

Dear Editors and Reviewers:

Thank you very much for your careful review and constructive suggestions with regard to our manuscript "**Pulmonary hypertension secondary to seronegative rheumatoid arthritis overlapping antisynthetase syndrome**" Those comments are helpful for us to revise and improve this article.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors describe an unusual case of PH secondary to Seronegative RA plus ASS. The case is well written and figures are legible too. Multiple Minor comments need to be addressed- 1.Please expand "IIM" in introduction section, Line 8. 2.Outcome/follow-up section, Line 3- "Cardiac ultrasonography revealed Mild PH"- Please define the source of classification of PH into mild, moderate & severe. Neither the recent ACC/AHA nor the ESC/ERS PH guidelines provide such a classification. 3.Outcome/follow-up section,Line 11- " Arpan can be relieved after regular " - the sentence doesn't make sense ..correct it! 4."The current treatment of PAH (Anritsu Tan Tablets 5 mg bid) was" - provide generic name of Anristu Tan tablet ! 5.Table 1- "Pulmonary artery pressure" - which one Mean or systolic or diastolic ? 6. Fig. 2 - Gradual widening of the pulmonary artery not appreciable in serial CT. Give Pulmonary Artery dimensions for better understanding. 7." Sparks et al. showed that depression, especially antidepressant use, is " - Any specific antidepressants use which is more prone to develop RA ? if yes add. 8."SNRA and depression" section can be trimmed. Not very relevant as the present case concerns regarding development of PH. 9.SNRA and ASS section, Line 4-"Radiotherapy erosion is occasionally found " - it should be "radiological erosions". 10. Why ws ASS diagnosed - mention which criteria - Solomon or Connor's? 11.Reference - 14 & 16 are duplicate 12.Reference - 17 & 19 are duplicate

Reply: Thank you for taking the time to review our article. We are very grateful to your meaningful comments and kind reminder. According your comments, we amended the relevant part in manuscript.

1. Thank you for pointing this, we have expanded idiopathic inflammatory myositis (IIM) in introduction section, Line 11.

2. Dear reviewers, We appreciate your reminder. Due to our oversight, a re-review of the literature revealed the limitations of our classification of the severity of pulmonary hypertension, which is only available in our

country. We have revised "Cardiac ultrasonography revealed Mild PH" to "Cardiac ultrasonography revealed PH". And we removed such classification in our text.

3. Thank you for your valuable advice, we have revised "Arpan can be relieved after regular" to "Joint pain was relieved after regular" in the Outcome/follow-up section, Line 13.

4. We have revised "Anristu Tan" to "ambrisentan" in the Outcome/follow-up section, Line 20.

5. RAP can be estimated by echocardiography, the estimation of systolic PAP is based on the peak tricuspid regurgitation velocity (TRV) taking into account right atrial pressure (RAP) as described by the simplified Bernoulli equation. We have changed Table 1- "Pulmonary artery pressure" into "Pulmonary systolic artery pressure"

6. Thank you for your advice, we have taken your suggestion and marked the dimensions in Fig. 2 for better understanding.

7. Considering your valuable suggestions:"SNRA and depression" section can be trimmed. Not very relevant as the present case concerns regarding development of PH. We have trimmed "SNRA and depression" in the discussion section. So we did not add antidepressants use which is more prone to develop RA.

8. Thank you for your valuable advice and we have trimmed "SNRA and depression" in the discussion section.

9. Thank the reviewer for this valuable comment. We have revised "Radiotherapy erosion" to "radiological erosions" in the SNRA and ASS section, Line 5.

10. Our patient's anti-J0-1 were strongly positive, and she had arthritis and ILD(not explained by other causes). according to the Connor et al.,2010 criterion, ASS was diagnosed.[1]

[1]. Marco, J.L. and B.F. Collins, Clinical manifestations and treatment of antisynthetase syndrome. Best Pract Res Clin Rheumatol, 2020. 34(4): p. 101503.

11. Thank you for the reminder, we have rechecked and removed the duplicate references.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Thank you for the opportunity to review this work. -1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes -2 Abstract. Does the abstract summarize and reflect the

work described in the manuscript? Yes. However, please provide the full term of this abbreviation in the Core tip: "ASS," "PAH," and "CTD." -3 Key words. Do the key words reflect the focus of the manuscript? Yes -4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes -5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Not applicable. -6 Results. Are the research objectives achieved by the experiments used in this study? Yes -7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Yes -8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Yes -9 Biostatistics. Not applicable. -10 Units. Does the manuscript meet the requirements of use of SI units? Yes -11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? There was "[J]" after every journal title in the reference. For example, "De Stefano L, D'Onofrio B, Manzo A, et al. The Genetic, Environmental, and Immunopathological Complexity of Autoantibody-Negative Rheumatoid Arthritis[J]. Int J Mol Sci, 2021,22(22)." Please remove "[J]" in the reference. -12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Yes -13 Research methods and reporting. The CARE checklist mentions the "strengths and limitations in your approach to this case." Therefore, please state the strengths and limitations of this case in the manuscript in the discussion section. -14 Ethics statements. Yes

Reply: Thank you for acknowledging some aspects of our article. It is our great honor to receive your active comments. Thank you very much. According your comments, we amended the relevant part in manuscript.

1. Based on your valuable advice, we have provided the full term of this abbreviation in the Core tip: "ASS," "PAH," and "CTD."
2. Thank you for the reminder, we have rechecked and removed "[J]" in the reference.
3. Thank the reviewer for this valuable comment. The CARE checklist mentions the "strengths and limitations in our approach to this case." Therefore, We have stated the strengths and limitations of this case in the manuscript in the discussion section. One strength of our case study is that it is the first report of this particular phenotype, but a limitation is that although cardiac ultrasound can screen for pulmonary hypertension, our patient did not undergo the gold standard test.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is an interesting case for reporting. It is worth noting that, the discussion section is rich and well arranged, and the most parts of the manuscript has a good spelling, grammar and syntax. In addition, the majority of bibliographic citations are update. However, before it becomes publishable, it still requires some improvement. Here are my comments: 1.The background section has been duplicated from the first paragraph of the introduction, it is incomplete and does not cover all of your research ingredients, and also, the importance of your article is not prominent enough. In this section, you must create an explicit view of why you are directed to write this topic. 2.In the case summary section be specific on the patient, and what have done for this individual, not on what this case study reports and definition of scientific facts. At the last sentences of this section explain the current situation of your patient. 3.Add one more keyword in your abstract, and make sure you checked all of them on Medical Subject Headings (MeSH). 4.The constructs and concepts in the introduction section are poor-organized. Include more general and specific background in the manuscript, and use more cohesion and coherence in sentences. The aim of your study, which must come in the last sentences, been located in the middle. 5.In the introduction section, there are some sentences which been left without citation. Provide references for All the sentences which finished by dot, and make sure that the entire of manuscript follow this maxim. 6.in the final diagnosis section, you have written the initial diagnosis; substitute it with final diagnosis. Sincerely Navid Faraji

Reply: Thank you for your recognition of our article. We are very grateful to your meaningful comments. According your comments, we amended the relevant part in manuscript.

1. Thanks to the reviewer, the background section has been duplicated from the first paragraph of the introduction, it is incomplete and does not cover all of our research ingredients, and also, the importance of our article is not prominent enough. In this section, we have created an explicit view of why we are directed to write this topic. We have taken your suggestions and revised the background section to complete and cover all of our research ingredients.

2. Thanks to the reviewer, we have taken your valuable suggestion and revised the case summary section on the following: specific on the patient, and what have done for this individual, At the last sentences of this section we have explained the current situation of our patient.

3. We checked all of keywords on Medical Subject Headings (MeSH) and We revised them.

4. Thank you very much for your meaningful advice. The constructs and concepts in our introduction section are poor-organized. We have

reorganized the introductory and background sections Including more general and specific background in the manuscript, and use more cohesion and coherence in sentences to make them more readable. In the last sentences, we have stated The aim of our study.

5. Thank you for the kind tip, we have added references to all the sentences which finished by dot.

6. In the final diagnosis section, We substitute initial diagnosis with final diagnosis.

Responses to science editor:

Thank you very much for your active comments.

Responses to company editor-in-chief:

Thank you very much for giving us this opportunity to revise our manuscript. According to the reviewers' comments, we have revised the manuscript. We have upload the Signed Informed Consent Form in Chinese, the original figure documents and the approval document of funding agency.