Author's response to reviews

Title: Asymptomatic primary tuberculous pleurisy with intense 18-fluorodeoxyglucose uptake mimicking malignant mesothelioma

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Author's response to reviews: see over
December 25, 2012

Dr. Jason Stout
Tonilynn Manibo
Editor,
BMC Infectious Disease

MS: 5050862398073859

Dear Dr. Stout:

Thank you very much for the useful recommendations for revision of my manuscript. We have followed the suggestions of the reviewers as we have revised our manuscript.

I hope our responses to the reviewers’ comments will allay their concerns, and place the manuscript in a publishable category.

Sincerely yours,

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ANSWER TO REVIEWER 1

Thank you very much for your thoughtful comments. Our responses are listed below.

The authors described the usefulness of FDG PET/CT in a case of tuberculous pleurisy. This case is original, interesting and well-described. I would suggest only minor revision. Please add this reference because it is related to the topic of this article.


Response: The above-mentioned article was extremely informative. We have added this article to the References section (No. 5) and the main points of this study have been incorporated into the revised manuscript as follows to describe more extensively the utility of PET-CT in the diagnosis and management of tuberculosis. Please see the response to the comment #3 from reviewer 2.

Line 5 page 4 in the revised manuscript

“However, it has been shown that inflammatory disorders, especially pulmonary tuberculosis, also induce FDG uptake in active lesions, which suggests that FDG PET results should be interpreted with caution [3, 4, 5]. Conventional or dual phase FDG PET can not effectively distinguish malignant disease from mycobacterium infections. Multi-tracer PET, a novel promising technology utilizing differences in tracer kinetics and decay, has been providing additional and complementary information to improve pulmonary nodule characterization [5].

The usefulness of FDG PET in the detection of mycobacterium infection sites has been shown in patients with miscellaneous infectious lesions or human immunodeficiency virus-associated fever of unknown origin [6, 7]. Moreover…….”

ANSWER TO REVIEWER 2

Thank you very much for your helpful comments. Our response is below.

This manuscript describes a case report of a patient with presumed tuberculous pleurisy, demonstrating that 18-FDG PET scan uptake decreased with treatment. The case report is straightforward, and the images are interesting. The fact that 18-FDG PET scans light up at sites of tuberculosis disease and that the intensity of uptake decreases with treatment has been well-described previously (e.g. Martinez V. et al, International Journal of Tuberculosis and Lung Disease 2012; 16: 1180), so I'm not sure how much of a contribution to the literature is represented by this case report. It would be greatly enhanced by a more extensive review of the utility of PET-CT in diagnosis and management of tuberculosis.

Response: The previous reports including the study by Martinez et al. demonstrated that FDG PET/CT was helpful not only for evaluating disease activity, but also for monitoring therapeutic
responses in pulmonary tuberculosis, tuberculous lymphadenitis, and skeletal tuberculosis, particularly in smear-negative patients. However, these reports did not include a case of primary tuberculous pleurisy, the pathogenesis of which is different from pulmonary tuberculosis. Therefore, we focused on FDG PET/CT images in the differential diagnosis of pleural disease. To enhance the contribution to the literature, we described more extensively the utility of PET-CT in the diagnosis and management of tuberculosis. Please see the response to the next major compulsory revision.

Major compulsory revision
1. The reading of a tuberculin skin test should be described by a single measurement (the transverse diameter of induration on the forearm), not a two-dimensional measurement--please correct this.

Response: Corrected in the revised manuscript as follows.

Line 18 page 6 in the revised manuscript
“However, the QuantiFERON-TB second generation (QFT-2G) test (3.02 IU/ml) and tuberculin skin test (10 mm induration) were both positive based on the Japanese criteria.”

2. While the diagnosis of tuberculosis is highly likely in this case, no positive culture was obtained. The authors should explicitly address this point.

Response: I agree with this comment. We have addressed this point in the revised manuscript as follows.

Line 3 page 7 in the revised manuscript
“Although no positive culture was obtained, other clinical data suggested that the diagnosis of tuberculous pleurisy was highly likely in this case and the patient received antituberculous therapy for 6 months (2HREZ/4HRE) without any side effects.”

3. The manuscript would benefit from a more extensive literature review to discuss the role of PET-CT in diagnosis of tuberculosis and evaluation of treatment efficacy. The paper mentioned above by Martinez and others (e.g. Via LE et al, Antimicrobial Agents and Chemotherapy 2012; 56: 4391) are two examples that come immediately to mind.

Response: We described more extensively the utility of PET-CT in the diagnosis of tuberculosis and evaluation of treatment efficacy with new references including the reviewers’ recommendations in the revised manuscript as follows.

Line 5 page 4 in the revised manuscript
“However, it has been shown that inflammatory disorders, especially pulmonary tuberculosis, also induce FDG uptake in active lesions, which suggests that FDG PET results should be interpreted with caution [3, 4, 5]. Conventional or dual phase FDG PET can not effectively
distinguish malignant disease from mycobacterium infections. Multi-tracer PET, a novel promising technology utilizing differences in tracer kinetics and decay, has been providing additional and complementary information to improve pulmonary nodule characterization [5].

The usefulness of FDG PET in the detection of mycobacterium infection sites has been shown in patients with miscellaneous infectious lesions or human immunodeficiency virus-associated fever of unknown origin [6, 7]. Moreover, it has been reported that FDG PET/CT is helpful not only for evaluating disease activity, but also for monitoring therapeutic responses in pulmonary tuberculosis, tuberculous lymphadenitis, and skeletal tuberculosis, particularly in smear-negative patients [5, 8-10]. Via et al. demonstrated that FDG-PET uptake in tuberculous pulmonary lesions was significantly reduced with as little as 1 week of treatment prior to changes in the volume and density of lesions in a rabbit model [10]. The absence of reduced FDG PET uptake in the early phase of treatment may suggest active tuberculosis due to a lack of adherence, drug resistance, or misdiagnosis [9].”