Reviewer’s report

Title: Lymphangioleiomyomatosis, multifocal micronodular pneumocyte hyperplasia, and sarcoidosis: more pathological findings in the same chest CT, or a single pathological pathway?

Version: 0 Date: 23 Mar 2017

Reviewer: Stephen Ruoss

Reviewer's report:

The case report manuscript submitted by Di Marco et al. represents an interesting discussion of a rather unusual clinical case they encountered. Their manuscript describes a patient with reported prior history of autoimmune hepatitis, though no corroborating data are included to confirm that diagnosis. More central to their presentation and discussion, they report that the woman has apparent TSC, with multi-organ features consistent with the diagnosis of TSC, and with reported prior genetic testing revealing a TSC1 mutation (corroborating genetic test data on this not supplied in the manuscript). They also describe features of mediastinal and hilar adenopathy on chest CT radiograph, as well as patchy skin involvement with an apparent dermatitis. The skin process was by report biopsied, with some of the features of the histology described, but with no supportive histological images provided in the manuscript.

The manuscript discussion of the patient's clinical circumstance and the test data raises a possible mechanistic link between sarcoidosis and TSC, the latter a disease for which there are substantial data directly linking mTORC1 dysfunction in disease pathogenesis. Di Marco et al. raise the possibility that sarcoidosis as well as TSC may be mediated in part by dysfunction or dysregulation of mTORC1, and reference a recent publication by Linke et al. in support of their pathogenetic speculation.

The manuscript provides very little data to directly support the intriguing pathogenesis speculation offered by the authors. In addition, clinical features suggesting sarcoidosis are not typically encountered in TSC or LAM, nor are features suggestive of TSC or LAM typically encountered in sarcoidosis. So while their report offers some rather intriguing and interesting speculation about possible shared cellular dysregulation pathways playing pathogenic roles in both sarcoidosis and TSC, establishing a clear link between these two diseases is not possible from the material included in the manuscript. The manuscript does function as an interesting alert to both clinicians and clinician-scientists that there may in fact be a mechanistic link, but establishing that link would require much work, and is clearly beyond the scope of this manuscript.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**  
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**  
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**  
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

**Declaration of competing interests**  
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.
I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.