Author’s response to reviews

Title: Meningitis and brain edema, rare presentation of minocycline-induced hypersensitivity syndrome

Authors:

Nicolas N Lefebvre (n.lefebvre@yahoo.fr)
Emmanuel E Forestier (emmanuel.forestier@chru-strasbourg.fr)
David D Farhi (farhidavid@yahoo.fr)
Veronique V Remy (veronique.remy@ch-cahors.fr)
Olivier O Lesens (olesens@chu-clermontferrand.fr)
Massa M Mohteshim-Zadeh (massa.mohseni-zadeh@chru-strasbourg.fr)
Yves Y Hansmann (yves.hansmann@chru-strasbourg.fr)
Daniel D Christmann (daniel.christmann@chru-strasbourg.fr)

Version: 3 Date: 8 March 2007

Author’s response to reviews: see over
Article: “Minocycline-induced hypersensitivity syndrome presenting with meningitis and brain edema: a case report.” (MS 1298757624125347)

Strasbourg, 2007-03-07

Dear Editor,

We thank you and the reviewers for the useful comments and suggestions to improve the text, please find attached the revised version of our article. Corrections and revisions requested by both reviewers have been made and all the recommendations for authors published online have been rigorously followed.

Here is a point-by-point response to the concerns expressed by the reviewers.

1. Reviewer 2: “The manuscript will require extensive editorial revision in all sections, in terms of spelling, correct grammar, writing style, etc. The authors use some words that I think are not in the context of what they meant to say”.
   Quality of written English: “Not suitable for publication unless extensively edited”

Answer: The manuscript was extensively re-worked by a native English-speaking medical epidemiologist. All the sections were reviewed and more appropriate wording used. The title was written according to instructions to authors.

2. Reviewer 2: “On physical examination, what were all the vital signs? Was a neurologic examination done and was it normal?”

Answer: Physical examination has been fully described in the text: the description of vital signs and neurological examination were added (they were normal).

3. Reviewer 2: “Was a biopsy of one of the lymph nodes performed to try to establish an etiologic diagnosis or exclude other etiologies?”
Answer: Because of the sudden onset of the disease, which rapidly resolved after withdrawal of minocycline and steroids, lymph node biopsy was not performed. Infectious agents (bacteriological or fungal) were not likely because of the favourable evolution (one year follow-up) without antibiotics. Viral infections could have been possible but all serologies were negatives at presentation and 2 weeks later. Moreover, testing for viral nucleic acid (PCR) in cerebrospinal fluid was negative. Malignancy (leukemia, lymphoma) was unlikely given the favourable evolution after a long follow-up. A biopsy would have been undertaken had the condition worsened early on.

4. Reviewer 2: “What cultures were specifically performed? Was culture of cerebrospinal fluid done for all infectious agents? In terms of the viral serologies, were acute and convalescent sera sent to attempt to identify recent exposure to specific agents? The authors state that several viral etiologies were negatives or cicatricials. I don’t understand their use of the term ‘cicatricial.’ »

Answer: In an effort to be concise, we removed exhaustive description of bacteriological cultures and viral serologies in the first manuscript. Culture and PCR testing of cerebrospinal fluid were done for bacterial and viral agents and were negative. This has now been included in this revised version.

Answer: Acute and convalescent sera were sent to attempt to identify recent exposure to multiple specific agents. This is exactly what we meant by the term ‘cicatricial’ (which is the French for convalescent in this context). We have made the correction in the text.

5. Reviewer 2: “What was the cerebrospinal fluid glucose concentration? Was HIV PCR done on spinal fluid? A repeat lumbar puncture would also have been useful to document normalcy.”

Answer: Glucose concentration in CSF was 3.1 mmol/L (included in the text). We agree that a repeat lumbar puncture could have been done to document return to normal. However, as the patient was feeling much better, we decided not to do it. Besides, a CT-scan was done after 2 weeks and was normal.

Answer: Unfortunately HIV PCR was not done in the CSF, but the HIV viral load was not very high and HIV meningitis was improbable in this context.

6. Reviewer 2: “In the discussion and a review of the references, it would appear that Knowles et al reviewed 13, not 11, cases. Did they find any similar cases of meningitis and brain edema when they reviewed the literature”
Answer: We have corrected the number of patients reviewed by Knowles et al. (13 and not 11).

Answer: We agree with reviewer 2 that we should have been more precise in our introduction and discussion, because we did not find any similar case of lymphocytic meningitis and brain oedema due to minocycline in the literature. We have corrected this element.

Furthermore, to reply to the general comment of reviewer 2, we have added in the discussion the elements of the diagnosis in terms of chronology, symptoms and differential diagnosis: according to all those criteria, hypersensitivity syndrome was very likely in our patient.

Answer to general comments:
We agree with reviewer 1 that increase awareness about potentially serious side effect of a widely prescribed drug should be communicated to clinician:

“This is an important case report on a rare adverse effect of minocycline. It will increase the awareness for adverse effects in this drug as a potential differential diagnosis of lymphocytic meningitis and brain edema.” (Reviewer 1)

Please keep us informed if any further information is needed.

Yours faithfully,