because of the growing risk of coinfection with Borrelia burgdorferi (Bb) as survival time and consequent potential tick exposure increases in HIV patients. The manuscript also raises several questions that beg for answers.

Major Comments

1. The authors report negative results for various HIV-related coinfections, but ironically they fail to mention coinfections with tickborne organisms such as Babesia, Anaplasma, Ehrlichia and Bartonella. Infection with all of these organisms has been reported in HIV patients (Vyas et al, Clin Infect Dis. 2007;45:1588-90; Falagas & Klempner, Clin Infect Dis. 1996;22:809-12; Talbot et al, Emerg Infect Dis. 2003;9:1123-7; Paddock et al, N Engl J Med. 1993;329:1164-7; Springer & Altice, Clin Infect Dis. 2003;36:e162-4; Lamas et al, Acta Trop. 2010;115:137-41), and like Bb these coinfections may be seronegative in the setting of HIV disease. The incomplete response to Bb therapy in the patient described in the manuscript might be attributed to inadequate treatment of a tickborne coinfection. Tickborne coinfections are also known to exacerbate LNB (Oleson et al, J Spinal Cord Med. 2003;26:168-71; Hongo & Bloch, Curr Treat Options Neurol. 2006;8:179-84; Eskow et al, Arch Neurol. 2001;58:1357-63), so diagnosis and treatment of these coinfections is important in the setting of LNB.

2. The authors state that persistent sequelae are "a very rare complication of LNB". To say the least, this statement is controversial. Studies in adults and children have shown persistent neurocognitive symptoms in a significant number of patients with treated LNB (Logigian et al, N Engl J Med. 1990;323:1438-44; Shadick et al, Ann Intern Med. 1994;121:560-7; McAuliffe et al, Appl Neuropsychol. 2008;15:208-19). Thus the persistent symptoms seen in the patient described by the authors may not be as uncommon as they assume.

3. Table 1 shows clinical data from the published reports of patients with LNB and HIV disease. Several modifications should be made to the Table: (a) Patient 1 had a CD4 T-cell count of 386/ul according to Table 1 in Reference 1. (b) It
would be better to show the normal range for CD4 T-cells in each study rather than the T-cell ratio, which is meaningless. (c) In addition to antiretroviral therapy, use or non-use of antibiotic prophylaxis should be listed for each patient (see #4 below). And (d) the V should be changed to F. In terms of the discussion of this Table, it is noteworthy that only Patient 3 met CDC criteria for AIDS based on a CD4 T-cell count under 200/ul. Thus LNB occurred in relatively healthy HIV patients, possibly explaining the relatively good outcome in these cases.

4. The reason that Bb infection is not described more often in HIV disease is unclear. Several explanations have been advanced, and the authors may wish to elaborate on them. The standard explanations are that the two infections occur in distinct populations, and that Bb infection may be masked by similar symptoms of HIV disease. These explanations are extremely weak. A more intriguing possibility is that prophylactic antibiotics given over the long term in HIV patients may prevent Bb infection, or that antiretroviral therapy itself may prevent Lyme disease. These possibilities raise issues about treatment of Bb that are important to consider. Along these lines, was the patient taking prophylactic antibiotics? If not, this should be clearly stated in the Case Report section.

Minor Comments
1. Was strain typing done for the Bb?
2. "Oligoclonal bands for B-cells were detected": This is a confusing sentence.

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.