Author’s response to reviews

Title: Nontuberculous Mycobacterium Infection Complicated with Haemophagocytic Syndrome: A Case Report and Literature Review

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Author’s response to reviews:

Dear reviewer and editor:

Thanks for your comments and suggestions. Here are our responses:

1. Page 6, Line 17: You mentioned about "Natural Killer (NK) cell activity was reduced”. Could you explain simply about which method do you used to test NK cell activity?

   This test was not available in our hospital. It was routinely conducted in a commercial clinical laboratory center (Hightrust Diagnostics). We consulted the laboratory staff about how they test NK cell activity. Because of the confidential agreement, we can only get an unofficially response from the center: NK cells from the patient’s blood sample were incubated with K562 cells for a period of time and then LDH level was measured to estimate how many K562 cells died. The amount of K562 cells that died after incubated with NK cells were compared with the amount of apoptosis of K562 cells during the same period of time. NK cell activity was then calculated using these data.

2. Page 6, Line 22: About autoimmune diseases, the serum markers shown in Table.1 are ANA and ANCA only. If other autoimmune profile has been checked but not be listed? There are many autoimmune disease would affect hemophagocytosis, such as systemic lupus erythematosus, rheumatoid arthritis, mixed connective tissue disease, adult-onset Still's disease... et al. If you check ANA and ANCA only, there will be many autoimmune diseases would be missed.
Besides ANA and ANCA, we also checked other autoimmune profiles including anti-ENA (anti-RNP, anti-Sm, anti-SSA, anti-SSB, anti-rRNP, anti-Scl-70, anti-Jo-1) antibodies, anti-PM-Scl, anti-dsDNA, anti-PCNA, ACA, AMA-M2, anti-histone antibodies, anti-CCP antibody, ACL, anti-β2GP1 antibody and LAC, which were all negative. The patient presented no rash, arthralgia, myalgia, alopecia, photosensitivity, oral ulcer, vulva ulcer, Raynaud’s phenomenon or other symptoms indicating autoimmune diseases. We will add the results of these profiles into our manuscript (Table 1).

3. Page 6, Line 37: If possible, mentioning anti-INF-gamma-Ab examination is not available at your hospital at this part might be better.

We will make the modification according to your suggestion (Case presentation section, paragraph 2, the last 2 sentences).

4. Page 6, Line 50: If HLH-2004 criteria is used for hemophagocytosis diagnosis, I think list the triglyceride/ fibrinogen/ sIL-2r data is better.

We tested triglyceride and fibrinogen level of the patient. Her triglyceride level was 2.62mmol/L and her fibrinogen level was 3.5g/L. sIL-2r was not tested because it was not available in our hospital at that time. Despite these results, our patient still met the diagnostic criteria of HPS according to HLH-2004 criteria (fever, splenomegaly, peripheral blood cytopenia, hemophagocytosis in bone marrow, low NK cell activity and hyperferritinemia). We will add these results into our manuscript (Table 1).

5. Page 6, Line 50: Could you list the prednisone dosage/ body weight ratio?

Prednisone was started with 1mg/kg/d. We will add this into our manuscript (Case presentation section, paragraph 3, the last sentence).

6. Page 6, Line 53-59: The treatment duration of amikacin is not listed.

Amikacin was continued for 1 month. We will add this into our manuscript (Case presentation section, paragraph 4, line 2).

7. Page 10, Line 9: In this part, you mentioned about the "count" of NK cell; however, in previous part (as question 1), you mentioned about "NK cell activity". What you checked is the cell activity or the cell count of NK cell? or both of them were checked?
We checked both NK cell activity (for diagnosis of HPS) and NK cell count (to screen for immunosuppressive conditions).

8. Page 11, Line 28-34: There are still other case reports about tuberculosis with hemophagocytosis. So, immunocompromised + HPS + granuloma in bone marrow biopsy should let us beware of the risk of TB or NTM infection. If adjusting the conclusion to "... and suspicion of possible mycobacterial (TB or NTM) infection" and listed the references of TB infection with HPS should be better.

We agree and will make the adjustment according to your suggestion (Abstract-conclusion, line4, Discussion section, paragraph3, the last 2 sentences).

9. Table 1: Please give more detail CBC data (MCV, MCH, MCHC) to give more data for the cause of anemia evaluation.

The patient had normal MCV, MCH and MCHC level (MCV 95.5fl, MCH 31.6pg, MCHC 335g/L). We will add this information into our manuscript (Table 1).

We sincerely thank you again for your comments and we have made some adjustment and clarification in our article accordingly, hoping to provide more information about our case.

Yours sincerely,

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