Dear editors,

Thank you very much for your helpful work, and we also very appreciate the valuable comments and suggestions from the reviewers. According to these comments, we have revised the manuscript very carefully. Attached below is a list of our point-by-point response to all the comments.

If any further information in regard to this paper is needed, please let us know.

Thank you for your help again!

Sincerely yours,

Xianzhi Xiong

Additive list 1:

Responses to the comments and questions from Reviewer 1

1) **Comment**: *Rhizopus microsporus lung infection has been reported frequently in a group of patients with poorly controlled diabetes and immunodeficiency, and in a case report, the authors reported no immunodeficiency or pre-existing disease. It is recommended that good blood glucose status on admission (e.g. HbAIc) and the presence of HIV infection (it would be important to mention that the patient is negative) be noted.*

Response: We have done corresponding tests for HbAIc and HIV, and the results are all negative, and the relevant results have been re-written in the manuscript.

2) **Comment**: *In the case of Rhizopus microsporus lung infection, surgical debridement may be considered, but it was not performed in this case. If you have any reason why local administration of amphotericin B was preferred over surgical intervention or why surgical intervention was inappropriate, please describe it. I hope these comments will be helpful.*

Response: Thank you very much for your good advice. Surgical resection is indeed one of the important therapies to deal with Rhizopus infection. We made consultation with the thoracic experts. Considering that the operation may be traumatic, and the patient's parents disagree with the lobectomy. Therefore, we started medical treatment.

Responses to the comments and questions from Science editor:

1) **Comment**: *Description of "Rhizopus microsporus lung infection is rare in immunocompetent patients and seldom reported" is confusing. As reported, "seven patients (29.2%) had no obvious predisposing risk factors", 29.2% is not rare yet.*

Response: We apologize that we don't give a clear description. This "rare" refers to the rare immunocompetent patient with Rhizopus microsporus lung infection reported. The "29.2%" refers to the patients with no obvious predisposing risk factors which were among all the immunocompetent patients with Rhizopus microsporus lung infection in that study.

2) **Comment**: *It is not adequate to the purposes of this case. The detection of microsporus in bronchoalveolar lavage fluid bymetagenomics next generation*

sequencing (mNGS) is not validated by the gold standards; "Considering both the effectiveness and safety, a treatment of combination of intravenous and inhaled using of AmB was performed. The intravenous dose of AmB was adjusted to 60 mg daily, combined with 10mg inhalation of AmB twice a day", the inhalation or local airway perfusion of Amphotericin B seemed to be based on personal experiencenot, but not approved by any guidelines. Although the response is good, it is not certain that "a combination therapy of intravenous, inhalation and local airway perfusion of Amphotericin B may be a promising strategy for the treatment of pulmonary mucormycosis". We don't know "inhalation or local airway perfusion of Amphotericin B " could play a work, therefore, the diagnosis and treatments might be a little bit misguided.

Response: Thanks for your good correction. Although in recent years, mNGS methods have been used to try to improve the detection and identification of pathogens and have become a topic of concern as routine pathogen identification tools, which provide a lot of evidence for early diagnosis. This method has not recommended as a basis for diagnosis in guideline. The diagnosis of pulmonary Rhizopus infection is still mainly based on the results of isolation and culture. Unfortunately, we did not get a positive culture result for this patient, so in this case it is insufficient to confirm the diagnosis of Rhizopus microsporus lung infection as we mentioned in the disscussion.

Secondly, it is true that there is no clear evidence-based medical support for nebulization and topical application of AmB in the airway. However, considering the adverse effects of intravenous use of AmB in patients, we proposed a new feasible

treatment. Although it showed good outcome in this patient, the main therapeutic effect might still be considered by the intravenous treatment. Whether this new method is effective or not may need more cases and controls in future.