Author's response to reviews

Title: Intracranial abscess due to Mycobacterium avium complex in an immunocompetent host: a case report

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Author's response to reviews: see over
Dear Dr. Logan
Executive Editor
BMC Infectious Diseases

Thank you and the peer-reviewers for your positive and constructive comments regarding our submission: “Intracranial abscess due to Mycobacterium avium complex in an immunocompetent host: a case report.” We have addressed all of your suggestions and would like to explain to you the following changes we have made in accordance to these suggestions:

1) Reviewer 1:
   a. Comment #1:
      i. Page 3, Lines 12-13. Bronchiectatic pulmonary MAC commonly occurs in older women without underlying lung disease. There has been some research on this that should be quoted on page 7, Lines 2-6
   b. Response #1
      i. Thank you for highlighting this additional information. We have included this information on Page 7, Lines 11-13.
      ii. Specifically, we wrote “Additionally, specific non-immunocompromised groups have shown a predisposition for MAC pulmonary infection; reports show an increasing prevalence of bronchiectatic pulmonary MAC disease in elderly women without underlying risk factors [11].”
   c. Comment #2
      i. Note is made that the patient is HIV-negative, but no mention is made of when that test was done. Was a test done during this illness?
   d. Response #2
      i. Thank you for pointing this out. The patient was indeed tested for HIV during this illness. We have now included this information on Page 6, Lines 1-2.
      ii. Specifically, we wrote, “Additionally, the patient was tested for HIV following abscess resection with negative results.”
   e. Comment #3
      i. Page 7, lines 15-17: 7/8 patients had some immunodeficiency, but what about the one remaining patient? You state that this is the first case of CNS MAC in an immunocompetent patient, but there appears to be one more.
   f. Response #3
      i. We apologize for the confusion and have made this comment more clear in the discussion section.
ii. **On page 8, Lines 2-8**, we wrote, “The additional immunocompetent case diagnosis is unclear as the patient presented with risk factors for MAC infection. The case describes a patient with chronic granulomatous meningitis who subsequently developed a secondary MAC brain abscess as a consequence of immunosupression due to prednisone therapy [12]. Moreover, the CD4 count was unknown. Our patient however, presented with a normal CD4 count, negative HIV status and without any existing co-morbidities”.

g. Comment #4
   i. Page 8, Lines 8-16: You should reference the ATS NTM treatment guidelines here, which are more pertinent for immunocompetent individuals. Azithromycin is a perfectly good alternative to clarithromycin and does not interact with rifabutin or rifampin.

h. Response #4
   i. We have now referenced (reference #19) the joint ATS/NTM treatment guidelines on Page 8 and 9.

   ii. **On Page 9, Lines 8-9**, we wrote, “Guidelines from the Centers for Disease Control and Prevention, American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA)…”

   iii. Additionally, **on Page 9, Lines 13-17**, we wrote, “Alternatively, azithromycin can be substituted for clarithromycin as it is efficacious and unlike clarithromycin, does not interact with rifabutin or rifampin in patients with AIDS [19]. In HIV patients, the United States Public Health Service and ATS/IDSA guidelines recommend minimum therapy for 12 months and 6 months of immune reconstitution [19]”.

i. Comment #5
   i. It would strengthen your paper to give more info about how the diagnosis was made. Since neoplasm was the leading differential, was culture even done up front? Or did a frozen section reveal granulomas, which gave a clue to send cultures?

j. Response #5
   i. Thank you for this suggestion. We have made the following changes:

   ii. **On Page 5, Lines 10-12**, we now wrote, “At the time, the etiology of the lesions was felt to be more likely neoplastic rather than infectious in the absence of any known immunocompromised state. Therefore, blood cultures were not obtained”.

   iii. **On Page 5, Lines 15-17**, we now wrote, “Upon incision the large left frontal lobe lesion was full of purulent material from which multiple
cultures were acquired. At this point, the differential favored intracranial abscess rather than neoplasm”.

2) **Reviewer 2:**
   a. **Comment #1:**
      i. P. 2 Line 14: the patient’s presentation was “uncharacteristic”; please clarify uncharacteristic of what

   b. **Response #1**
      i. Thank you for your suggestion. **On Page 2, Line 14-15**, we now wrote “The patient’s presentation was uncharacteristic of MAC infection in immunocompetent hosts, as he developed subacute, progressive symptoms that included severe frontal headaches, left eyelid swelling, blurry vision, and diplopia, without any pulmonary or systemic manifestations”.

   c. **Comment #2**
      i. P. 2 line 18: would change sentence to: MAC was the only pathogen that grew from intraoperative tissue cultures

   d. **Response #2**
      i. This has been changed per your suggestion on Page 2, Lines 18-19.

   e. **Comment #3**
      i. P. 4 Case presentation. Please list medications, including any herbals, over-the-counter. If none, please state that patient denied any history of immunosuppressive medications (or report if this was not elicited). Also report if any family history of autoimmune disease or other relevant conditions.

   f. **Response #3**
      i. Thank you for your suggestion. **On Page 4, Lines 9-11**, we now wrote, “The patient was not using any current medications and he denied a history of immunosuppressive drugs. Moreover, his family history was only positive for hypertension, without any mention of autoimmune disease”.

   g. **Comment #4**
      i. P. 5 second paragraph. Please report if AFB blood cultures were obtained and result? Also results of routine bacterial blood cultures?

   h. **Response #4**
      i. We have addressed this **on Page 5, Line 22 - Page 6, Line 2**.

         ii. Specifically, we wrote, “Intraoperative bacterial, anaerobic and fungal cultures however were all negative. Routine blood cultures, AFB blood
cultures and QuantiFERON® TB Gold test were also negative. The patient’s sputum culture however was positive for AFB. Additionally, the patient was tested for HIV following abscess resection with negative results.”

i. Comment #5
   i. Add CD4% to absolute count

j. Response #5
   i. On Page 6, Line 3, we have added the CD4% (32%) to the absolute count.

k. Comment #6
   i. P. 5 second paragraph, please delete “however” when reporting result of QFT blood test, as we do not necessarily expect this to be positive in a case of active mycobacterial disease (better test for latent infection)

l. Response #6
   i. Thank you. We have made this change per your suggestion. This is reflected on Page 5, Line 23.

m. Comment #7
   i. The patient had a positive AFB sputum smear. Please report when the AFB sputum cleared.

n. Response #7
   i. On Page 6, Line 14, we wrote, “Sputum AFB was negative at 7-months.”

o. Comment #8
   i. Please provide more detail about the patient’s clinical resolution. What specific symptoms/signs resolved and over what time period? Where there any follow-up radiology studies?

p. Response #8
   i. On Page 6, Lines 11-15, we wrote, “The patient’s neurological symptoms, exophthalmous, diplopia and mass effect fully resolved over the following 6-months. The blurry vision persisted, but was corrected with glasses. Sputum AFB was negative at 7-months. Furthermore, follow-up MRI at 8-months was negative for intracranial abscess”.

q. Comment #9
   i. P.6. 1st paragraph in discussion is redundant with introduction. May delete this paragraph altogether.

r. Response #9
We have deleted this paragraph per your suggestion.

Comment # 10
i. P.8 please comment on CNS penetration of the drugs.

Response #10
i. On Page 9, Lines 1-6, we now wrote, “The penetration of anti-NTM drugs to CNS infections is further complicated by the relatively impermeable blood-brain barrier (BBB). Ethambutol and the macrolides only reach sufficient CSF concentrations in the presence of meningeal inflammation [20]. Although rifampin shows greater efficacy in penetrating the BBB than the other drugs, it may be below the minimum inhibitory concentration level for some microbial strains [20, 21].”