Reviewer's report

Title: Outcome of Hospitalized Patients with Tuberculous Pleurisy: Clinical Impact of the Disease Extent

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Reviewer: Rafal Krenke

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General comments

The manuscript by Shu et al. is an extensive analysis of the relationships between different clinical, radiological and laboratory features and the outcome in patients with tuberculous pleurisy. The authors performed an interesting study which add some data to the existing literature on the prognosis in patients with tuberculous pleural effusion. The background and objectives are clearly presented and convincing. The methods used by the authors are generally correct (with some critical comments listed below). The results are clearly described and showed in four tables and one figure. The strength of the study is a relatively large and homogenous (all patients with M. tuberculosis positive pleural fluid culture) group of patients. The major weakness of the study is its retrospective character and relatively high percentage of patients lost to follow-up (only 52.7% of subjects had been reevaluated after 6 months of treatment). The interesting findings are those that pleuropulmonary involvement and delayed diagnosis (lack of pleural tissue for evaluation) were strong predictors of increased in-hospital mortality. Although my general opinion on the manuscript is positive, I also have to point out some statements, methods or data which raised my doubts or even criticism.

Minor essential revisions

The statement that the gold standard for the diagnosis of TP is mycobacterial culture of PE and respiratory specimens sounds controversial. It is well known that pleural tissue studies are equally specific but more sensitive than pleural fluid evaluation. If so, I would rather say that pleural biopsy is the gold standard or, at least, a reference procedure in the evaluation of suspected tuberculous pleurisy. Since the combined sensitivity of direct microscopy and pleural fluid cultures were reported far below 50-60% in the majority of previous series, I suppose this was probably not higher in the reviewed study. Thus, I believe it might be important to realize that the patients evaluated by Shu et al. were not the consecutive patients with tuberculous pleurisy but selected patients with positive pleural fluid culture. The true number of patients with tuberculous pleurisy treated in the authors’ institution between 2001 and 2008 was probably approximately twice as large. I am not sure whether the results and conclusion could be directly extrapolated to patients with tuberculous pleurisy and negative pleural fluid culture. This limitation was noted by the authors and mentioned in
the discussion.

It seems to me that the criteria the authors used to distinguish between the isolated pleurisy group and pleuro-pulmonary group are imprecise. If the criteria for the diagnosis of isolated pleural involvement were 1) negative culture for M. tuberculosis of all respiratory samples and 2) the absence of pulmonary parenchymal lesions compatible with TB in chest radiographs, the patients meeting none or only one of these criteria were classified into the pleuro-pulmonary group. Thus, I am afraid that the latter group might have included patients with tuberculous pleurisy and old, inactive post-TB parenchymal abnormalities (e.g. fibro-cavitary lesions).

The total number of patients in the study group (205) is not consistent with the sum of patients with different indications for in-hospital management (massive and/or loculated PE – 51pts, prolonged symptoms – 51 pts, intolerant fever or dyspnea – 99 pts, and presence of lung mass - the remaining 14 pts. If this is because some patients had more than one indication for hospitalization it would be better to avoid referring to the 14 subjects with lung mass as the remaining patients, because it seems somewhat confusing. After subtracting (51+ 51+ 99) from 205 we receive 4, not 14 patients.

The authors have not described the general way of data presentation. In two tables mean and SD, while in one median and SD are presented. If the distribution of all variables was normal, mean # SD should consequently be used, if not, data should rather be presented as median and IQR. I have some doubts whether the distribution of all data was normal but I assume that this had to be a case, when t-test was used to evaluate differences between various groups.

Citing their previous study, the authors state that in patients with neutrophil-predominant TP and parenchymal lung involvement they had found in-hospital mortality of 36%. The data presented in the original paper show, however, that 13% of patients had no parenchymal lesion. Thus, I believe there were not only patients with tuberculous pleurisy and parenchymal lung involvement but also some patients with isolated tuberculous pleurisy in that study group.

Minor issues not for publication

Although the general linguistic impression is good, the authors should make an additional effort to eliminate some errors. The examples are presented below.

• There are two identical sentences in the manuscript: Patients were followed for at least 6 months after index PE samples were collected, or until death or loss of follow-up.

• After 6-month treatment, 108 (52.7%) patients had followed in our hospital.

• In addition to previous study showed high mortality in hospitalized TB patients [8], our previous study revealed that in patients with neutrophil-predominant TP and parenchymal lung involvement had in-hospital mortality was 36%.

• Because the patients with isolated pleurisy were more likely to present with
local (chest pain) and systemic (fever) inflammatory symptoms and less likely to have hypoalbuminemia, it is possibly that pulmonary involvement represents an extensive and serious infection in a compromised and malnourished host.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.