Author's response to reviews

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

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Author's response to reviews: see over
Leiden, 9 August 2010.

Dear Editor and Reviewers,

Thank you for giving us the chance to resubmit our manuscript. Below are our point-to-point answers to the final concerns of the reviewers.

Reviewer 1
1. On 2 occasions (lines 36 and 157) they refer to “biologic” recovery. I believe they mean “microbiologic”.
   A: We adjusted the text accordingly.
2. In lines 158 and following, they refer to “sequelae commonly...”. I think the word “commonly” is potentially misleading as most systematic studies show these sequelae to be infrequent. I similarly think the statement that “neurologic sequelae are more frequently found in patients in whom treatment is delayed” is potentially misleading. True neurologic sequelae (as opposed to nonspecific symptoms in the absence of evidence of nervous system damage) ensue when a nervous-system-damaging event occurs. The longer the patient has the infection, the greater the opportunity for such an event to occur. If a facial palsy occurs on day 3, there can be permanent sequelae. If it occurs on day 90, sequelae are neither more nor less likely. Similarly for the very rare event described here – encephalitis.
   A: We adjusted the text. We would like to explain our hypothesis: This patient had an infection of unknown duration. But complaints had started only three months ago. In the reference of Hansen et al (ref 18) it is described that some patients present with an encephalomyelitis with an altered gait. These patients have complaints that are longer (>6 months) than in our described patient. However, in that article patients respond to the therapy. It is stressed that this response and recovery is often slower than in the patients with earlier stages of diseases, but nonetheless marked. Secondly it is described by the article of Shadick et al (ref 20) that (measurable) sequelae are more likely to take place in patients where treatment is delayed. But sequelae, though generally infrequent, most often consist of neurocognitive impairment, fatigue and complaints of paresthesia. We agree with the reviewer that is beyond a doubt that in prolonged infection damage is more prone to occur, and therefore also sequelae of the disease. What we try to show is that with a relatively short duration of illness this patient suffers from severe damage already, with minimal recovery over 4 years.
3. The conclusion that Lyme encephalomyelitis may be more severe in HIV infected patients can be neither proven nor disproven by one case report. This disorder is very rare. The fact that it occurred in one patient with HIV is very interesting, but cannot be taken as proof of the assertion. A more appropriate conclusion might be “When focal encephalomyelitis occurs in an area endemic for B burgdorferi infection, this infection should be considered as a rare possible cause. This case raises the possibility that this disorder might be more severe in immunocompromised individuals, such as those with HIV infection.”
   A: We understand the reviewers concerns and have adjusted the text to fit the suggestion of the reviewer better.
We have taken the reviewers comment to heart. The reviewer is correct about the prevalence of canine babesiosis and the case written by one of the co-authors of an HGE/anaplasma case near the German border. We have sent 10 samples from 2004-2010 to the National Institute of Health (RIVM) for analysis on Babesia, Ehrlichia and Anaplasma. They performed serology as they considered that the best diagnostic measure. There were no signs of infection in these sera. We therefore conclude that these pathogens played no role in this specific case. Bartonella serology and CSF PCR was performed and both were found negative.

We sincerely hope we have responded to the reviewers concerns adequately. Any questions that remain we are happy to answer,

Sincerely,
Nathalie van Burgel