Author’s response to reviews

Title: Thyroid Rosai-Dorfman disease with infiltration of IgG4-bearing plasma cells associated with multiple small pulmonary cysts

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Author’s response to reviews:

PULM-D-18-00531R1: A case report of Rosai Dorfman disease: thyroid infiltration with emperipolesis and increased IgG4-positive plasma cells associated with multiple pulmonary cysts

Point-to-point reply:

We thank the editor and reviewer 2 for their comments on the revised version of our manuscript. Please find below a detailed point-to-point reply taking all concerns into consideration. We revised the manuscript accordingly and strongly hope that it is now acceptable for publication.

1. Please rename the "Introduction" heading so that it appears as "Background" in both the Abstract section and in the main text. The manuscript was revised accordingly.

2. Please rename the "Discussion" section to "Discussion and Conclusions". The manuscript was revised accordingly.

3. Please remove the cover letter, the CARE checklist, and the response to reviewers from the file inventory, as they are no longer needed at this stage of the editorial process. The manuscript was revised accordingly.

4. Please revise your manuscript according to the reviewer comments found at the end of this email.
E Radzikowska (Reviewer 2): I think that in this case lung disease is not sufficiently documented, but other aspects of this rare case are very good presented. Birt-Hogg-Dube syndrome (BHDS) has a wide clinical presentation, and over than 140 mutations of foliculin gene have been identified. There are about 30% of patients with BHDS have only lung cystic lesions, so the statement, that lack of kidney and/or skin lesions excludes the BHDS is not truth.

We agree with the reviewer that the lack of renal cancer and/or skin lesions does not exclude BHDS, an autosomal dominant syndrome characterized by cutaneous fibrofolliculomas, multiple lung cysts, spontaneous pneumothorax and renal cancer. There was no lung disease in the family history of the patient and there was no evidence for extrapulmonary manifestations of BHDS in our case. However, as pointed out in our first response to the reviewer’s comment the distribution of the cysts in our case is not suggestive for BHDS. The cysts in BHDS are multiple, thin walled and in the majority of patients seen in the peripheral lung zones at lung bases and along the mediastinum, they are unique, since they abut or encase the proximal portion of the lower pulmonary veins, disproportionate in number of paramediastinal elliptical (floppy) cysts, generally less in number and bigger in size compared to LAM (Escalon JG et al AJR Am J Roentgenol. 2019; 212:1–5. Isolated Cystic Lung Disease: An Algorithmic Approach to Distinguishing Birt-Hogg-Dubé Syndrome, Lymphangioleiomyomatosis, and Lymphocytic Interstitial Pneumonia). In contrast, the multiple small and thin-walled lung cysts in the presented case were higher in number and diffusely distributed throughout the lung parenchyma, more resembling the distribution in LAM. (Raoof S et al Chest, 2016,150:945, ref 10 in our manuscript). This notion has now been added to the discussion and conclusions section on page 5.

5. When submitting your revised manuscript please ensure you do so as a single clean copy without any tracked changes, colored or highlighted text, as these are no longer required at this stage of the editorial process. The manuscript was resubmitted without any tracked changes, colored or highlighted text according to the request of the editor.