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Jin-Lei Wang, Ph.D.
Editor-in-Chief, *World Journal of Clinical Cases*

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Dear Dr. Wang,

Thank you very much for your recent communication, indicating that our manuscript, 81862 may be suitable for publication in *World Journal of Clinical Cases*. We also express our gratitude to the referees for providing positive reviews and useful suggestions, which have guided us to improve our manuscript. In this letter, we provide detailed, point-by-point responses showing how we have followed the reviewers' suggestions to revise our manuscript.

We sincerely hope that our revised manuscript will now be considered scientifically significant, of high research quality, and appropriately edited for publication in *World Journal of Clinical Cases*.

Thank you very much for your consideration. We look forward to hearing from you at the earliest convenience.

Sincerely,

Yuan Liu

Referee 1

- 1. This is a very good paper of an important issue, and of a particular case. I have some minor concerns to raise, that might be addressed easily: 1. It is hard to believe that an extrapulmonary TBC would heal / improve with three months regimen of INH etc. Furthermore, please specify exactly what kind of regimen was used: any quinolones? Guidelines suggest a longer treatment than three months, however: please consult and quote relevant sources.*

Response: Firstly, thank you for your endorsement. Secondly, we apologize for these confusions and make clarifications in the revised manuscript. Surely, TB treatment usually takes 6 months or more. We planned a standardized anti-tuberculosis treatment of 2HRZE/4HR, but the patient stopped the drug because of gastrointestinal discomfort during the 3rd month of treatment and suspended for 2 weeks, then he continued to take the medicine again for 3 months. So the total time is six months. Thank you very much for raising this question, and we will provide more details about the patient's treatment in the treatment section in the revised manuscript.

- 2. Figure 1 has very interesting data, so I find it very confusing and of no help to mix up all images together. Kindly produce separately: ---a MRI image of the thigh, with explanations, sequences used, (gadolinium enhancement?) ---the intraoperative / surgical image*

Response: Thank you very much for your consideration. We split and rearranged the original Figure 1. In the revised manuscript, Figure 1 contains important preoperative imaging data. Figure 2 shows the intraoperative picture and the histopathological results of the resected specimen, and we marked the sequence used in the MRI picture. This patient had a non-contrast MRI, so no contrast agent was used.

- 3. What about the nodules in the thorax CT? Then the case was not a merely extrapulmonary TBC.... In such a setting, a three-months regimen would even be more inadequate to ensure healing.*

Response: The patient had no history of tuberculosis exposure, no systemic

symptoms of tuberculosis such as fever or loss of weight, and previous tests did not support the diagnosis of tuberculosis. And his CT results, although showing scattered nodules, do not support the diagnosis of tuberculosis. We fully agree that a three-months regimen would even be more inadequate to ensure healing. We explained this earlier in question 1.

Referee 2

1. In the present case, the acid-fast stain (AFS) in the surgical specimen was positive and pathological finding was compatible for tuberculosis (TB). These findings can reach the diagnosis of TB. Why do you perform NGS?

Response: Thank you very much for your consideration. The patient had similar symptoms of abscess and rupture in the left thigh in 2018, when the patient underwent debridement surgery in another hospital, and bacterial culture, tuberculosis-related tests such as acid-fast stain (AFS) and tuberculosis culture were negative. Considering that the patient was a middle-aged male with normal immune function, no history of tuberculosis exposure, no systemic symptoms of tuberculosis such as fever or loss of weight, and previous tests did not support the diagnosis of tuberculosis, we performed NGS testing on the surgical specimen to clarify the diagnosis and detected *Mycobacterium tuberculosis* sequences at last. Subsequently, in order to confirm our diagnosis, we further contacted the pathology department for AFS of the surgical specimen. The surgical specimen was stained several times in the pathology department, and a small number of acid-fast bacilli were eventually found, which further confirmed the accuracy of our diagnosis.

2. What is the standard process in such case which TB could not be ruled out? In my opinion, AFS and TB culture should be routinely performed for the surgical specimen, and TB PCR should be further applied in AFS positive case. If no positive results, NGS has its role in this situation.

Response: For patients with suspected TB, AFS, tuberculosis (TB) culture, and PCR may be routinely followed for TB diagnosis, but NGS may be more advantageous in

this case with recurrent abscesses and all previous TB-related tests were negative. In the revised manuscript, we will be more detailed and logical in describing the case. We will add the important negative test results previously performed in the section of history of present illness.

3. *The authors mentioned NGS has a low cost in the introduction. What is the cost of AFS, culture, PCR, and NGS in your organization? The authors should provide the information.*

Response: We apologize for these confusions and make clarifications in the revised manuscript. This sentence does not refer to the economic cost, we actually want to say that repeated AFS and repeated culture etc. have consumed too much energy cost of doctors and patients. We deleted this sentence and made the paper clearer. In fact, the price of NGS in our hospital is about 6 times the price of AFS, about 3000 RMB.

4. *The treatment periods were only 3 months. What was the decision based on? The treatment seemed not follow the TB treatment guideline.*

Response: We apologize for these confusions and make clarifications in the revised manuscript. Surely, TB treatment usually takes 6 months or more. We planned a standardized anti-tuberculosis treatment of 2HRZE/4HR, but the patient stopped the drug because of gastrointestinal discomfort during the 3rd month of treatment and suspended for 2 weeks, then he continued to take the medicine again for 3 months. So the total time is six months. Thank you very much for raising this question, and we will provide more details about the patient's treatment in the treatment section in the revised manuscript.

5. *The Certificate of English Editing was insufficient. The authors should provide the official certificate of what organization performing the English Editing.*

Response: We provided the official certificate of what organization performing the English Editing in the revised version.