Author's response to reviews

Title: Clinical spectrum of intrathoracic Castleman disease: a retrospective analysis of 48 cases in a single Chinese hospital

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Version: 4 Date: 7 February 2015

Author's response to reviews: see over
Dear professor Catia Cornacchia and Ms Hazel Joyce Delos Santos,

Please consider our manuscript entitled “Clinical spectrum of intrathoracic Castleman disease: a retrospective analysis of 48 cases in a single Chinese hospital” for publication as a research article in the BMC pulmonary medicine. It’s the revised version of this manuscript. I have re-edited my manuscript according to the reviewer suggestions. Respond to reviewers will be attached in the second part of the cover letter. Two thoracic surgeons are added to the author list according to the reviewer’s suggestion. All listed authors agreed with this change and every author has sent the confirmation of the this changes to the editor.

Thorax is the common place to develop Castleman disease (CD), but there is no systemic clinical analysis for intrathoracic CD. In order to facilitate the recognition, diagnosis, and treatment of this uncommon disease, we now describe the clinical and radiological characteristics of 48 intrathoracic CD patients in our hospital. Intrathoracic multicentric CD (MCD) was more common than unicentric CD (UCD) in our hospital. MCD was older, more symptomatic and sicker than UCD. Hyaline vascular variant were more common in UCD. All of UCD showed mass in various intrathoracic locations and surgery resection was performed for all and all were alive. Mass, pleural effusion, bronchiolitis obliterans and diffuse pulmonary shadows, including lymphocytic interstitial pneumonia-like images, multiple nodules of different size and sites, patchy, ground-glass opacities and consolidations were showed in our MCD. Most of MCD cases were arranged with chemotherapy and their prognosis were worse than UCD’s.

We believe this study will be of great interest to pulmonologist, hematologist as well as the general readership. This study has not been submitted elsewhere for
publication consideration. All authors have read and agreed to this submission and declare no conflicts of interest. We hope this study is of sufficient novelty and importance for publication. Thank you for your consideration and I look forward to hearing from you.

Sincerely yours,

Hui Huang

Respiratory medicine department
Peking Union Medical College Hospital
Beijing, China
Respond to the reviewers:

Dear professor Amelie Guihot,

Thank you very much for your pertinent and impressed suggestions. That’s very kind of you to do so. I will revise my manuscript following your comments.

Explanations for major compulsory revisions:

1. (1) Thank you for your suggestions. I reviewed Dossier’s manuscript about the analysis of HHV-8 related CD cases and Fajgenbaum’s review about HHV-8 and HIV negative idiopathic MCD (Blood. 2014 May 8;123(19):2924-33). It was said that HHV-8 infection drove the hypercytokinemia in all HIV-positive patients and some HIV-negative patients. And HHV-8 related CD cases showed own clinicopathological characters, regardless of HIV infection. As HHV-8 associated tests, including peripheral blood samples and pathological specimen, were not done for all our patients, we are not sure whether the differences between Dossier’s and ours are related to HHV-8 infection or not. I have discussed these information in our manuscript.

2. Yes, since there is no significant difference between the intrathoracic and extrathoracic group in our hospital’s CD cases, I have cancelled table 1 in our manuscript. Thank you. At the same time, I have added the detailed chest CT findings of UCDs and MCDs in our paper as following your advice (Table 2).

3. Thank you for your suggestions. The name of the pathologists who have supervised the analysis has been quoted in the article. They were also the co-author of our paper. The detailed diagnostic criteria for CD was added to the revised version, which was edited by our pathologist.

Explanations for minor essential revisions:

1. Thank you for your suggestions. The respiratory CD had been replaced by intrathoracic CD in the revised version. And the inappropriate expressions, eg, including “HIV was not so
popular", “can be manifested as” and “it can be classified as unicentric OR multicentric”, were re-edited in the revised version.

2. The detailed information about the detection of HIV-antibody was added to our revised version. The detailed chest CT findings of our enrolled cases was listed in the Table2. The detailed information about the autoantibodies for our all cases was also added to the revised version of our manuscript.

3. Our study is a retrospective study and some of the information about prognosis was acquired by phone and/or mail. As some patients and/or their families were short of medical knowledge, they could not tell their detailed medical information in their local hospital during the follow-up period. And four cases with MCD were lost to follow-up. None of the rest 44 cases had occurred lymphoma. I’m afraid that I cannot describe the information about the occurrence of flares and remission episodes for MCD clearly and accurately. I’m totally sorry for that.

Sincerely yours,

Hui Huang

Respiratory medicine department

Peking Union Medical College Hospital

Beijing, China
Dear professor Mohamed A Regal,

Thank you very much for your pertinent and impressed suggestions. I will re-edit my manuscript following your comments.

**Explanations for your comments**

1. Thank for your suggestions. I have invited two of our thoracic surgeons (Cheng Huang and Ying zhi Qin) to be the co-authors of our paper. Both of them have made great contributions to the diagnosis and treatment of our enrolled cases. They deserved it. Thank you for your reminder. All authors in the author list have sent the confirmation of this changes to the editor.

2. According to your suggestions, respiratory CD has been replaced by intrathoracic CD.

3. Surgeries, either for biopsy or curative, were important for the diagnosis and treatment for CD cases. So, all related surgeries that were performed in our enrolled cases were listed in the Table3 in the revised version.

4. ”diagnostic surgery” means the surgery was performed for biopsy. I have replaced it with “exploratory surgery for biopsy” in the revised version.

5. The detailed chest CT findings of our enrolled cases was listed as Table2 in the revised version.

Sincerely yours,

Hui Huang

Respiratory medicine department

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