Manuscript NO: 72674 revision

Dear Editor,

Many thanks for your consideration of our manuscript “Serum-negative sjogren's syndrome with minimal pathologic nephropathy as the initial presentation: A case report” (Manuscript NO: 72674). We appreciated comments and suggestions from the reviewers. We have responded to the comments in this letter and submitted a revised version of the manuscript that addressed the points as reviewers suggested. The relevant reviewers’ comments (**in bold**) and our responses were presented below.

We hope that the revised version of our manuscript will be acceptable for publication in the journal of *World Journal of Clinical Cases*.

I look forward to hearing from you soon.

Sincerely yours,

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Point-by-point responses to the reviewer' comments:

First of all, we thank all the reviewers for their positive and constructive comments and suggestions.

Reviewers' comments:

Reviewer #1:

1. In Case Presentation, the reasons supported the final diagnosis of pSS should be revised for clarity. The phrase like "SS was not exclude…." is not the positive description for the final diagnosis.

Answer:

Thank you for the comment. I have adjusted the language and removed phrase like "SS was not exclude...". The final diagnosis was sjogren's syndrome combined with nephrotic syndrome in the Case Presentation. (Line 97)

2. When was this patient discharged from the hospital?

Answer:

The patient was discharged from the hospital on December 09, 2020. (Line 99-100)

3.Justification of final diagnosis of an atypical pSS should be the first priority in the Discussion section and the following issues should be discussed: Negativity of SS-A and SS-B antibody serology was significantly more common in later-onset pSS, compared to early-onset pSS. A 43-year-old female patient was presented in this case report, which is later-onset according to the classification of Wei et al. (2021). Wei L, Zhifei X, Xiaoran N, Meilu L, Yang L, Yixuan L, Xiuying R, Yashuang S, Jingjing C, Shaoying G, Liu Y, Lijun S, Fengxiao Z, Wen Z. Patients with early-onset primary Sjögren's syndrome have distinctive clinical manifestations and circulating lymphocyte profiles. Rheumatology (Oxford). 2021 Apr 20:keab367. doi: 10.1093/rheumatology/keab367. Epub ahead of print. PMID: 33878180. Notably, a positive ANA test is also common in healthy individuals. Li QZ, Karp DR, Quan J, Branch VK, Zhou J, Lian Y, Chong BF, Wakeland EK, Olsen NJ. Risk factors for ANA positivity in healthy persons. Arthritis Res Ther. 2011 Mar 2;13(2):R38. doi: 10.1186/ar3271. PMID: 21366908; PMCID: PMC3132017.

Answer:

In the first paragraph of this discussion, I have explained the rationale for the final diagnosis of atypical pSS. The diagnosis of Sjogren's syndrome was based on the 2016 ACR/EULAR pSS classification criteria. We discussed that serologically negative SS-A and SS-B antibodies are significantly more common in late-onset pSS, compared to early-onset pSS, which have more pronounced clinical manifestations and enhanced activation of the cellular immune system..MSGB should be considered if pSS were suspected in the patients without typical pSS symptoms or specific autoantibodies.(Line 106-124)。

4.For better logic flow and readability, awkward sentences and grammatical errors should be corrected. For example; "Therefore, early diagnosis and realization of the effect of pSS on kidney disease is important." This statement did not reflect the scope of this case report. "However, under the current laboratory diagnostic technology, the corresponding autoantibodies cannot be detected in the serum of some pSS patients,…" Did Authors refer to the limited diagnostic technology of their hospital?

Answer:

We have refined the language and removed inappropriate expressions, such as "Therefore, early diagnosis and realization of the effect of pSS on kidney disease is important" and "However, under the current laboratory diagnostic technology, the corresponding autoantibodies cannot be detected in the serum of some pSS patients,…."

Reviewer #2:

1. The authors described a case of nephrotic syndrome. Evidence including lip salivary gland inflammation and decreased tear flow suggests that SS may be the cause. Renal tubular atrophy and interstitial fibrosis were occasionally observed under light microscopic analysis in this case. Interstitial inflammatory cell focal aggregation is a common pathological manifestation of renal damage in SS. Please highlight these findings in figures.

Answer:

We have circled in red the focal aggregation of interstitial inflammatory cells in Fig. 1B and 1C. (Line 82-83)

2. Differential diagnosis of other autoimmune diseases are needed.

- Answer: I have added more antibody tests for identification in Table 1. The current medical history describes that the patient has no dry mouth, no need to take dry food with water, no dry eyes, no flake tooth loss, no parotid gland enlargement, no joint pain, no hair loss, no light allergy, no oral ulcer,no systemic skin sclerosis. In laboratory examination, anti dsDNA and anti SM antibodies were negative, and complement C3 was normal. In conclusion, systemic lupus erythematosus and other immunological diseasescan be excluded..(Line169-178).

3. Please check more autoantibodies to identify what constitutes ANA in the case. ..

Answer：In Table 1, more autoantibodies were added to determine the ANA composition in this case (mainly including RF, anti-RNP, anti-ACA, anti-scl-70, anti-A-Fordrin and anti-JO-1). (Line63-69)