Reply to the reviewer's comments

Dear Editor and Reviewer:

Thank you for your patience and professionality of pointing out the deficiency of our case report.This time,we have revised the manuscript seriousiy.The following is my reply to the questions raised by the reviewer

1. While the authors make a good effort to present a case of gouty arthritis complicated by systemic inflammatory response syndrome and HLH, the presentation, writing and case description needs significant revision and correction. There is intermixing of the term"infection", "sepsis" and "systemic inflammatory response syndrome" which is very confusing as gout can induce SIRS but NOT cause infection or sepsis, unless there is evidence of secondary infection in a gouty arthritis. I would recommend the authors to frame the case report better and keep infection and SIRS as two distinct entities. And if there was evidence of any bacterial growth, only then use the term sepsis or infection.

   Author's reply:On the first day of admission, our patient developed gouty tophi rupture of the right ankle joint, and secreted a white viscous and odorous secretion. The results of laboratory examination on admission showed that the WBC 26.45 × 10^9/L 、 PCT 2.84ng/ml and CRP205mg/L.What's more, On the first night of admission, the patient developed high fever, dyspnea and other clinical symptoms. The bacterial culture results of secretion in the later stage indicated that the patient was infected by methicillin-resistant Staphylococcus. According to the relevant diagnostic criteria of sepsis(1), the patient met the diagnostic criteria of sepsis. In view of your question about the intermixing of the term"infection", "sepsis" and "systemic inflammatory response syndrome, we explained the diagnosis of sepsis in the multidisciplinary expert consultation section.

2. The text is well written, but I think that if the focus was to alert to the

possibility of secondary hemophagocytic syndrome, it would be important to highlight relevant and essential symptoms/signs for the diagnosis. and also, the modification in the antibiotic regimen was not clear: there was an invasive fungal infection.

Author's reply:Hemophagocytic syndrome is a rare disease of immune system destruction, which is also the first time in our clinical work. We have a relatively clear understanding of its related clinical signs by consulting the relevant literature and consulting the hematologist. In addition to the clinical symptoms and signs (fever, hepatosplenomegaly), laboratory examination (hemocytopenia, hypertriglyceridemia, ferritin > 500ng / L), bone marrow biopsy found hemophiles is of great significance for the diagnosis of the disease(2,3), which we mentioned in the multidisciplinary expert consultation and discussion section.In addition, for the part of antibiotic treatment process proposed by you, we reorganized the treatment plan of antibiotics according to the course of the disease. For the specific plan, please refer to the treatment section of the manuscript

3. Your case report is fascinating, but there were several grammar and punctuation mistakes. I suggest the authors use the proper tool for grammar check.You described the clinical case of sepsis-related haemophagocytic syndrome due to infected gouty tophi. However, this point was not clearly stated in the introduction, where you wrote: "we report a rare case of sepsis and secondary HPS caused by giant gouty tophi rupture". So, I suggest underlining the pathogenetic mechanism: infected gouty tophi rupture->sepsis-> HPS.About the case presentation, I suggest rewriting in discursive way the section on multidisciplinary expert consultation. It is essential to know the clinical management avoiding personal reference to the single clinicians. Indeed, this aspect should be emphasized because it represented the cornerstone for the proper clinical management of your patient.About antibiotic therapy, you stated: "Piperacillin Sodium and

Sulbactam Sodium for infection (4.5g q8h iv) for 4d. When the results of bacterial culture indicated that methicillin-resistant Staphylococcus was infected, We gived vancomycin (0.5g q12h iv) when the patient has repeated infection. In addition, we were given colchicine (0.5 mg bid) for 2d, celecoxib (0.2 g bid) for 2d, methylprednisolone (12 mg qd) for 2d to control the acute attack of gout, and febuxostat(40 mg qd) for 3wk to inhibit uric acid formation. When the patient diagnosed haemophagocytic syndrome, We changed the antibiotic program to imipenem cilastatin sodium for injection (1g q8h iv) for 1d, moxifloxacin hydrochloride sodium chloride injection(400mg qd iv) for 1d, linezolid injection (300ml q12h iv) for 1d. After the infection was stable, we changed the antibiotics to voriconazole (200mg q12h iv) for 2d and linezolid injection (300ml q12h iv) for 2d." This part was very confounding, and I did not understand why you administered some drugs for only one day. Moreover, the time sequence for switch therapy was unclear. This part should be completely rewritten.According to my suggestions, the discussion section should be implemented. It can be useful to provide a literature revision about the topic. According to my analysis, I suggest major revision.

Author's reply:According to your suggestion, we briefly describe the pathogenesis of infection caused by gouty tophi rupture, which leads to sepsis and secondary hemophagocytic syndrome in the last part of the introduction. Secondly, for the multidisciplinary expert consultation section, we reorganize the multi-disciplinary consultation opinions according to the time node according to the development process of the disease. Finally, in the aspect of clinical management of antibiotic use scheme, we described the adjustment and use of antibiotic scheme and the specific effect in detail according to the development process of the disease, and described again in the discussion section, and added relevant literature for theoretical support.

In view of the relevant grammatical errors in the manuscript, we revised the English grammar and polished the language again.

Reference

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2 Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. N Engl J Med. 2003;348(2):138-50.[PMID:12519925.doi:10.1056/NEJMra021333]

3. Sadaat M, Jang S. Hemophagocytic lymphohistiocytosis with immunotherapy:brief review and case report. *J Immunother Cancer*. 2018;6(1):49. Published 2018 Jun 5. doi:10.1186/s40425-018-0365-3

Thank you for your valuable advice so that we could found the deficiency of our case report.It's a great learing opportunity for us.We are pleasant to receive the professional reviewers and improve our study and manuscript according to your guidance.

Best regards,

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