Author’s response to reviews

Title: Pulmonary fungus ball caused by Penicillium capsulatum in a patient with type 2 diabetes: a case report and literature review

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Author’s response to reviews: see over
Dear Editors,

Thank you very much for your letter and advice on our letter of case report (MS 9615314579494818).

We have revised the manuscript in light of the comments, provided a point-by-point response to the concerns, and would like to re-submit it for your consideration. The amendments are highlighted in red in the revised manuscript, and all authors have seen and approved the revised manuscript.

Additionally, we added Chao Zhang in the authors list because he performed the in vitro susceptibility test of the *P. capsulatum* isolates.

We hope that the revision is acceptable, and we look forward to hearing from you soon.

With best wishes,

Yours sincerely,

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Firstly, we would like to express our sincere thanks to the reviewers for the constructive, positive and professional comments on our manuscript.

Replies to Reviewer1 (Brunella Posteraro)
1. We have added the two articles (Clin Infect Dis. 2012 54:e8-e19 and Mycopathologia. 2013;175:57-67) into references of the manuscript according to the reviewer’s suggestion, for better emphasizes the ever-increasing importance of penicilliosis.
2. In abstract, we deleted the first sentence and the abstract started as “Following the recent transfer…….” in accordance with the reviewer’s suggestion in background section; the penultimate sentence also revised as “…·based on the morphological analysis of microscopic and macroscopic features and on the ribosomal internal transcribed spacer (ITS) sequencing” in case presentation part; also, we revised conclusions to a unique sentence.
3. In background of the text, we revised the entire background section such as combined second and third sentences;
4. With regard to the growth on CYA and YES of our clinical isolate, we have not gone into details about the microscopical features of the *P. capsulatum* isolate on CYA and YES culture. Actually, it is common practice in *Penicillium* (and *Aspergillus*) species taxonomy to only describe the micromorphology on MEA, and the agar media CYA and YES are only used on macroscopical analysis and often show atypical structures. Also, the sentence starting with “Growth on MEA plates incubated at ……….” has to be referenced with the Figure 3.
5. As for the figure 4 comment, we have added some taxonomic details about the cited Ramigena section to make it more understandable for readers.
6. In conclusions of the text, we deleted the first sentence and modified other sentences as suggested in the first paragraph; In second paragraph, we substituted “and” with “but” in the first sentence, and modified other sentences as the reviewer’s suggestion; Also, we deleted the sentence starting with “In this
case, "infection" and substituted the term “symptoms” with “clinical manifestations” in the last sentence in third paragraph.

7. We have Modified the list of the references according to new insertions, and the reference numbers within the text.

8. In legends, we have used “Histologic” instead of “Histological” in Figure 2 in light of the reviewer’s suggestion.

9. In Figure 4, “NT” means “Neotype”, and “T” means “Type”.

10. Last but not least, the revised manuscript has been edited by two native English speakers from American Journal Experts Company.

Replies to Reviewer 2 (Morena Caira)

1. The patient was treated with caspofungin. When was it started? Can the authors provide susceptibility test?

Our answer: The patient was treated with caspofungin (70 mg/day, 14 days) and fluconazole (400 mg/day, 90 days) at once after pulmonary lobectomy. Compared with the other two P. capsulatum strains (ATCC10420, ATCC48735) from environment, our clinical isolate (CBS134186) has just been evaluated to six antifungal agents (amphotericin B, voriconazole, itraconazole, ketoconazole, fluconazole, 5-fluorocytosine) using CLSI M38-A2 broth microdilution method. There is no significant difference of antifungal susceptibilities between the P. capsulatum strains isolated from environment and clinical source. We also find that fluconazole and 5-fluorocytosine are not suitable for antifungal treatment on P. capsulatum infections. The data showed in Table 1.

Table 1. Antifungal susceptibilities of P. capsulatum isolates from environment and clinical source (µg/mL)

<table>
<thead>
<tr>
<th></th>
<th>amphotericin B</th>
<th>voriconazole</th>
<th>itraconazole</th>
<th>ketoconazole</th>
<th>fluconazole</th>
<th>5-fluorocytosine</th>
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<tr>
<td>ATCC10420</td>
<td>1</td>
<td>1</td>
<td>0.25</td>
<td>0.125</td>
<td>&gt;64</td>
<td>16</td>
</tr>
<tr>
<td>(P. capsulatum)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATCC48735</td>
<td>1</td>
<td>0.5</td>
<td>0.25</td>
<td>0.0625</td>
<td>&gt;64</td>
<td>32</td>
</tr>
<tr>
<td>(P. capsulatum)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>CBS134186</td>
<td>0.5</td>
<td>0.5</td>
<td>0.25</td>
<td>0.0625</td>
<td>&gt;64</td>
<td>32</td>
</tr>
<tr>
<td>(P. capsulatum)</td>
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</tbody>
</table>
2. The authors reported the result of beta-d-glucan test, while galactomannan has not been reported. Was it available?
Our answer: There is no data on galactomannan test in our case report, for galactomannan test is not available in our hospital yet.

3. Did the authors check beta-d-glucan after caspofungin treatment? Results of both microbiological and radiological tests confirming the good results should be provided.
Our answer: No, we did not check beta-d-glucan test after antifungal treatment mainly due to the patient is poor. Frankly, she was not willing to pay for other diagnosis cost when she found she have been recovery. Maybe we could check beta-d-glucan test after antifungal treatment if we met another similar patient.

4. Literature revision has not been comprehensively reported in the text, so I suggest to modify the title. (please remove “literature revision” from the title)
Our answer: Yes, we have removed “literature revision” from the title.

5. Last but not least, the whole revised manuscript has been edited by two native English speakers from American Journal Experts Company.