Reviewer’s report

Title: An unusual case of acute lupus haemophagocytic syndrome: a test of diagnostic criteria

Version: 0 Date: 28 Dec 2016

Reviewer: Sae Ochi

Reviewer's report:

This is an interesting case in which HLH preceded onset of SLE, so it might be worth publishing in the Journal of Medical Case Reports. However, I think several major points need to be answered before acceptance.

1. As sputum culture was positive for colitis, her first presentation might be explained by hemophagocytosis related to sepsis. Her CRP was negative, so it is not strongly suspected, but at least you need to mention about this differential diagnosis in discussion. Also it is better you show the result of blood culture.

2. There are little information about the titre of each parameters. For example, lymphocyte counts, titres of ANA, ds-DNA antibodies, AST, ALT, triglyceride, IgG, IgM, IgA, C3, C4, CH50, anti-platelet antibody, haptoglobin, soluble IL-2 receptor, etc. It might be better you add a table that summarises the laboratory findings of first and second admission.

3. It is also required to show the images of hemophagocytosis as well as that of immunofluorescence patterns of renal biopsy, otherwise we cannot see the process of diagnosis. Please add figures that represents your laboratory findings.

4. Negative finding of bone marrow cannot fully rule out malignant lymphoma (ML), which can also present positive auto-antibody. Did you examine monoclonality of immunoglobulin or genetic test for ML? If not, please explain how you made diagnosis of exclusion.

5. It is not just the difference of diagnosis criteria that delayed the diagnosis of this case. It is really rare that a patient showed negative ANA at the time of first clinical symptom of SLE, because HLH usually occur due to hyper-cytokine status due to autoimmune reaction. What is your speculation of negativity of ANA on her first admission? Is there any other trigger for HLH, or you think HLH might have triggered production of autoantibody? You described some in the first paragraph of Discussion section, but there is no explanation about how you made exclusion diagnoses. I strongly recommend you to discuss the differential diagnoses of hemophagocytic syndrome first, then explain how you excluded each disease, and discuss why you think this is the manifestation of SLE in discussion.
Minor points

1. Human immunodeficiency virus also present nephritis and positive autoantibodies, which resemble type IV lupus nephritis. So I am interested how you ruled out HIV. What was the 'screen of hepatitis B, C, and HIV'? Did you measure HIV-antibody, or did you conduct Western blot? Please clarify it.

2. Also, ruling out infection is important in such a case, because hemophagocytic syndrome due to viral infection may also show temporal remission by treatment with corticosteroid. Which kind of EBV antibody did you measure? Did you measure serum EB-DNA? Also, which antibody did you measure to exclude CMV infection? And usually, CMV antigenemia needs to be measured to exclude CMV infection. Please clarify the methods you used to exclude these infections.

3. The patient presented alopecia on first admission. Did you conduct skin biopsy? If not, do you think this is dermatological symptom of SLE? If it is so, there must be sign of inflammation, such as rash. If not, what is your diagnosis about this alopecia?

4. Also, her first symptom was confusional episodes. Do you think this is the symptom of NP-SLE? What is your diagnosis? Please explain.

5. Page 4, paragraph 3: Please add the unit of platelet counts (/mm3).

6. Page 4, paragraph 3: please spell out ABST and IV.

7. In the abstract you described 'coombs test', but in main manuscript you mentioned 'direct antiglobulin test'. It might be better the description is consistent.

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