Responses to the Editor's and Reviewer's Comments

February 9, 2024

Dear reviewer and the editorial staff of ***World Journal of Clinical Cases*****,**

We wish to re-submit the manuscript titled "**Systemic lupus erythematosus in a 15-year-old female with multiple splenic nodules: A case report**" (Manuscript NO.: 92121, Case Report).

We express our sincere gratitude for your detailed review and careful scrutiny of our manuscript. We thank the Editor and the reviewer for their thoughtful suggestions and insights, from which our manuscript has immensely benefited. Through the accurate comments made by the reviewer, we now better understand the critical issues in our paper. Accordingly, we have revised the manuscript and made the necessary changes in accordance with the Editor's and reviewer's insightful suggestions. The revisions made in the paper are highlighted in yellow for ease of identification.

Our point-by-point responses to the reviewer's comments are provided below.

We acknowledge that the quality of our manuscript has improved owing to the considerable efforts of the reviewer and Editor. Hence, we hope that our revised manuscript will be considered and accepted for publication in the ***World Journal of Clinical Cases***.

Thank you for your consideration. I look forward to hearing from you.

Reviewer's Comment:

1. In this case, the authors performed CT, RBC-SPECT, PET-CT for the patient to identify the etiology and nodule nature, however, MRI has also been emphasized in upper abdominal disease. The authors' preference for CT was based on lupus enteritis. Should MRI examinations be considered in the subsequent identification? If so, what is the value of the test compared to other examinations.

Author's reply:

We thank the reviewer for these insightful comments. Normally, the signal of the adult spleen on MRI, when compared to the liver, is hyperintense on T2 weighted-imaging and hypointense on T1-weighted imaging. Specifically, the spleen exhibits a high signal on diffusion-weighted imaging. In the case of hemangioma, it typically appears as hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Additionally, peripheral enhancement with centripetal filling on later phase imaging may be observed. Lymphoma, on the other hand, usually presents as hypo-enhancing compared to the rest of the splenic parenchyma. Therefore, when MRI is performed, it is possible to differentiate between hemangioma and lymphoma using MRI alone. However, compared to PET-CT, it may be challenging to differentiate focal infiltrating lymphoma, which exhibits little tissue contrast between normal splenic parenchyma.

In this case, the patient sought opinions from the radiologist and oncologist after undergoing AP-CT. At the time, the patient presented with a LDH level of 544 U/L (normal range: 135-250), persistent fever, and multiple lymph node enlargements, including a palpable left sterno-clavicular lymph node. In particular, the differentiation of lymphoma and the selection of the biopsy location were crucial. As such, RBC spect scan and PET-CT were initially recommended. This decision also took into account the examination costs and schedules at our clinic.

Upon reflection, we now recognize that MRI would have been a good alternative imaging tool to differentiate between hemangioma and lymphoma, as suggested by the reviewer.

REFERENCES

1 **Ito K,** Mitchell DG, Honjo K, Fujita T, Uchisako H, Matsumoto T, Matsunaga N, Honma Y, Yamakawa K. MR imaging of acquired abnormalities of the spleen. AJR Am J Roentgenol 1997; 168: 697-702 [PMID: 9057518 DOI: 10.2214/ajr.168.3.9057518]

2 **Saboo SS**, Krajewski KM, O'Regan KN, Giardino A, Brown JR, Ramaiya N,

Jagannathan JP. Spleen in haematological malignancies: spectrum of imaging findings. Br J Radiol 2012; 85: 81-92 [PMID: 22096219 DOI: 10.1259/bjr/31542964]

3 **Rabushka LS**, Kawashima A, Fishman EK. Imaging of the spleen: CT with supplemental MR examination. Radiographics 1994; 14: 307-332 [PMID: 8190956 DOI: 10.1148/radiographics.14.2.8190956]

2. Periarteriolar necrosis was observed in this study, while aseptic necrosis and infarction were also observed in a previous study, based on your insights, weather this explain the occurrence of splenic infarction in patients with SLE. It would be nice to have more discussion.

Author's reply:

We appreciate these valuable comments by the reviewer. Splenic infarction occurs when the blood supply to the spleen is compromised, typically due to occlusion of an artery or vein. In autoimmune diseases, such as systemic lupus erythematosus (SLE), splenic infarctions may occur occasionally. In SLE, symptoms related to blood clots can arise, leading to impaired blood circulation in the spleen. Many SLE patients exhibit positive antiphospholipid antibodies, which potentiate thrombosis by upregulating surface adhesion molecules and releasing proinflammatory cytokines. The activation of vascular and immune cells by antiphospholipid antibodies further enhances thrombosis through these mechanisms.

The patient in this case has an anticardiolipin antibody IgG level of 46.0 GPL (<23), whereas the lupus anticoagulant and anti-beta2 GPI antibody tests were negative. This positive antiphospholipid antibody finding is believed to be associated with pathological periarteriolar necrosis. The patient is currently receiving low-dose aspirin, and there have been no occurrences of thrombotic events since starting this treatment.

We also explained the relationship between splenic infarction and SLE in the Discussion section. **Additionally, the Reference section was revised, specifically on page 8, lines 10-13, and on page 10, lines 13-21**):

Discussion section

Many SLE patients show positive antiphospholipid antibodies, and these antibodies are involved in splenic infarction and necrosis through the upregulation of surface

adhesion molecules and the release of proinflammatory cytokines and procoagulants.

Reference section

11 **Wand O**, Tayer OE, Khoury S, Hershko AY. A practical approach to infarction of the spleen as a rare manifestation of multiple common diseases. *Ann Med* 2018; 50: 494-500 [PMID: 29929401 DOI: 10.1080/07853890.2018.1492148]

12 **David G**, Doruk E. Diagnosis and Management of the Antiphospholipid Syndrome. *N Engl J Med* 2018; 378: 2010-2021 [PMID: 29791828 DOI: 10.1056/NEJMra1705454]c

13 **Arnold MH**, Schrieber L. Splenic and renal infarction in systemic lupus erythematosus: association with anti-cardiolipin antibodies. *Clin Rheumatol* 1988; 7: 406-410 [PMID: 3229088 DOI: 10.1007/BF02239202]

REFERENCES

1 **Wand O**, Tayer OE, Khoury S, Hershko AY. A practical approach to infarction of the spleen as a rare manifestation of multiple common diseases. Ann Med 2018; 50: 494-500 [PMID: 29929401 DOI: 10.1080/07853890.2018.1492148]

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3 **Arnold MH**, Schrieber L. Splenic and renal infarction in systemic lupus erythematosus: association with anti-cardiolipin antibodies 1988; 7: 406-410 [PMID: 3229088 DOI: 10.1007/BF02239202]

3. It might be better to add scale bars to Figure 3, even if it's stated in the description.

Author's reply:

We thank the reviewer for pointing this out. In line with the reviewer's comment, we added scale bars to Figures 3 and 5 as follows:

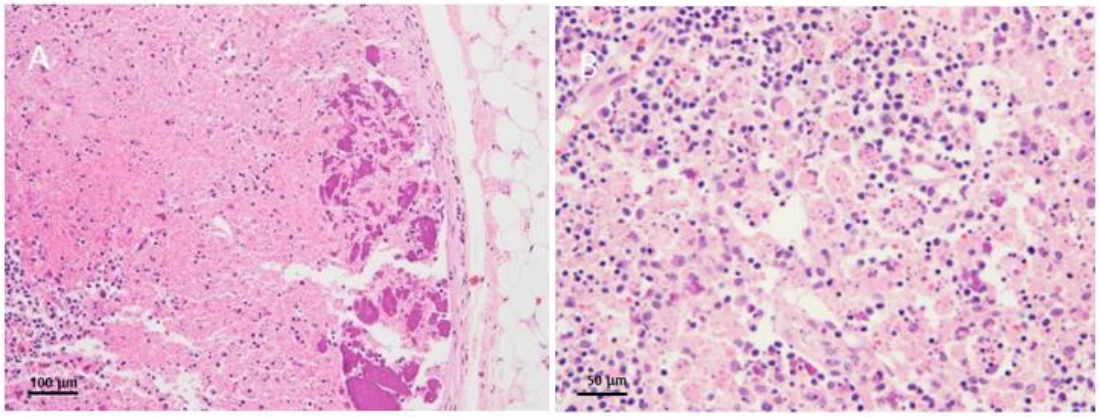

Figure 3 Histopathological findings of the lymph node. A: Lymph node biopsy reveals extensive subcapsular necrosis with hematoxylin bodies (hematoxylin and eosin stain, x200); B: Higher magnification shows abundant crescentic histiocytes, abundant karyorrhectic debris, and small hematoxylin bodies (hematoxylin and eosin stain, x400).

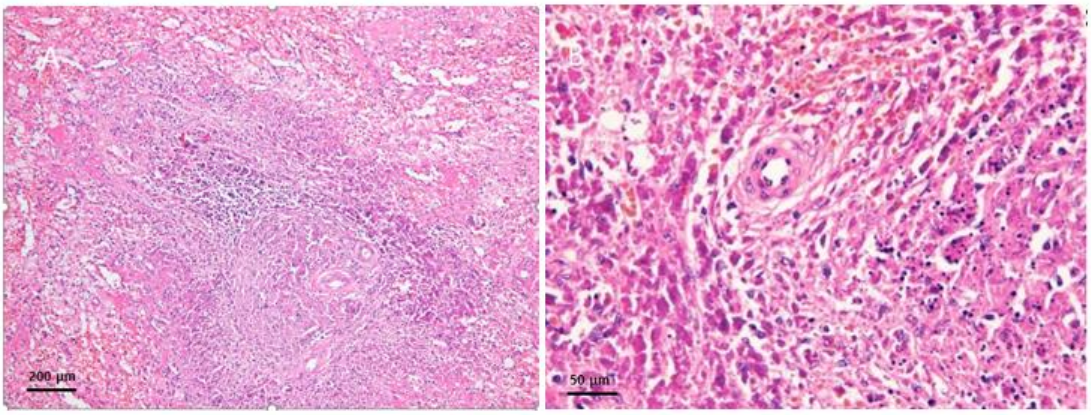

Figure 5 Histological findings of the spleen. A: Extensive periarteriolar necrosis with hematoxylin bodies (hematoxylin and eosin stain, x100); B: Higher magnification of hematoxylin bodies and abundant karyorrhectic debris (hematoxylin and eosin stain, x400).