

## **Inactivated COVID-19 vaccine triggering hemophagocytic lymphohistiocytosis in an immunocompetent adult - A case report**

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10-Feb-2022

Ref.: Ms. No. JCTRes-D-22-00009

**INACTIVATED COVID-19 VACCINE TRIGGERING HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN AN IMMUNOCOMPETENT ADULT- A CASE REPORT.**  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Mar 12, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The manuscript is well written and clearly presents the case of HLH following administration of Sinopharm's SARS-CoV-2 vaccine.

The authors should make the following modifications and clarify:

1) Did the patient have an active SARS-CoV-2 infection at time of presentation? This needs to be reported. SARS-CoV-2 can itself induce HLH, see e.g.,

<https://pubmed.ncbi.nlm.nih.gov/34518190/>

<https://pubmed.ncbi.nlm.nih.gov/34086418/>

Please incorporate this into the manuscript.

2) Please address all available literature regarding vaccine-induced HLH, including but not limited to:

<https://pubmed.ncbi.nlm.nih.gov/34862234/>

3) Figure 3 needs a legend to indicate what each line represents.

4) Table 2 right column header should read "Patient's values"

5) Please indicate in the discussion whether there is a DD other than HLH that could encompass the clinical symptoms exhibited by your patient. At this stage, the case is presented as a causal relationship between the vaccination and HLH. Since it is only a single case, the drawing of definitive conclusions is precarious and should be done with extra caution.

6) Figure 1 legend should explain what the arrows point to.

7) Please remove grammar/spelling errors such as some odd capitalizations (e.g., page 11, line 11, Hypofibrinogenemia, mL versus ml is inconsistently used, etc.).

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Authors' response

Dear Editor,

Subject: Submission of revised manuscript "Ref.: Ms. No. JCTRes-D-22-00009

INACTIVATED COVID-19 VACCINE TRIGGERING  
HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN AN  
IMMUNOCOMPETENT ADULT- A CASE REPORT.”

Thank you for your email enclosing the reviewer's comments. We have carefully reviewed the comments and have revised the manuscript accordingly. Our responses are given in a point-by-point manner below. Changes to the manuscript are marked with red.

We hope that the revised manuscript is suitable for publication and look forward to hearing from you in due course.

Sincerely,

Dr. Saqib R. Khan  
Aga Khan University Hospital, Pakistan

**Reviewers' comments:**

1) Did the patient have an active SARS-CoV-2 infection at time of presentation? This needs to be reported. SARS-CoV-2 can itself induce HLH, see e.g.,

<https://pubmed.ncbi.nlm.nih.gov/34518190/>  
<https://pubmed.ncbi.nlm.nih.gov/34086418/>

Please incorporate this into the manuscript.

**Answer: Page 3, line 21,22: We have added a statement in which we mention that we ruled out active COVID-19 infection in the patient as his COVID-19 PCR was negative. Furthermore, we have included both the above-mentioned references as [12] and [13]. We have also adjusted the sequence of the references accordingly**

2) Please address all available literature regarding vaccine-induced HLH, including but not limited to:

<https://pubmed.ncbi.nlm.nih.gov/34862234/>

**Answer: Page 6, line 13,14,15: The above-mentioned relevant case has now been included in the article and a comparison is also drawn with our case.**

3) Figure 3 needs a legend to indicate what each line represents.

**Answer: We have added the legend in Figure 3 and mentioned what each line corresponds to.**

4) Table 2 right column header should read "Patient's values"

**Answer: Table 2 right column now read “Patient’s values” as suggested**

5) Please indicate in the discussion whether there is a DD other than HLH that could encompass the clinical symptoms exhibited by your patient. At this stage, the case is presented as a causal relationship between the vaccination and HLH. Since it is only a single case, the drawing of definitive conclusions is precarious and should be done with extra caution.

**Answer: Page 3, line 28,29: We have added our list of differentials in the case presentation section**

6) Figure 1 legend should explain what the arrows point to.

**Answer: The Figure 1 legend has been corrected as per suggestion.**

**“Figure 1: (A, B)- Bone marrow smear showing hemophagocytosis histiocyte (arrow) with engulfed red blood cells and platelets (hemophagocytosis).”**

7) Please remove grammar/spelling errors such as some odd capitalizations (e.g., page 11, line 11, Hypofibrinogenemia, mL versus ml is inconsistently used, etc.).

**Answer: We have checked all the grammatical errors and have adjusted our manuscript accordingly.**

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2<sup>nd</sup> Editorial decision  
11-Mar-2022

Ref.: Ms. No. JCTRes-D-22-00009R1  
INACTIVATED COVID-19 VACCINE TRIGGERING HEMOPHAGOCYTIC  
LYMPHOHISTIOCYTOSIS IN AN IMMUNOCOMPETENT ADULT- A CASE REPORT.  
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers: