

Dear editor

I would like to resubmit the attached manuscript, titled “Multiple cranial nerve palsies with small angle exotropia following COVID-19 mRNA vaccination in an adolescent: A case report” (file name "78193_Auto_Edited.docx")

The manuscript has been carefully rechecked, and the necessary changes have been made. All the coauthors agree to the changes made and the responses provided.

I hope that the revised manuscript is now suitable for publication in your journal

Sincerely

Saeyoon Kim

Sysnow88@hanmail.com

Name of journal: World Journal of Clinical Cases

Manuscript NO: 78193

Manuscript type: Case report

Title: Multiple cranial nerve palsies with small angle exotropia following COVID-19 mRNA vaccination in an adolescent: A case report

Reply to editorial comments:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Please see the attached file

Dear reviewer

Thank you for all the valuable recommendations and insights, which we believe have enriched the

manuscript and give us more balanced perspective of our research. The manuscript has been carefully rechecked. Our replies are marked in blue color as follows and the necessary changes have been made in revised manuscript according to your suggestions.

1. Abstract – the grammar in the conclusion should be corrected (first line is not well written, second line – "is my be").
 - Thank you for your comment and we apologize for this error. We edited this point as follows;
The etiology of this adverse effect following vaccination was thought to be immunological.
2. Introduction – This part is well written and describe the relevant background for this case.
 - Thank you for your comment. We have tried to provide sufficient background on our case.
3. Case description – The case is described comprehensibly; the evaluation was in-depth with all relevant diagnostic tests. Was any other infectious serology taken, such as CMV, EBV and others?
 - We are glad that you spotted this point. At the time of our patient's visit, there were no symptoms or signs of infection, and the inflammation markers (CRP, ESR) were normal. So, no other virus tests were performed but as you suggested, our study would have been more convincing if additional serology tests had been performed to rule out other infections
4. Discussion – There are several issues the authors should address:
 - (4-1) I think this part is missing a discussion on neuromuscular manifestations of COVID-19 disease and comparison to those by the vaccine. This topic is important in order to highlight that although the vaccines might have such adverse effects, they also prevent from severe disease which can cause similar and worse outcomes. The authors should address the following article which describes neuromuscular manifestations in COVID-19 patients: <https://link.springer.com/article/10.1007/s00296-022-05106-3>

- Thank you for your comments. And we carefully reviewed the article that you mentioned kindly. In this case, our patient was negative for SARS-CoV-2 from nasopharyngeal swabs. So, we did not discuss the complications of COVID-19 infection. But as you suggested, cardiac complications such as myocarditis and cardiac dysfunction have been reported in adults^[1,2]. It is known that the disease course of COVID-19 in children is milder than in adults, but cardiac complications such as cardiogenic shock and myocardial dysfunction also have been reported^[3]. Therefore, it is important to consider vaccination according to the patient's underlying disease and the risk of complications from COVID-19. We added this part on revised manuscript.

➤ (4-2) Was there a link found in previous studies between the vaccines and an immune-mediated neuromuscular phenomenon? I think an example of such can be added. Were inflammation markers elevated in previous cases? A comparison can be made with this case.

- Thank you for your comment. Cosby et al. reviewed immune-related vaccine adverse events by searching PubMed for articles published between January 1945 and August 2018 and reported neuromuscular phenomenon such as Guillain–Barré syndrome (GBS)^[4]. And other Immunologically mediated neurological complications were also reported^[5,6]. About cranial nerve palsies, there are several studies reporting CN palsies following other vaccines. According to US Vaccine Adverse Event reporting system, the most commonly reported vaccine was seasonal influenza vaccine, followed by Hemophilus influenzae type b and Human papillomavirus vaccine^[7,8]. We added this part to our revised manuscript.
- And thank you for pointing out this part. We reviewed previous, but little was mentioned about the level of inflammation markers. In a case report of GBS following by COVID-19, C-reactive protein was within normal limit but further studies are needed^[9].

➤ (4-3) Were vaccines for other infectious diseases have been reported to cause similar side effects? Is it a unique phenomenon of this specific vaccine? Was it previously reported in COVID-19 vaccines other than the Pfizer-BioNTech?

- Thank you for your comment. According to US Vaccine Adverse Event Reporting System, there were three reports of multiple cranial nerve palsies after influenza vaccination ^[8]. Therefore, it does not seem to be a unique phenomenon of COVID-19 vaccine.
- Cranial nerve palsies after other types of COVID-19 vaccine such as Moderna and AstraZeneca have been reported.^[10] However, further researches are needed to investigate whether there are significant differences between vaccine types.

References

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- 2 Guidon AC, Amato AA. COVID-19 and neuromuscular disorders. *Neurology* 2020; **94**: 959–969.
- 3 Rodriguez-Gonzalez M, Castellano-Martinez A, Cascales-Poyatos HM, Perez-Reviriego AA. Cardiovascular impact of COVID-19 with a focus on children: A systematic review. *World J Clin cases* 2020; **8**: 5250.
- 4 Stone Jr CA, Rukasin CRF, Beachkofsky TM, Phillips EJ. Immune-mediated adverse reactions to vaccines. *Br J Clin Pharmacol* 2019; **85**: 2694–2706.
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2009. *Vaccine* 2011; **29**: 6920–6927.
- 6 Ullah MW, Qaseem A, Amray A. Post vaccination Guillain Barre syndrome: a case report. *Cureus* 2018; **10**.
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- 8 Woo EJ, Winiecki SK, Ou AC. Motor palsies of cranial nerves (excluding VII) after vaccination: reports to the US vaccine adverse event reporting system. *Hum Vaccin Immunother* 2014; **10**: 301–305.
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- 10 Sriwastava S, Sharma K, Khalid SH, Bhansali S, Shrestha AK, Elkhooly M, Srivastava S, Khan E, Jaiswal S, Wen S. COVID-19 vaccination and neurological manifestations: a review of case reports and case series. *Brain Sci* 2022; **12**: 407.

Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Thanks for the review.

Language Quality: Minor language polishing mentioned by reviewer was corrected.

Scientific Quality: The above-mentioned contents have been added to the revised manuscript.

Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Please provide the original figure documents.

Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

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Thanks for the review

We attached figures by using PowerPoint. These figures are original so added "copyright information"

as you suggested.

The revised manuscript was improved by additional contents.