Author's response to reviews

Title: Successful diagnosis of tuberculous lymphadenitis by loop-mediated isothermal amplification of cutaneous samples from an ulcerated surface lesion: a case report

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Author's response to reviews: see over
Professor Michael Kidd  
Editor-in-Chief  
*Journal of Medical Case Reports*

Dear Professor Kidd,

Ref.: MS: 1816313622124178

Thank you for your e-mail dated April 22, 2014. We are grateful to the reviewers for their valuable comments and have revised the manuscript in accordance with the reviewer comments. Our point-by-point responses are provided after this letter.

We hope that our manuscript it is now suitable for publication in the *Journal of Medical Case Reports*.

Thank you for reconsidering our study.

Sincerely,

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RESPONSE TO REVIEWER 1

We are grateful to Reviewer 1 for the critical comments and useful suggestions. We have taken all of the comments and suggestions into account in the revised version of our paper. Changes to the manuscript are indicated by underline.

Comments to authors: This MS explain the diagnosis of TB lymphadenitis by LAMP method compared with other conventional assays and PCR assay. The technique accurately identified the case within 90 min. The whole MS has to be edited by the native English speaker.

Response: The paper has been edited by a native English speaker familiar with the field.

Major comment 1: In Fig. 3, the authors should add the gel pictures of PCR and LAMP to confirm the result of commercial LAMP kit.

Response 1: For PCR detection of M. tuberculosis, we used a commercially available test named the Cobas TaqMan MTB assay (Roche Diagnostics, Rotkreuz, Switzerland). Therefore, the PCR product was identified automatically as an M. tuberculosis-specific gene, according to the manufacturer’s instructions. For the LAMP product, a highly specific nucleotide extension was detected using four primers to recognize six distinct regions on the target by visually observing turbidity and fluorescence without gel imaging. Accordingly, we changed the following text as follows(p. 5, line 15-17):

“…and M. tuberculosis DNA was unequivocally identified in the positive culture by means of the Cobas TaqMan MTB assay (Roche Diagnostics, Rotkreuz, Switzerland) [5].”
**Major comment 2:** In the discussion part, the authors should discuss more on other LAMP reports for identification of TB.

**Response 2:** We changed the text as follows (p. 6, line 18 - p. 7, line 1):

“In contrast, LAMP could amplify the *M. tuberculosis*-specific DNA rapidly under isothermal conditions [8]. A recent meta-analysis of 10 studies to estimate the diagnostic accuracy of LAMP for pulmonary TB revealed a sensitivity of 80.0% (95% CI, 78–83%) and a specificity of 96.0% (95% CI, 95.0–97.0%) [9]. Furthermore, LAMP, which in combination with PURE has recently been established as a diagnostic technique requiring only limited equipment and manpower, provides an accessible, cost-effective, rapid, and more appropriate molecular diagnostic tool for TB in the field setting [6]. All procedures, including the time for sample preparation, could be performed within just 1.5 h.”

**Major comment 3:** The author mentioned that LAMP assay need only 90 min to complete. Is it included the time for sample preparation? The author should mention about this in the discussion part.

**Response 3:** We added the following text (p. 7, line 1-3):

“All procedures, including the time for sample preparation, could be performed within just 1.5 h.”

**Minor comments:** The author should give a reference and some detail for PCR assay on page 5.
Response: We changed the text (p. 5, line 15-17) as follows:

“…and *M. tuberculosis* DNA was unequivocally identified in the positive culture by means of the Cobas TaqMan MTB assay (Roche Diagnostics, Rotkreuz, Switzerland) [5].”
RESPONSE TO REVIEWER 2

Thank you very much for your valuable comments.

Comments to authors: This is an coherent, authentic and very interesting case report, which also has a significant diagnostic value. In my opinion, you should underline not only the diagnostic value of the new molecular method used but also the performance of this procedure in specific sample types, such as swab samples.

Response: We agree that additional information on this procedure with specific sample types, including swab samples, will be valuable. We are currently investigating this point and intend to report it in a later paper.
RESPONSE TO THE EDITOR

Comments: Please also ensure that your revised manuscript conforms to the journal style (http://www.jmedicalcasereports.com/info/instructions/). It is important that your files are correctly formatted.

Comment 1: Please change the description of the patient’s gender to “male”.

Response 1: We have changed the two instances of “man” to “male”.

Comment 2: Please include the Ethnicity of the patient in the Abstract and Case presentation sections.

Response 2: We have added the Ethnicity of the patient (Japanese) to p.3, line 9 and p.4, line 22.

Comment 3: Please change the ‘Case Report’ section header to ‘Case Presentation’.

Response 3: We have changed this term (p. 4, line 21).

Comment 4: Please include an acknowledgement section at the end of the manuscript before the reference list. Please acknowledge anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria
for authorship. Please also include the source(s) of funding for all authors. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements.

**Response 4:** We have added an Acknowledgements section (p. 9, lines 3-4).