

Answers to the editor

We answered all of the reviewers' comments as follows by point-to-point.

We provided the ORCID number of each author (page2)

The pictures we provided in the manuscript are clearest (page20)

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Answers to reviewer (Reviewer's code: 00049331)

1. Title should be "Epstein–Barr virus-associated hemophagocytic syndrome in patients with ulcerative colitis on azathioprine: A case report" instead of "Epstein–Barr virus-associated hemophagocytic syndrome during treatment for ulcerative colitis: A case report".

We added " with azathiopurine" after "during treatment "according to the native English editor and other reviewer.

2. This case presentation should be checked by native English speaker. After correction according to recommendations, this case is acceptable for publication.

We asked native English editor to check our manuscript and attached the certification.

Answers to reviewer (Reviewer's code: 00522179)

1. This is an interesting case report. Author, please provide the following information:
EBV DNA PCR quantitative before and after treatment

Answer) We checked EBV DNA PCR quantitative just after starting treatment not before treatment. We added the data in the manuscript (page 9).

2. Was CMV DNA checked?

Answer) Yes, we checked CMV IgG and was negative. We added “CMV IgG was negative.” In the manuscript (page9).

3. Laboratory data after successful treatment of VAHS and at latest follow up

Answer) We added lab examination data after improvement from VAHS in the manuscript (page 9).

Answers to reviewer (Reviewer's code: 03520161)

1. The authors reported here an interesting case of EBV associated hemophagocytic syndrome in patient with UC. Overall the case is well written and interesting which shed light on the rare catastrophic side effect of azathioprine treatment. is it important to note, that the current guidelines in IBD world is to test the EBV status before commencing treatment with azathioprine, usually it is not recommended to start azathioprine therapy if the patient has not been exposed to EBV given the increased risk of infection such as acute primary EBV infection, i suppose as occurred in this case.

Answer) We did not check EBV infection before azathiopurine treatment. We should have checked EBV infection before treatment, however, EB-IgM is positive and EBNA is negative in our case; therefore, we think that VAHS was caused due to primary acute EBV infection in our case.

2. I have few issues: 1- is the EBV status was examined before treatment with azathioprine, and if it was negative why it was begun?

Answer) We did not check EBV infection before azathiopurine treatment.

3. does that patient was informed about the risks of treatment? does the patient was in regular follow-up and lab examination

Answer) We informed the patient about the risks; infection, bone marrow suppression, and so on. We added lab examination data after improvement from VAHS in the

manuscript (page 9).

4. 2- in the title it should be written "during treatment with azathioprine"

Answer) We added " with azathiopurine" after "during treatment " according to the native English editor.

5. 3- please add the number of EBV PCR copies to the text 4- in the case presentation section,

Answer) We checked EBV DNA PCR quantitative just after starting treatment not before treatment. We added the data in the manuscript (page 9).

6. correct primo to "primary

Answer) We corrected.

7. " 5- insert all the lab results into table, it is easier for the readers to absorb that overall the case is interesting and worthy to be published after revisions, however, if the EBV status before commencing treatment with azathioprine negative, this issue should be addressed in the conclusion section with recommendation to carefully prescribe this medication in such cases. It should be remembered that hemophagocytosis is a fatal disease and caution should always be implemented to avoid this fatal consequences.

Answer) We added lab examination data after improvement from VAHS in the manuscript (page 9) instead of insertion of all the lab data into table. We checked EBV DNA PCR quantitative just after starting treatment not before treatment. Therefore, we added that "It should be remembered that hemophagocytosis is a fatal disease and caution should always be implemented to avoid this fatal consequences."