

Dear Reviewers:

Thank you for your comments concerning our manuscript entitled “Multi-systemic melioidosis in a patient with type 2 diabetes in a non-endemic area: A case report”(ID: 89623). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval.

Reviewer #1:

1. The manuscript tries to achieve too many things to assess the impact of unique case of multi-systemic melioidosis, which occurs in non-endemic regions and there publishing this case report to enhance the awareness for melioidosis in non-endemic regions, but failed to justify the novelty of their model. The authors need to narrow down their study focus. I encourage the authors to provide more in-depth evidence on focused points for claiming the accuracy.

The report on melioidosis discussed herein originates from Wuhan, China, located in the central part of the country within a temperate region. Wuhan is not considered an endemic area for melioidosis, and there have been no previous reports of this disease in the region. The local hospitals had minimal awareness of melioidosis, leading to a lack of recognition among medical staff. Due to this insufficient understanding, a case of cutaneous melioidosis in a patient was misdiagnosed as undifferentiated connective tissue disease, resulting in the administration of steroid therapy, inadvertently promoting the progression of the illness. During the hospitalization, *B. pseudomallei* was cultured from the patient's blood and urine. However, due to the limited awareness of melioidosis, the neurological manifestation of the disease was not promptly recognized, and it was mistakenly diagnosed as a cerebral hemorrhage. The convoluted diagnostic journey of this case serves as an illustrative example highlighting the challenges in diagnosing melioidosis, emphasizing the need to enhance awareness among healthcare professionals.

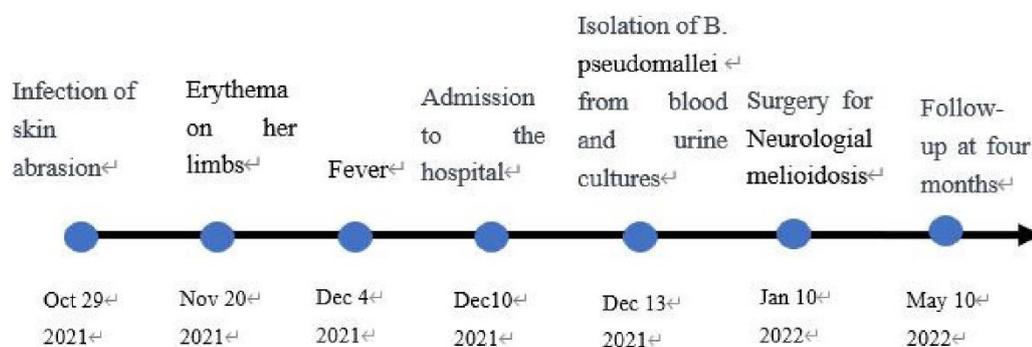
The patient's fall occurred outdoors in an area regularly cleaned and maintained, yet the source of *B. pseudomallei* remained unidentified. This limitation underscores the importance of meticulous clinical reporting. In future endeavors, greater attention will be given to conducting thorough clinical research. The primary objective of reporting this case is to enhance awareness of melioidosis, especially among healthcare professionals in non-endemic regions, to prevent misdiagnosis and oversight.

2. First of all the patient history data is very much complex and confusing, the authors should provide a detailed timeline of the case with detailed working

profession (whether the patient was a farmer, gardener and planter or involved with agriculture related works, etc.).

Due to a lack of awareness regarding melioidosis, the patient's condition was not promptly recognized as glanders, leading to early and non-standardized treatment. This complexity resulted in a convoluted course of diagnosis and treatment. To elucidate the progression of the illness, we constructed a detailed case timeline based on the onset of symptoms and the corresponding treatment strategies at different time points. We have created a comprehensive timeline in accordance with your suggestion; however, we seek guidance on whether this timeline is suitable for inclusion in the article.

The patient, a retiree residing in Wuhan, has not been involved in agricultural, horticultural, or planting activities, and this information has been supplemented in the article.



Timeline of the case

3. The author must mention a separate paragraph mentioning the ethical approval from which approval committee. Hope a written consent letter was also filled out by each patient.

We have provided a detailed description in a separate section regarding the ethics and patient consent for publishing this article. The patient has also signed a written consent form, which has been included as an attachment.

3. Throughout the manuscript the authors should referring to a bacterium in a paper, should underline or italicize the names in the text.

We have italicized the names of bacteria in the article.

5. The resolution of figure 2 images are poor. The author should provide better resolution pictures. Diffusion-weighted imaging (DWI) could have been better.

We consulted with the radiologist, and the imaging pictures we provided were selected to be representative from the patient's radiological examinations. We invited the radiologist to review the patient's cranial DWI (Diffusion-Weighted Imaging) examination, and it was noted that the DWI images did not effectively illustrate the

patient's lesions. Additionally, the cranial DWI examination was only completed during episodes of seizures, and for the other instances of cranial MRI examinations, DWI was not performed. Therefore, DWI images were not included in our set of pictures.

6. The author should include more data (B. pseudomallei-specific CD4+ IFN- γ T-cells and CD8+ IFN- γ T-cells, IgG1 and IgG2) under Laboratory test results of the Patient section to strengthen the manuscript.

Due to a lack of understanding of the disease at that time, we were not familiar with the role of B. pseudomallei-specific CD4 and other tests. Furthermore, the hospital lacked the technical capability to conduct B. pseudomallei-specific CD4+ IFN- γ T cells, CD8+ IFN- γ T cells, IgG1, and IgG2 testing. Consequently, these examinations were not carried out. This experience reminds us that in future work, especially for unique cases, it is essential to refer to more literature and enhance the monitoring of specific disease markers to achieve more precise diagnoses.

7. The author should mention whether the melioidosis patient had a history of chronic renal failure, hematologic diseases, connective tissue diseases, chronic liver diseases, and tuberculosis or not.

The patient has type 2 diabetes but has not progressed to diabetic nephropathy, and there is no evidence of chronic kidney dysfunction. Additionally, the patient does not have any blood system diseases, connective tissue disorders, chronic liver disease, or pulmonary tuberculosis. These modifications have been incorporated into the document.

8. Throughout the manuscript, there are several language mistakes. Therefore, I recommend the paper should undergo professional language editing before it can be published.

We submitted the article to a professional language editing service for revision, and we have also uploaded the proof of the modifications.

9. There are several typos and grammatical mistakes which could have been corrected before the final submission.

You mentioned the textual and grammatical errors in the article, and we have already enlisted the services of a professional language editing company for corrections.

Yours sincerely,
Feng Zhou

30 Dec, 2023