Author’s response to reviews

Title: Intracranial actinomycosis of odontogenic origin masquerading as auto-immune orbital myositis: a fatal case and review of the literature

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Author’s response to reviews:

Dear Mr. Belibasakis,

Thank you for your positive response and the additional comments on the manuscript “Intracranial actinomycosis of odontogenic origin masquerading as auto-immune orbital myositis: a fatal case and review of the literature”. We have addressed these final suggestions and provide a point-by-point description of the changes made to the manuscript. Please find this description attached below.

Yours sincerely,

Gijsbert J. Hötte
Reviewer 1:
No additional comments

(Reviewer 2):

General comments:
1. Thank you for the thorough answers to my comments. Now having had the answers I understand that the only finding suggestive of actinomyces infection was the brain autopsy sample with gram positive filamentous bacteria. Therefore, actinomycosis diagnosis is probable but actinomyces was not definitely shown to be the causative agent. The authors should bring this up as a weakness/uncertainty of the study in the discussion. The appearance of the timeline has greatly improved in revision!
*** To clarify the uncertainty of our diagnostic process we have made additional changes to the text (lines 186-187 and 240-241)

Detailed comments:
1. Line 46. Autopsy showed actinomycotic meningoencephalitis > Autopsy showed bacterial aggregates suggestive of actinomycotic meningoencephalitis
***This is a valid point and we have changed it in the text (line 46)
2. Line 63. Actinomycetacae > Actinomycetaceae
Not all genera in this family are known to belong to the commensal flora of the oropharyngeal cavity. Actinomyces, Nocardia and Streptomyces are not the three genera of Actinomycetes/Actinomycetaceae. Please correct the facts and update the bacterial classification or leave it out of the manuscript.
*** “Actinomycetaceae (often called Actinomycetes) are a family of bacteria belonging to the normal commensal flora of the oropharyngeal cavity. Actinomyces, Nocardia and Streptomyces are three genera of Actinomycetes and are known to rarely cause intracranial infection of odontogenic origin” has been replaced by “In the order of Actinomycetales, Actinomyces is a genus of the Actinomycetaceae family, whereas Nocardia is a genus of the Nocardiaceae family. Both genera belong to the normal commensal flora of the oropharyngeal cavity and are known to rarely cause intracranial infection of odontogenic origin” (lines 63-69)
3. Line 67. As the actinomycosis diagnosis was based only on the staining result in the autopsy brain sample, the word "presumed" should be moved in front of the word "intracranial", i.e. "presumed intracranial and intra-orbital actinomycosis…"
*** This is a valid point and we have added the word “presumed” (line 70)
4. Line 88. Borrelia burgdorferi > Borrelia burgdorferi, Treponema pallidum > Treponema pallidum
*** We assume that the reviewer has suggested to write these names in Italic (perhaps this has been omitted in the decision letter we received). The font of both Borrelia burgdorferi and Treponema pallidum has been changed to Italic (line 91).
5. Line 117. Staphylococcus aureus > Staphylococcus aureus
*** We assume that the reviewer has suggested to write these names in Italic (perhaps this has been omitted in the decision letter we received). The font of Staphylococcus aureus has been changed to Italic (line 120).
6. Line 138. "…of abnormal…" > should it be "…or abnormal…"
*** The word “of” has been changed to “or” (line 139)
7. Line 158. Regarding classification, please remove the beginning of the sentence and start the
sentence by "Actinomyces and Nocardia…"

*** The beginning of the sentence has been removed (line 160)

8. Line 159. Actinomycetaceae > Actinomyces

*** Actinomycetaceae has been changed to Actinomyces (line 161)

9. Line 161. microaerophilic > microaerophilic, Actinomyces requires > Actinomyces species require

*** Microaerophilic has been changed to microaerophilic. Actinomyces requires has been changed to Actinomyces species require. (line 163-164)

10. Line 254. Targeted assays for which microorganisms?

*** “Additional targeted 16S rRNA assays turned out negative” has been replaced by “Additional targeted 16S rRNA assays, in order to distinguish Actinomyces from Nocardia, turned out negative due to poor quality of the RNA” (lines 243-244)

11. Line 285. …the first report of actinomycotic orbital…. > …the first report of probable actinomycotic orbital….

*** The word probable has been added to the text (line 273)

Additional changes:

1. Department of Cranio-maxillofacial Surgery has been replaced by Department of Oral and Maxillofacial Surgery (line 14)

2. Department of maxillofacial surgery has been replaced by department of oral and maxillofacial surgery (line 99)