Author's response to reviews

Title: Lyme neuroborreliosis in HIV-1 positive patients successfully treated with oral doxycycline: case series and literature review

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Author's response to reviews: see over
Cover Letter

Revised version of “Lyme neuroborreliosis in HIV-1 positive patients successfully treated with oral doxycycline: case series and literature review”

The authors are most thankful for the referees’ work and are of the opinion that the revision has significantly improved the article. Here follows a point-by-point description of changes made in response to the concerns raised by the referees.

General changes
  • Patient ethnicity has been added to all case presentations.

Referee 1: Unn Ljøstad
  • The language has been checked throughout the article.

Referee 2: Pia Forsberg
  • Abbreviations have been checked throughout the article.
  • The Swedish Medical Products Agency recommended treatment for Lyme neuroborreliosis is oral doxycycline, either 200 mg bid for 10 days or 100 mg bid for 14 days. As two of the patients in the article were treated somewhat longer, the reference to the Swedish Medical Products Agency has been omitted.
  • In Case reports, Patient 1: paragraph on hyponatremia has been rewritten.
  • In Case reports, Patient 1: paragraph that describes increase in CD4 cells has been omitted for clarity.
  • In Case reports, Patient 1: in paragraph on follow up six months later had been added “data not shown”. In the Materials and Methods section has been added a paragraph describing repeated lumbar punctures for some of the patients.
• In Case reports, Patient 2: last paragraph, this patient did not undergo a lumbar puncture at follow up after six months.

• In Case reports, Patient 3: paragraph on improvement of symptoms has been rewritten to be more specific. Dysgeusia (altered sensation of taste) has been changed to “change of taste of coffee”.

• Regarding opportunistic infections: for all patients bacterial and fungal CNS infections were ruled out by negative culture of CSF, cryptococcosis was ruled out by negative antigen test of CSF, viral infections were ruled out by PCR analyses for the most common neurotropic viruses, neurosyphilis was ruled out by negative syphilis tests of serum and CSF. The last sentence of the second paragraph of the Discussion section has been altered to specify this.

• In Discussion, second paragraph: the two borrelia serology samples for patient 4 were not analysed in parallel. The first sample was positive for IgM, negative for IgG; the second sample was positive for both IgM and IgG.

• In Discussion, fourth paragraph: sentence on atypical clinical picture has been rewritten for clarity.

• In Figure 1: patient number has been added to each line.

• In Table 1: abbreviations have been checked and reference values have been added for numerical values.

Referee 3: Franc Strle

• In Abstract, Introduction: second sentence has been rewritten according to the referee’s suggestion.

• In Abstract, Case Presentations: first sentence has been rewritten according to the referee’s suggestion.
- 3 -

- In Abstract, Conclusion: “LNB” is changed to “Lyme neuroborreliosis”, second sentence has been rewritten according to the referee’s suggestion.

- In Introduction, first paragraph: last sentence has been rewritten according to the referee’s suggestion.

- In Method and Material: First sentence has been rewritten according to the referee’s suggestion; dosage for oral doxycycline has been included in the last sentence.

- In Case reports, Patient 1: the patient’s admission to hospital has been specified.

- In Case reports, Patient 2: the patient’s admission to hospital has been specified.

- In Case reports, Patient 2: the duration of treatment is in accordance with what is now stated in the Method and Material section

- In Case reports, Patient 4: sentence on patient’s symptoms has been rewritten according to the referee’s suggestion.

- In Discussion, first paragraph: second sentence has been rewritten according to the referee’s suggestion.

- In Discussion, second paragraph: regarding the sentence “all the patients displayed a rapid response to anti-Borrelia treatment”; Case report, Patient 2 has been rewritten to clarify that symptoms started improving shortly after treatment initiation.

- In Discussion, third paragraph: previously published cases have been thoroughly reviewed; the patient previously described as having “headaches and myalgia” had only headache at the time of diagnosis of LNB.
In Discussion, fourth paragraph: on the severity of symptoms being influenced by the impaired immunity in patients with HIV-1 infection; a sentence have been added stating that the mechanism by which this might happen is unknown.

In Discussion, fourth paragraph: posterior circulation refers to the vertebro-basilar part of the cerebral circulation.

In Discussion, fourth paragraph: “normal pressure hydrocephalus caused by LNB” has been changed to “normal-pressure hydrocephalus in patients with LNB”.

In Discussion, sixth paragraph: “in the acute stage of the Borrelia infection” has been changed to “at time of diagnosis of the Borrelia infection”.

In Conclusions, “atypical neurological symptoms” has been changed to “neurological symptoms”.

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