Author’s response to reviews

Title: A case of localized tracheobronchial relapsing polychondritis with positive matrilin-1 staining

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Angelo Gaffo (Reviewer 1)
This is an interesting case report. The authors present a case of a patient with underlying systemic sclerosis who has tracheobronchial inflammation and on biopsies is found to have positive staining for matrilin-1 in the tracheal tissue but not in the auricular cartilage.

Response: We are very grateful for the reviewer’s kind and thoughtful comments to improve the quality of our manuscript. We have addressed the reviewer’s comment one by one, with each comment and response represented as C and R, respectively.

C1-1: The title is quite confusing and I do not believe it conveys properly what was done. I do not pretend to re-write the report for the authors but might suggest: "A case of localized tracheobronchial relapsing polychondritis with positive matrilin-1 staining"

Response: We appreciate the reviewer’s suggestion for our title. We have changed our title as the reviewer suggested.

C1-2: The authors use "trachea-bronchiole" throughout the manuscript but, like in ref 14, "tracheobronchial" seems the right way to describe this.

Response: We also appreciate the reviewer’s suggestion about the usage of medical terminology. We have corrected all the term “trachea-bronchiole” to “tracheobronchial”.

C1-3: The references the authors present for matrilin proteins are outdated. I could find updated references with a simple PubMed search. The authors might consider updating the background and discussion.

Response: We appreciate the reviewer’s suggestion about our reference. We have re-searched and updated our reference regarding matrilin proteins [reference 4] in Background on page 6, line 83 to 84 and in Discussion on page 9, line 159 to 161.

C1-4: Doubt a case reports needs a whole methods section. The immunochemical technique could be included in the case report itself.

Response: We appreciate the reviewer’s suggestion about the description of the immunochemical method. We have deleted the section of “Methods” and described it within the “Case presentation” on page 7, line 118 to 121.

C1-5: This patient had systemic sclerosis in the background. Any discussion of the role this could have played in the presentation? Also would mention in the discussion that RPC commonly presents in association with other autoimmune diseases.

Response: We appreciate the reviewer’s important suggestion. We have discussed the occasional coexistence of RPC with other autoimmune diseases on page 9, line 148 to 152.
C1-6: Please review spelling throughout the manuscript - many mistakes, e.g; "cartridge" for "cartilage"; "matrillin" is misspelled many times. This makes the manuscript not-acceptable at the moment

Response: We really appreciate the reviewer for pointing out our misspellings. We have carefully read through our manuscript and corrected those mistakes.

C1-7: Please clarify why this patient had an ear biopsy. Was it to clarify diagnosis of RPC (medical care) or to explore the issue of matrillin (research). If the former is true then an ethics committee/IRB and a consent would have been needed.

Response: We appreciate the reviewer’s valuable comment about the ear biopsy. In this case, we conducted the ear biopsy to clarify the diagnosis of RPC because a previous report [reference 11] demonstrated the usefulness of ear biopsy for proving cartilage inflammation irrespective of ear symptoms. We have mentioned this point on page 7, line 111 to 113.

C1-8: Probably more insight is needed from the authors on the implication of this finding - if confirmed - for RPC. Will it be important in clarifying pathogenesis, diagnostic testing, therapeutics?

Response: We appreciate the reviewer’s useful comment. We believe that our finding supports the possibility that matrilin-1 is involved in the pathogenesis of localized tracheobronchial RPC. However, immunochemical staining of matrilin-1 in the tracheal tissue would not be useful for the diagnosis of RPC at present, because there has been no report that compared the expression levels between RPC patients and normal subjects. Further studies are needed to clarify this point. We have discussed this point on page 10, line 178 to 181.

Adrian Schreiber (Reviewer 2)

The manuscript by Maikiguchi et al. "A case of matrilin-1 positively stained trachea-bronchiole localizing type in relapsing polychondritis" describes a patient with RPC with positivity of matrilin-1 expression in tracheal specimen.

The authors present an interesting case which could potentially put in further evidence for a role of matrilin-1 in the autoimmune destruction process.

However, in the current from the manuscript has some limitations which should be addressed by the authors.

Response: We are very grateful for the reviewer’s kind and thoughtful comments to improve the quality of our manuscript.

C2-1: The histology figures are of very low quality and makes it very hard to follow the conclusion of the authors. This has to be improved.
Response: We apologize to the reviewer for the trouble in interpreting the histology figures due to the low quality. We have now corrected the histology figures.

C2-2: The manuscript would greatly benefit from the measurement of autoantibodies against matrilin-1 in the index patient. I would suggest to include a measurement.

Response: We appreciate the reviewer’s thoughtful and significant suggestion. There were some difficulties in measuring the amount of anti-matrilin-1 antibody. First of all, as far as we know, there is no commercially available method to measure it. Furthermore, to interpret this patient’s result, we will also need to prepare serum from RPC patients without airway involvement or other articular cartilage destructive diseases such as rheumatoid disease, as well. Second, we did not preserve this patient’s serum and, inconveniently, he was transferred to another hospital for further medical treatment several months ago. The reviewer’s thoughtful comment remains to be solved in the future. However, this time we have noted this issue as a limitation on page 9, line 164 to 166.

C2-3: Minor points: There are some misspellings which should be edited.

Response: We really appreciate the reviewer for pointing out our misspellings. This comment was also pointed out by reviewer 1. We have carefully read through our manuscript and corrected those mistakes.