Reviewer's report

Title: Acute kidney injury induced by thrombotic microangiopathy in a patient with haemophagocytic lymphohistiocytosis

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Reviewer: Jin-Shuen Chen

Reviewer's report:

The manuscript “Acute kidney injury induced by thrombotic microangiopathy in a patient with haemophagocytic lymphohistiocytosis” by Bae et al presented a case in renal TMA associated HLH. In this article, the authors provided a lot of information to describe the case, but the article still is open to criticism.

General comments:
1. Under the condition of thrombocytopenia, if this kind of patient needs to receive any invasive procedures, such as renal biopsy, the risk of bleeding should be considered. So, the authors need to provide the data of PT/PTT and whether any methods of bleeding prevention were used on the patient. That will help readers follow their strategies easily.

2. Cytotoxic therapy for the patient is very important information, so the actual dose of drugs should be shown on either Table 2 or in context.

3. For the issue of acute renal failure, the picture of the tubular region should be included in Figure 3A.

4. Why does the ferritin level increase with treatment?

5. In Table 1, the authors summarized and analyzed the similar cases; this table should be included in the Discussion.

Minor comments:
1. The article is readable with only a few minor diction errors.
   e.g. P8, para2, line16, “TMA in HLA”, not HLA, is HLH

   P15, Figure 3, H&E stein, not stein, is stain 2. Use of abbreviations: when using abbreviations, you should give the complete phrase at the first use. And some abbreviations should be presented clearly in the text. For example, CRP, LDH, HCV, TMA, AKI… should be corrected. Check all abbreviations and correct similar problems.

3. Some reference forms were not correct. Please recheck

1. The language needs some improvement. Please find a native English speaker to revise the language for you.
2. Use of abbreviations: when using abbreviations, you should give the complete phrase at the first time using them. And some abbreviations should be presented clear in the text. For example, CRP, LDH, HCV, TMA, AKI... should be corrected. Check the whole abbreviations and correct all the similar problems.

3. Nephrotic syndrome associated with haemophagocytic lymphohistiocytosis has been well discussed in previous literatures. Please well discuss if this patient has nephrotic syndrome or nephritic syndrome. Figure 1 did not show triglyceride and total cholesterol.

4. In this patient, authors said hepatitis C antigen was positive but AST and ALT levels were normal, which suggested that HCV was in an inactive state. Do you check any anti-HCV antibody or RNA in this patient?

5. Some references forms were not correct. Please recheck

1. In the article, as the Table 1 shows, to date, numerous mediators of inflammation have been implicated in the development and progression of lupus nephritis and these include cytokines, chemokines and glycosaminoglycans. Why were type 1 INFs, IL-6, TNF#, and hyaluronan selected for review? Particularly in the part of INTRODUCTION to the article, authors mentioned that “serum levels of various inflammatory mediators are increased in patients with lupus nephritis (table 1) and these include IL-6, TNF#, IFN# and hyaluronan.” However, that is insufficient to support their claim for the critical role of these four mediators.

2. As the title is “Mediators of inflammation and their effect on resident renal cells-implications in lupus nephritis,” my suggestion is that the main resident renal cells should be reviewed. As we know, resident renal cells include mainly 1) glomerular cells and 2) tubular cells. In glomerular cells, there are mesangial cells, endothelial cells and podocytes. As for tubular cells, proximal, Helens loop, distal and cortical collecting duct cells are included. In the progression of lupus nephritis, the role of these resident renal cells should be addressed in orderly fashion. Otherwise, the authors should consider changing their title.

3. As per the title, my suggestion is that the main implications should be pointed out and summarized in the end of each section. Implications may include clinical applications or the future directions of basic research, etc. For example, as in the part of IFN, authors mentioned that “Intriguingly, this would suggest that the expression of IFN-inducible transcripts could either result in a milder form of renal injury or be protective against glomerular damage. Whether the presence of this signature is a cause of consequence of disease remains to be fully defined.” As other mediators could have the similar implications, a precise summary of each section would make the article more persuasive.

Specific comments:
First of all, page number should be inserted, to help reviewers point out their comments clearly.

In the part of ABSTRACT:
1. Line 8, the word “whereas” is strange, does the authors mean “and”?
2. Based on the content of the article, the article not only focuses on their effects on resident renal cells but also the production of mediators and the implications. The authors should clarify these ideas.
3. Abbreviations, such as IFNs, IL-6, and TNF-#, should be clarified.

In the part of INTRODUCTION:
1. In the first paragraph, last sentence “Lupus patients follow a relapsing-remitting pattern in which the frequency of flares differs between individual patients” is strange, and does not seem to connect to the rest of the paragraph.
2. In the second paragraph, the authors should address clearly about their main ideas: Why were IL-6, IFNs, INF-# and HA selected to be reviewed? What resident renal cells will be focused on? What implications will be pointed out?

In the parts of IL-6, TNF-#, INFs and HA:
In each section, authors reviewed a lot of information, but it is a little bit chaotic. Based on their claim, my suggestion is that each section may include the following data: 1). Once Ag-Ab, what resident renal cells respond to produce these mediators either by evidence from in vivo or in vitro? As B cell, T cell, monocyte, et. are not important, suggest you cut this mention. 2) What are the current possible mechanisms for these mediators inducing the progression of lupus nephritis? 3) What are the possible implications for these mediators after review. The authors could clarify these points.

In the part of Table 1:
So many inflammatory mediators are involved in the pathogenesis of lupus nephritis, but authors used the sentence “serum levels of various inflammatory mediators are increased in patients with lupus nephritis (Table 1) and these include IL-6, TNF-#, IFN-# and hyaluronan (HA)” to describe Table 1. This is not comprehensive enough. The idea and statement should be reorganized.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests