Author's response to reviews

Title: Bilateral pleural effusion and interstitial lung disease as unusual manifestations of Kikuchi-Fujimoto disease: case report and review of the literature

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Author's response to reviews: see over
Dear Sir:

We are grateful for your comments and the reviewers’ proof-correction. My colleagues and myself have just reviewed the manuscript achieving some obvious improvement, in our opinion. Please excuse one of MY mistakes: I forgot to include all the data from pleural fluid. Regarding the inclusion of microphotographs of the lymph node examined, we recently acquired the necessary technology and have included a third figure with the histopathological content. We emphasized all the grammar and syntax corrections performed in red letter case, so that they can be better appreciated.

Subsequently, we will try to give a point-by-point response to the reviewers’ remaining queries and comments:

1) Reviewer: Antoni Hrycek
   a. In fact, Aota Y et al. reported one case of pleural effusion due to KFD in 2006\(^1\). We reviewed English literature and did not record this paper, which is written in Japanese. Nevertheless we took into account the data included in the abstract, written in English: we omitted our case as the “first case of isolated KFD with pleuropulmonary involvement”, and we changed our conclusion.
   b. Really, Chen HC et al. was repeated in reference numbers 4 and 6. Please accept our apologies.

2) Reviewer: Krystyna Galazka
   a. Our colleague Laura Zaldumbide performed a more detailed description of the histopathological picture of the lymph node examined, and provided us with a microphotograph of the case with typical features of KFD. Crescentic or non-phagocytic histiocytes could be observed between various other types of histiocytes like tingible body macrophages or foamy histiocytes. Unfortunately, we did not determine the presence or the expression of myeloperoxidase antigen in the histiocytes of our patient.
   b. We also performed most of the language corrections she suggested.
3) Reviewer: Kyung-Yil Lee
   a. We actually assume that our report has some limitations, mainly the lack of lung or even pleural pathologic findings, and the absence of immunological contributions for a better understanding of KFD. We must argue that, due to our limited technical resources, our point of view is basically clinical: we report one case of isolated KFD with bilateral pleural effusion and interstitial lung disease, and its excellent improvement with prednisone treatment. Furthermore, lung or pleural biopsy were not necessary for the diagnosis and clinical management of the patient, so we did not perform them.
   b. We tried to shorten the title, but we were unable to do so without losing essential information regarding the report.
   c. We added to the manuscript the normal ranges of laboratory data, and the immunoglobulins levels, as the reviewer suggested. We did not determine the lymphocyte subsets and the complement. We utilized antinuclear antibodies (ANA) as autoantibody screening. Due to the main usefulness of fluorescence antinuclear antibodies (FANA) in the prediction of KFD recurrences, we obviated them.
   d. We added the characteristics of the removed lymph node and the patient’s clinical evolution during the next days, as the reviewer suggested.
   e. There is no specific treatment for patients with KFD, the disease is usually self-limited and only in cases with severe clinical course and/or multiple relapsing symptoms, could corticosteroids offer some benefit in the opinion of some authors, on the basis of pathogenic and immunologic considerations. To date there is no algorithm regarding the duration of the prednisone treatment. In our case, like in others, the clinical and analytical improvement during follow-up appointments were essential.

4) Reviewer: Maria Hatzistilianou
In our opinion we could conclude that our patient suffered from isolated KFD, and differential diagnosis was correctly performed regarding SLE:

i. The patient never met the validated revised ACR criteria for SLE\(^5\).

ii. Typical findings of SLE were not observed in the lymph node biopsy: necrotic and thrombosed blood vessels, necrotizing neutrophilic infiltrate and the pathognomonic haematoxylin bodies\(^6\).

iii. We performed ANA as autoantibody screening at the time of KFD diagnosis and during follow-up evaluation, as recommended by some authors\(^2\).

iv. The follow-up of the patient for two years should also be seriously considered: nowadays he is asymptomatic and autoantibody screening remains absolutely negative.

5) Reviewer: Fevzi Altuntas

a. We agree with the reviewer that the co-existence of an autoimmune thyroid disease would support an interesting relationship. Unfortunately, as we pointed out in the manuscript, the hyperthyroidism of our patient was due to toxic multinodular goiter. It is an occasional consequence of long standing simple goiter. This disease is more common in areas of endemicity, like ours (Lower Deba County, Basque Country-Spain), and genetic and environmental factors seem crucial in its pathogenesis, rather than autoimmunity.

We had the opportunity of reviewing and correcting our manuscript with a Dutch colleague who is in possession of the Proficiency level of English language. My colleagues and I hope you will find it of interest for being published in your Journal.

Best regards

Alberto Garcia-Zamalloa MD
REFERENCES