Author's response to reviews

Title: Multidrug Resistant M. tuberculosis from Multiple Cutaneous Abscesses in a Patient with Polymyositis: Response to treatment

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Author's response to reviews: see over
Answers to the comments of the Reviewer (Mr. Hendrik Simon S Schaaf)

Thank you very much for your concern and comments. We definitely think that your concern regarding the article is true. We followed your comments and modified the article. The article has been thoroughly revised; there are new inclusions of relevant facts in ‘Background’ as well as in ‘Discussion’, which will definitely strengthen the presentation. Many new angles have been explored and many new thought provoking scientific reasonings were included, which we think will give the article a new dimension. The language has been made more lucid and presentable. We hope that you will now find it suitable for publication.

Please note in the text that the parts, which are modified and corrected, are colored blue and the new inclusions are colored red.

Answers to General Comments

1. It was a case of polymyositis, not pyomyositis. We are sorry for the mistake. The first sentence in the abstract has now been corrected.

Answers to Major Compulsory Revisions

1. The treatment of the first episode was supervised for first 2 months (now included in text).

   It is well documented that the history of previous tuberculous treatment is misleading in majority of the patients (Van Rie A, Warren R, Richardson M, Gie RP, Enarson DA, Beyers N et al.: Classification of drug-resistant tuberculosis in an epidemic area. Lancet 2000, 356: 21-24, now included in text) and we also believe that history of compliance is notoriously unreliable.

   Here, the patient gave a history of regular intake of drug and we documented his statement.

2. Resistance to all the first line and most of the second line drugs (which the patient did not receive) was the worth mentioning finding of the report. It is rare and
hardly reported before. It might be a case of endogenous reactivation with multi-
“drug resistance in previously treated case” where the mode of resistance is not
exactly known (point mutation?) or it can be labeled as an evidence of multi-
“drug resistance in new case”, which might better explain the acquisition of
resistance against all those drugs, to which the patient was not exposed. These
two possibilities are discussed in details this time (Ref: Van Rie A, Warren R,
Richardson M, Gie RP, Enarson DA, Beyers N et al.: Classification of drug-
Multidrug resistance rate is higher in HIV-infected patients (Raviglione MC,
O’Brien RJ: Tuberculosis. In: Harrison’s Principles of Internal Medicine; eds:
eds, Vol. 1, 2001, p. 1024-1035). Therefore, it was speculated that other
immunocompromised persons are more likely to develop MDR tuberculosis,
though there was no supporting evidence. Rapid development (within 6 months)
of MDR TB in our case initiated the idea.
3. The INH-concentrations were 1µg/ml and 10 µg/ml. It is now corrected in the
text.
We agree to your comment that all the drugs have shown high-level resistance.
We also believe that there are chances of cross-resistance between amikacin and
kanamycin, and between sparfloxacin and ciprofloxacin. Now the question
comes: Why had we chosen that particular regimen and how the patient was
cured?
To answer the first question, I would likely to mention that it was really become a
challenge for all of us to save the life of the patient with very limited options for
treatment since the strain was resistant to 9 drugs. While formulating the
treatment protocol, we also had to keep in mind the availability of the drugs in the
hospital and in the surrounding areas, and the purchasing capacity of the patient.
The particular regimen was decided at last with 4 first line drugs (though high-
level resistant) and 2 other drugs like kanamycin and sparfloxacin ignoring the
chance of cross-resistance.
It is rightly mentioned by you that reconstitution of the immune system has played a major part in saving the life of the patient. The immunosuppressive drugs (like steroid and methotrexate) were stopped at the onset of the treatment for the second time (now clearly mentioned in the text), only with the intention to give a chance to the immune system to recover and fight back. It helped. It has now mentioned in discussion.

4. Cultures were done from the sputum as well as from the aspirated pus during the initial and second admissions of the patient. It is now mentioned in the case report.

Number of cultures from different samples, both on initial diagnosis and follow up, is now mentioned.

All the tests (including nitrate reduction test, which we failed to mention) were done for the second time to reconfirm the isolate. Now mention in the case report. Exogenous reinfection was definitely another possibility of acquiring the infection and we are grateful for your suggestion. This time we discussed that possibility with appropriate references (the reference you suggested is also included).

Answers to Minor Essential Revisions

1. The abstract has been modified according to your suggestion.
2. We tried to improve the language as far possible. We are very grateful to Ms. Maria Alice A Telles, the second reviewer of the article, for her intriguing effort to correct the language as well as the presentation of our article. We modified and corrected the language of the article according to her suggestions and corrections.
3. The new terminologies like ‘drug resistance in previously treated case’ and ‘drug resistance in new case’ are included along with the reference.
4. Full forms are written before abbreviations.
5. The biopsy report is discussed in details in discussion.
6. Analysis of restriction-fragment length polymorphisms (RFLP) is useful in this study, because different strains of M. tuberculosis can be reliably distinguished

7. The stage at which the miliary pattern appeared on chest radiograph is mentioned in case report.

8. The term “miliary TB of non-reactive type” is explained in discussion with reference.
Answers to the comments of the Reviewer (Ms. Maria Alice A Telles)

Thank you very much for your intriguing effort to correct our article to make it publishable. We are grateful to you. We followed your suggestion and corrected the article accordingly.

We humbly want to mention our opinion regarding one correction:

Resistance is higher and more rapidly acquired in HIV-infected patients (I don't agree with this, if you are sure about this you need to include a reference here).

We have corrected the statement in the text as - Multidrug resistance is higher in HIV-infected patients.

(References:
