

Dear Editor,

Thank you for your email and the reviewer's comments concerning our manuscript entitled "Pulmonary sarcoidosis: a novel sequelae of DRESS – a case report" (ID: 80024). We thank the reviewer for the very helpful comments. We revised the manuscript according to the recommendations. We provide below with a brief "List of changes" in the revised manuscript, followed by our answers to the referee's comments.

List of changes: (The manuscript has been modified using Microsoft Word Track Changes)

1. Page 7 line 23-30, page 8 line 1-9, and we added references [9] and [10].
2. Page 2 line 24-26.
3. We added a new figure (figure 1) and adjusted the figures order.
4. We added Physical examination and Laboratory examinations according to "*List of common issues in revised manuscripts by authors and comments*".
5. We sent our revised manuscript to AJE and edited further.

Reviewer #1:

Specific Comments to Authors: The authors have reported a case of pulmonary sarcoidosis secondary to Allopurinol induced DRESS- the authors should be commended on approaching this rare but important clinical entity. The article flows well on the whole with enhancement from clinical and pathological images. It may be worthwhile to have a brief discussion of differential diagnoses of non-caseating granulomas included within the case. Would politely remind the authors to adhere strictly to scientific writing to avoid losing the impact of their article. 'At a follow-up of 6 months after the treatment withdrawal, the patient's situation stayed stable and he was satisfied with the results of the treatment.' could be rewritten as Following a 6-month follow-up of completion of treatment, the patient's clinical condition remained stable with no clinical evidence of relapse. The initial results with follow-up results could be tabulated to make it easier for the reader to follow. Was ACE levels measured and/or monitored? Kindly include this.

Response to Reviewer #1: Thank you for your summary. We really appreciate your efforts in reviewing our manuscript. We have revised the manuscript accordingly. Our point-by-point

responses are detailed below.

Detailed reply to reviewer's comments:

Comment 1: *It may be worthwhile to have a brief discussion of differential diagnoses of non-caseating granulomas included within the case.*

Response to comment 1: We are grateful for the suggestion. To be more clearly and in accordance with the reviewer concerns, we have added a more detailed interpretation regarding the differential diagnoses of non-caseating granulomas. More detailed statistical analysis was added on page 7 line 23-30, page 8 line 1-9. The revised content in our manuscript now reads:

The differential diagnoses of noncaseating granulomas are briefly listed below[9,10]: (1) Hypersensitivity Pneumonitis (HP): The hilar lymph nodes are not affected, and granulomas are mainly located in the peribronchiolar region. Due to the predominance of CD8+ suppressor lymphocytes in HP, bronchoalveolar lavage can provide some diagnostic basis. (2) Chronic Beryllium Disease (CBD) and Silicosis: CBD is usually referred to as “sarcoidosis of known cause”. It is important to take an accurate exposure and occupational history to exclude conditions such as berylliosis or silicosis. (3) The sarcoid-like reaction: Noncaseating granulomas may be seen in a number of settings, including malignancy (e.g., solid neoplasm, Hodgkin's disease, and non-Hodgkin lymphoma), drug toxicity and subsequent medical device implantation. (4) Common variable immunodeficiency (CVID): The presence of low serum immunoglobulin levels, a history of recurrent infection, the presence of areas of organizing pneumonia and follicular bronchiolitis may be helpful in the diagnosis. Our patient did not meet the abovementioned criteria and was finally diagnosed with pulmonary sarcoidosis.

The corresponding references are:

9 Bernardinello N, Petrarulo S, Balestro E, Cocconcelli E, Veltkamp M and Spagnolo P. Pulmonary Sarcoidosis: Diagnosis and Differential Diagnosis. *Diagnostics* (Basel, Switzerland) 2021; 11: [PMID: 34573900 DOI: 10.3390/diagnostics11091558]

10 Tana C, Donatiello I, Caputo A, Tana M, Naccarelli T, Mantini C, Ricci F, Ticinesi A, Meschi T, Cipollone F and Giamberardino MA. Clinical Features, Histopathology and Differential Diagnosis of Sarcoidosis. *Cells* 2021; 11: [PMID: 35011621 DOI: 10.3390/cells11010059]

Comment 2: *Would politely remind the authors to adhere strictly to scientific writing to avoid losing the impact of their article. 'At a follow-up of 6 months after the treatment withdrawal, the patient's*

situation stayed stable and he was satisfied with the results of the treatment.' could be rewritten as Following a 6-month follow-up of completion of treatment, the patient's clinical condition remained stable with no clinical evidence of relapse.

Response to comment 2: We agree with the comment and re-wrote the sentence on page 2 line 24-26.

Comment 3: *The initial results with follow-up results could be tabulated to make it easier for the reader to follow.*

Response to comment 3: We are grateful for the suggestion. To be more clearly and in accordance with the reviewer concerns, we have added the figure 1.

Comment 4: *Was ACE levels measured and/or monitored? Kindly include this.*

Response to comment 4: Thank you for your careful review. We did not measure ACE levels. The diagnosis of pulmonary sarcoidosis is based on radiologic and pathological findings. Angiotensin converting enzyme (ACE) is a widely used biomarker in sarcoidosis with suboptimal sensitivity and specificity, and some of the sarcoidosis patients had no high serum ACE values. For our patient, after other causes of granulomas had been ruled out, sarcoidosis was diagnosed based on the evidence of chest radiographic findings and noncaseating granulomas on biopsy.

Reviewer #2:

Specific Comments to Authors: Dear Authors, this is a well-written manuscript with an interesting message to deliver. The diagnostic work-out and intellectual background of your case support the conclusion that the pulmonary sarcoidosis was interestingly connected to DRESS syndrome after allopurinol administration. Best Regards

Response to Reviewer #2: Thank you for your careful review. We really appreciate your efforts in reviewing our manuscript.

Sincerely Yours,

Yuqi Hu & Ai Cui on behalf of all the authors.