Reviewer’s report

Title: Paradoxical response to disseminated non-tuberculosis mycobacteriosis treatment in a patient receiving tumor necrosis factor-alpha inhibitor: a case report

Version: 2

Date: 30 January 2014

Reviewer: David Cohn

Reviewer’s report:

General Comments

This is an interesting and unique case report of a patient with relapsing polychondritis treated with a TNF# inhibitor (adalimumab) who developed disseminated MAC infection, and then significantly worsened after initiation of appropriate antimycobacterial therapy and discontinuation of the anti-TNF# inhibitor, presumed to be due to a paradoxical reaction. The case is well documented by the description of clinical course, microbiological and radiographic findings. There are numerous structural or grammatical changes which should be made as suggested below.

Major Compulsory Revision (Recommendation)

A thorough literature search should be re-done to ensure there are no prior case reports of NTM with paradoxical reactions in HIV-uninfected patients (as there are with tuberculosis), including those that may be embedded in series of opportunistic infections in patients treated with TNF# inhibitors.

Minor Essential Revisions

1. P3 p1 Abstract Add …revealed “new” granular...
2. You use the term M. intracellulare and M. avium complex (MAC) interchangeably throughout the manuscript. I would suggest using one or the other. Was the isolate definitely speciated as M. intracellulare, as opposed to MAC, or not? If yes, perhaps state that it was M. intracellulare when you first report the culture results, and use MAC in the rest of the manuscript. If not, use MAC throughout.
3. P3 p2, P4 p1, P7 p1 Change “mediastinum” to “mediastinal”
4. P4 p1 Delete …in “the” tuberculosis…
5. P4 p1, P8 p1 Change “reduce’ to “decrease”
6. P4 p2 Delete “The” clinicians…
7. P4 p 2 Change “got” to “get”
8. P4 p2, P10 p3 Change “adequate treatment” to “optimal management”
9. P5 p1 After …“fungal infections.” add additional references from the literature
on opportunistic infections with biological agents

10. P5 p1 Add ..with” known” NTM...

11. P5 p2 Delete …tuberculosis “infection” after...

12. P6 p1 What was the dose (or dose range) of prednisolone used?

13. P6 p1 For IGRA and anti-MAC antibody assays, add in parentheses the manufacturers of tests that were used

14. P6 p1 Change “manifestation” to “manifestations”

15. P6 p2 For CRP, give normal range or upper limit of normal for your lab after 13.81 mg/dl

16. P6 p2 For “almost”, do you mean “all”?

17. P7 p1 Change …“the” to “this” NTM...

18. P7 p1 If you are going to use abbreviations, for rifampicin, I would use “RIF” instead of “RFP” and for ethambutol, “EMB” instead of “EB”

19. P7 p1 Change the “4-month treatment” to “4 months of treatment”

20. P7 p1 Move “increased” to after “lymphadenopathy”

21. P7 p1 Paragraph break at “Because”...

22. P7 p1 Before “We then changed..”, add “After ? months of antimycobacterial therapy with CAM, RIF and EMB...”. It appears this change in therapy occurred later than the 4 months referred to above (looks like about 6 or 7 months in Figure 2 ??)

23. P7 p1 Change …“the” to “this” NTM...

24. P7 p1 Change …abscesses “still enlarged.” to “continued to enlarge.”

25. P7 p1 Change …nodes “were enlarged” to “enlarged more” with...

26. P8 1 Delete ..in “the” tuberculosis...

27. P8 p1 Change …”has now been” to “was” increased...

28. P8 p1 Change …“has now been” to “was” increased...

29. P8 p1 Change sentence to read “The clinical course, culture results, treatment regimens and CT scan images are shown serially in Figure 2”

30. P8 p2 Change “Conclusion” to “Discussion”

31. P8 p2 Change …“about RP case complicating with NTM” to “of a RP case with NTM as a complication”.

32. P8 p2 Change …“is” to “has been” reported “in Thailand and Taiwan”...“MAC” to “NTM”, and IFN- # “antibody” to “autoantibodies” (as described in ref 5)

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35. P9 p1 Add …including “the use of” infliximab...

36. P9 p1 Change to …average “ time from the initiation of biological agents to
the development of NTM was 10 months”...”similar to” our case...
37. P9 p1 Change “included” to “reported”. “the adequate” to “to appropriate”
38. P9 p1 Change “indicated” to “had a” …paradoxical “effect” to “reaction”
39. P9 p2 Add references after sentences on definition of IRIS (e.g., Meintjes et al) and IRIS in HIV-infected patients (e.g., Shelburne et al, Burman et al, Lawn et al, Narita et al)
40. P9 p2 Change “during active” to “after the initiation of” antiretroviral...
41. P9 p3 Change …patients “who…infection”…to “with tuberculosis” after...
42. P10 p1 Add …evidence “to recommend a specific course of action” in...
43. P10 p2 Change …case “indicated paradoxical effect” to “had a paradoxical reaction” to...
44. P10 p2 Please double check that there are no case reports of NTM paradoxical reactions in HIV-negative patients
45. P10 p2 Delete …“unlike tuberculosis treatment.”
46. P14 Legend Figure 2 Add …clinical course, “microbiological results, treatment regimens” and computed...

Level of interest:An article of importance in its field

Quality of written English:Needs some language corrections before being published

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