Author’s response to reviews

Title: Earliella scabrosa-associated Postoperative Endophthalmitis after Phacoemulsification with Intraocular Lens Implantation: a Case Report

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Author’s response to reviews:

Dear editors and reviewers,

Thank you for your letter and for the reviewers’ comments on our manuscript entitled “The First Case Report of Earliella scabrosa-associated Postoperative Endophthalmitis after Phacoemulsification with Intraocular Lens Implantation” (ID: [BOPH-D-17-00446]). All of these comments were very helpful to use while we revised and improved our paper. We have carefully studied these comments and made corrections that we hope will meet with your approval. [The changes in the revised manuscript are marked in red.]* The responses to the reviewers’ comments are provided below.

Reviewer 1#:

1. Reviewer’s Comment: There is a recent human case report of opportunistic infection suspected by Earliella scabrosa (PMID: 28221210). Some of the descriptions in the abstract and conclusion should be changed because this is not the first case of human infection by Earliella scabrosa. And also the article should be cited in this article.

Response: What the Reviewer states is true. Thus, the statement “Earliella scabrosa (an agent of white rot on wood) has never been reported in infectious human disease” was corrected and changed to “Earliella scabrosa has never been reported as an infectious agent in the human eye”; the statements “To the best of our best knowledge, this is the first case report of a human infection associated with Earliella scabrosa ”were corrected as “Here we report a case of a human eye infection that was associated with Earliella scabrosa.”; the statement “However, this organism has not yet been implicated in human infections” was deleted. Additionally, the previous study recommended by the reviewer (PMID:28221210) was cited in the Discussion.
section as “Notably, a recent case report published by Desmond Shi-Wei Lim et al. was the first to document that this organism can infect humans [10]. In Lim’s report, this pathogen caused cutaneous fungal septic emboli in an immunocompromised child, resulting in mortality”. This study was also added to the reference section.

2. Reviewer’s Comment: It would be better if the author could add a detailed history of the patient within one month of cataract surgery. The ophthalmic history of this period is difficult to accept in a few points.

   a. If the endophthalmitis started within 3 days of surgery, how was the infected eye maintained for one month only with levofloxacin topical medication without antifungal therapy?

   b. Why did the eye surgeon continue to administer levofloxacin eye drops alone for one month without providing other treatment options such as intravitreal injection?

   c. Was there any occupational or environmental risk factor that could increase exposure to Earliella scabrosa in the patient or surgery hospital?

   d. In the first human infection case with Earliella scabrosa was an opportunistic infection in the immune-compromised state and resulted in mortality despite a massive antifungal agent (PMID: 28221210). However, for this case, the patient was not in a severely immune-compromised state (though the patient had diabetes) and the clinical course was very mild. How can you explain this discrepancy?

Response: We have re-written the “Case presentation” section according to the Reviewer’s suggestion. The detailed history of the patient within one month of cataract surgery was described as follows: “One month before admission, the patient underwent phacoemulsification and IOL implantation in a local hospital. Within 72 hours of this surgery, he presented at a private clinic with irritation, redness and reduced vision in the right eye. The patient was treated with antibacterial medications (levofloxacin eye drops, six times per day) for 3 days, and it was suggested that he present for a subsequent visit 3 days later. However, the patient missed this follow-up visit, and he applied the levofloxacin eye drops for one month. At one month after his presentation at the private clinic, his signs and symptoms had not improved. It was at this time that the patient was referred to the Hainan Province Eye Hospital (Haikou, China).”

   a. According to the patient’s statement, he should have completed a subsequent visit after he was told to apply the levofloxacin eye drops for 3 days. However, he failed to complete this visit, and he continued to use the eye drops for one month before he was referred to Hainan Province Eye Hospital.

   b. According to the patient’s statement, he presented at a private clinic instead of a local hospital. The doctor in the private clinic suggested a subsequent visit after he told the patient to apply levofloxacin eye drops for 3 days. However, the patient failed to complete the later visit.
c. Environmental risk factors were not assessed because the surgery was performed in a local hospital before the patient was referred to Hainan Province Eye Hospital.

d. In consideration of the Reviewer’s suggestion, we have explained this discrepancy in the discussion section as follows: “We noticed that there is considerable discrepancy between the prognoses described in Lim’s and this report. In Lim’s report, this pathogen resulted in death despite the use of massive antifungal treatment. However, in this case, the course was mild. One potential reason for this discrepancy is that the characteristics of the site of initial presentation were different. In the child described in Lim’s report, the skin was the initial site of infection. The vascular network within the skin may have facilitated the formation of vascular emboli by fungal hyphae, resulting in the dissemination of the infection and multi-organ involvement. On the contrary, the vitreous of the eye can, to some extent, restrict the dissemination of a pathogen because it contains no blood vessels and is a poor nutritional source for invading agents. Another potential reason was that there were differences in the general physical condition of the two patients. The adult patient had type II diabetes but was in generally stable physical condition. However, the child described in Lim’s case was in poor physical condition during the course of admission. In addition to the fungal infection, the child had severe idiopathic aplastic anemia and was suffering from graft failure, intracranial hemorrhage and multiple bacterial infections. The child’s death may therefore have been the result of multiple diseases.”

3. Reviewer’s Comment: Is the sequence of the amplified ITS PCR product in a strain isolated in this study 100% similarity to Earliella scabrosa using the National Center for Biological Information (NCBI) GenBank database? If not, please add a similarity percentage to Earliella scabrosa and then provide information about other possible organisms and percentages of the similarity.

Response: As the reviewer commented, “The sequence of the amplified ITS PCR product from the strain isolated in this study was analyzed using the National Center for Biological Information (NCBI) GenBank database and identified as Earliella scabrosa (KR706165)” was corrected as “The sequence of the amplified ITS PCR product that was obtained from the strain isolated in this study was analyzed using the National Center for Biological Information (NCBI) GenBank database and identified as Earliella scabrosa (KR706165, identity 99%). A sequence alignment revealed that this sequence shared 91% similarity with Trametes sp. and 89% similarity with Ganoderma sp.”

Reviewer 2#: 

1. Reviewer’s Comment: Abstract. Visual acuity has to be expressed in Snellen chart. "2/20 in the right eye" please correct.
Response: In accordance with the reviewer’s comment, the statements “the patient’s visual acuity improved from light perception to 2/20 in the right eye” was corrected to “the patient’s visual acuity improved from light perception to 20/200 in the right eye.”

2. Reviewer’s Comment: What do you mean? Please explain. (an agent of white rot on wood)

Response: “An agent of white rot on wood” is a characteristic of the fungus Earliella scabrosa. We did not feel that it was necessary to describe this trait in the abstract, and it therefore was deleted. The statement “Earliella scabrosa (an agent of white rot on wood) has never been reported in infectious human disease” was corrected to “Earliella scabrosa has never been reported as an infectious agent in human eyes”.

3. Reviewer’s Comment: Case presentation: "corrected visual acuity of 2/20."?

Response: In accordance with the reviewer’s comment, the statement “One week after surgery, the patient obtained a best-corrected visual acuity of 2/20” was corrected to “One week after surgery, the patient obtained a best-corrected visual acuity of 20/200.”

4. Reviewer’s Comment: Did the patient received antimicotic therapy?

Response: This patient underwent surgery (including an IOL explantation with capsular bag removal and a 23G pars plana vitrectomy combined with a silicone oil tamponade) only to remove the pathogen. Antimicotic drugs would have been used during the course, though none were applied in this case. . The intraocular irrigation solution used during the surgery contained 1 mg/0.1 ml vancomycin, which was included to treat any resulting bacterial infection. Fortified tobramycin and levofloxacin eye drops were administered after the vitrectomy, and their use was continued for six days. One week after surgery, the patient obtained a best-corrected visual acuity of 20/200.

5. Reviewer’s Comment: Conclusion must be Discussion - you discuss a lot of published data. Response: In accordance with the reviewer’s comment, the title of the “Conclusion” section was corrected to “Discussion and Conclusions”.

We would like to express our great appreciation to you and the reviewers for the comments you have provided regarding our paper. If you have any further queries, please do not hesitate to contact us.

Kind regards,

Hong He