RE: World Journal of Clinical Cases-79983

December 28, 2022

Name of Journal: World Journal of Clinical Cases
Manuscript NO.: 79983
Column: Case Report
Title: Unusual presentation of systemic lupus erythematosus as hemophagocytic lymphohistiocytosis in a female patient: A case report

Dear Editors:

Thank you very much for giving us an opportunity to improve our paper. We have revised the manuscript according to the reviewers' constructive comments and suggestions. You may find our answers to the reviewers on the following pages. If any other concerns exist, please let me know at your first convenience.

Looking forward to hearing from you.

Best wishes,

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Reviewer #1:

Dear authors, Thank you for this interesting case report. I have proposed some changes and had some questions I have added directly to the revised manuscript. However, the most intriguing part for me is that I think that the diagnosis of the patient as having TTP is not clear enough, as well as the genetic testing report. I think these warrant some clarification.

Answer: Thanks for your suggestion. The patient in our case showed negative result of ADAMS13, however not meet the diagnosis criteria of TTP [1]. We modified the discussion part on page 8. We also added detailed explanation of genetic testing report on page 6 ("Further diagnostic work-up" part).

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This MS is a well-written, potentially interesting case report. Some concerns are arisen which should be addressed adequately.

1. Hemophagocytic lyphohistiocytosis as an initial presentaion of SLE has already been reported. Thus, it is needed to clearly describe what kind of points are novel.

Answer: We appreciate your comments very much and agree with you. SLE is an autoimmune condition that is strongly associated with HLH [2]. In SLE patients, the estimated prevalence of co-occurrence of sHLH has been reported to be 0.9%–4.6% [3].

The novelty of our case report is that this is the first case of an SLE patient with a disease course accompanied by sHLH, thrombotic microvascular disease, and infection. As a rare case of a young female with SLE accompanied by HLH. The patient presented with TMA and infection on the second admission to our hospital, which was an essential reminder for clinicians during treatment of SLE patients complicated with HLH. Besides, we also did whole exon gene sequencing to screen for genetic diseases and found positive mutations in LYST gene, ATM gene and FERMT1 gene. We have added the statement on page 8 (discussion part).

2. It is nice to use a table which summarized previously reprted cases with the same condition. The authors should discuss the similarity and diferrences between prreviously reported cases and this case.

Answer: Thanks for your suggestion. The previous study has systematically reviewed the characteristics of patients with SLE and MAS [4]. The study demonstrated that MAS development in SLE patients led to highly intensive care unit admissions and in-hospital mortalities with presence of infection, and thrombocytopenia. Similar to the review, the patient in our case report showed dramatically increased levels of ferritin, which formed an important part of the diagnostic criteria. We have added the statement on page 8 to page 9 (discussion part).

3. Why this patient develop this condition? In-depth soeculation should be represented.

Answer: Because of methylprednisolone and immunosuppressant treatment, the patient presented with infection and TMA, which was an essential reminder for clinicians during

treatment of SLE patient complicated with HLH. We have added the statement on page 7.

Reviewer #3:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: Please add more explanation about genetic testing and recommendation for genetic testing for patients with SLE and suspected HLH
Answer: Thanks for your suggestion. We also added a detailed explanation of the genetic testing report on page 6 (Further diagnostic work-up part).

References:

1. Zheng XL, Vesely SK, Cataland SR, Coppo P, Geldziler B, Iorio A, Matsumoto M, Mustafa RA, Pai M, Rock G, Russell L, Tarawneh R, Valdes J, Peyvandi F. ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020;**18**:2496-2502. [PMID:PMC8091490 DOI: 10.1111/jth.15010].
2. Patel AR, Desai PV, Banskota SU, Edigin E, Manadan AM. Hemophagocytic Lymphohistiocytosis Hospitalizations in Adults and Its Association With Rheumatologic Diseases: Data From Nationwide Inpatient Sample. J Clin Rheumatol. 2020;**Publish Ahead of Print**. DOI: 10.1097/rhu.0000000000001670].
3. Gupta D, Mohanty S, Thakral D, Bagga A, Wig N, Mitra DK. Unusual Association of Hemophagocytic Lymphohistiocytosis in Systemic Lupus Erythematosus: Cases Reported at Tertiary Care Center. Am J Case Rep. 2016;**17**:739-744. [PMID:PMC5065291 they have no conflicts of interest. DOI: 10.12659/ajcr.899433].
4. Aziz A, Castaneda EE, Ahmad N, Veerapalli H, Rockferry AG, Lankala CR, Hamid P. Exploring Macrophage Activation Syndrome Secondary to Systemic Lupus Erythematosus in Adults: A Systematic Review of the Literature. Cureus. 2021;**13**:e18822. [PMID:PMC8592789 DOI: 10.7759/cureus.18822].