OPEN PEER REVIEW

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As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

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An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Immune Thrombocytopenic Purpura in a Child with COVID-19: A Case Report"

Author(s): Marjan Tariverdi, Maliheh Mohammadzadeh Esini, Hanie Pazarkar, Zahra Naghmehsanj, Nazanin Farahbakhsh

Review Timeline:

Submit Date: 2 Nov 2020
Revised Date: 22 Apr 2021
Accepted Date: 29 Apr 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Shahnaz Armin: Associate Editor | Revision (0) — 8 Nov 2020

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: Reviewer | Revision (0) — 8 Dec 2020

Dear AE,
There are many of good information related to confirmation of ITP in this case duo to Covid 19, but I think this presentation still needs some more informations and mild revision for complete informations .
They include:
1-retic count, Direct and indirect Coombs test of patients.
2- peripheral Blood smear in patient , sister and father. The presentation of the low plate in the family is at the same time with pos covid in father and patient and neg in sister, but underlying familial thrombocytopenia and other causes should be discussed more.

3- Is there a history of thrombocytopenia in other people of families?
4- Rising of plate after second time of treatment (Methyl and....) is 20000/ UL or 200000/UL . if 20000/ul , so it does not mean as response to treatment.
and the the result and follow up of patient-related to thrombo- cytopenia and the result of covid evaluation needs more discussion.
Thanks.

REFEREE: Reviewer | **Revision** (0) 10 Dec 2020

Dear AE,
ITP in children often is triggered by any type of viral infection. Also SARS-COV-2019 cause thrombocytopenia with some mechanisms such as immune response to platelet antigens and direct effect on bone marrow. This is not a new phenomenon. In this setting, your patient cured by corticosteroid puse and not with Hydroxychloroquin.
COVID-19 present with different clinical symptoms include:
1. ARDS
2. pancytopenia
3. Kawasaki-like
4. meningoencephalomyelitis
5. gastroentrocolitis
Thanks.

REFEREE: Associate Editor | **Revision** (0) 11 Dec 2020

Dear EIC,
Please the authors follow the reviewer's comments and reply in a point-by-point manner.
Please highlight new changes in the manuscript.
English copy-editing is warranted before the next submission.
Thanks

REFEREE: EIC | **Revision** (0) 11 Dec 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response to reviewers

Dear Sir/Madam:

In response to your comments on the manuscript entitled "Immune thrombocytopenic purpura in a child with COVID-19: A case report", we addressed every issue as follows:

Associate Editor 1:

1. **Reviewer's comment:** The presentation of the case in addition to the history of his father and sister is not clear, please completely divide and clear all dates for these three persons.
   Our response: The presentation of the case and the history of close family members and the dates were clarified.
2. **Reviewer's comment:** In the evening of the same day (May 28th), his father's nasopharyngeal swab turned out positive for SARS-CoV-2 on reverse transcriptase polymerase chain reaction (RT-PCR) testing. why after 18 days father did test?
   Our response: The delay in testing the father with regard to COVID-19 was because of the low socioeconomic status of the family and lack of health insurance, which was added to the manuscript.
3. **Reviewer's comment:** What was your explanation for abnormal LFT in first admission and it was still abnormal in first day of second admission?
   Our response: It appears that the abnormal LFT on first admission may have been due to the immune response to COVID-19 infection. Although LFTs were still abnormal on the second admission, the liver enzymes had declined compared to the first admission. We had suspected the potential causes of elevation of liver enzymes such as CMV and EBV; however, the patient had tested negative for both.
4. **Reviewer's comment:** It was very helpful if you can check antibody COVID from his sister the cause for this discrepancy the total condition or other organ failure in cases with lower platelet, in this case no other organ involvement except liver and hematologic manifestation, no DIC or end organ failure
   Our response: The patient's sister had been checked for anti-SARS-CoV-2 antibody and the results were negative. The patient himself also tested negative for COVID-19 antibodies. The antibody results were added to the manuscript.
5. **Reviewer's comment:** This patient was also treated as ITP with IVIG and corticosteroids and had a good recovery regarding her platelet count. In comparison to our study, this case progressed to a more severe disease and her ITP was treated with IVIG.... it was good response or progressive case???
   Our response: Their case responded well to IVIG while our case was more progressive and the reason for this has been discussed and added to the manuscript.

6. **Reviewer's comment:** Our patient showed improvement with this drug…..you can't say your patient had good response to chloroquine because at same time you used steroid
   Our response: Chloroquine and corticosteroids are both considered as treatments for COVID-19 and we can say that our patient improved with COVID-19 treatment.
7. **Reviewer's comment:** was resistant to IVIG while responded to hydroxychloroquine and corticosteroids ….it was not resistance because platelet increase to 20000 at first admission but may be the effect of activation of virus was the cause of second decline of platelet
   Our response: The purpose of this case report was to introduce a case of ITP following COVID-19 infection and not the treatment per se. Given the good response of the patient to IVIG during his first admission, we first thought that he was a case of ITP irrespective of COVID-19 infection; however, when his platelet count decreased again and his COVID-19 test turned out positive, we suspected that ITP was due to COVID-19 infection and our suspicion was confirmed when he responded to hydroxychloroquine (to decrease viral replication) and corticosteroid (to decease the inflammatory response).
8. **Reviewer's comment:** viral testing in thrombocytopenic patients should be considered for timely diagnosis of COVID-19 and taking necessary measurements ….in addition to isolation, treatment of COVID
   Our response: The sentence was rephrased and corrected.

Reviewer 1:

1. **Reviewer's comment:** Retic count, direct and indirect Coombs tests of the patient.
   Our response: These results were added to the manuscript.
2. **Reviewer's comment:** peripheral Blood smear in patient, sister and father. The presentation of low plate in family is the same time with positive COVID in father and patient and neg in sister, but underlying familial thrombocytopenia and other causes should be discussed more.
   Our response: BPS had been performed for the patient and the results were added. The father and the sister had no BPS results but only bone marrow aspiration. There was no underlying familial thrombocytopenia.
3. **Reviewer's comment:** Is there history of thrombocytopenia in other people of family?
   Our response: There was no such history in other family members.
4. **Reviewer's comment:** Rising of platelets after second time of treatment (Methyl and….) is 20000/ UL or 200000/UL . if 20000/ul, so it does not mean as response to treatment. and the result and follow up of patient related to thrombocytopenia and result of COVID evaluation needs more discussion.
   Our response: The platelet count increased to 20,000/µl and regarding the diagnosis of ITP this increase is acceptable. As a matter of fact, in other cases of ITP the goal of treatment is a platelet count of 20,000 and values above this do not require treatment.

Reviewer 2:

1. **Reviewer's comment:** ITP in children often is triggered by many types of viral infections. Also, SARS-COV-2019 cause thrombocytopenia with some mechanisms such as immune response to platelet antigens and direct effect on bone marrow. This is not a new phenomenon. In this setting your patient cure by corticosteroid pulse and not with hydroxychloroquine.
   COVID-19 present with different clinical symptoms include:
   1.ARDS
   2.pancytopenia
   3.Kawasaki-like
   4.meningoencephalomyelitis
   5.gastroentrocolitis
   Our response: Although ITP following other viral infections is not uncommon, whichever the mechanism they will respond to IVIG as the treatment of choice regardless of the trigger. However, the goal of this case report was to present a case with ITP following COVID-19 infection who only responded to the treatments of COVID-19 with corticosteroids among them.

Sincerely,

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (1) 1 Feb 2021

Dear EIC
The reviewer(s) have recommended publication, but also suggest some major revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (1) 6 Feb 2021

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response to reviewers

Dear Sir/Madam:

In response to your comments on the manuscript entitled "Immune thrombocytopenic purpura in a child with COVID-19: A case report", we addressed every issue as follows:

Associate Editor 1:

Reviewer's comment: *Use a similar date format for all recorded dates in the whole manuscript body. For example "May 26, 2020"*

Line 5: add patient's age and sex → patient's age and sex were added.
Line 6: remove this part: "and a family history of immune thrombocytopenic purpura (ITP)" → this part was removed.
Line 7: remove "hydroxychloroquine and" → this part was removed.
Line 10: replace "is thrombocytopenia" with "SARS-CoV-2 induced immune thrombocytopenic purpura (ITP)" → thrombocytopenia was replaced with SARS-CoV-2-induced ITP
Line 38: add the first presentation date → the date was added.
Line 38 initiated with ITP signs and symptoms while in line 42 the authors state that "He was admitted with suspicion of COVID-19"??? Did the author intended to say "ITP"?--> we intended to say ITP and COVID-19 was replaced by ITP
Line 44: Remove: "With regard to close family members," → this part was removed.
Line 50: It seems that "possible ITP" is better words.--> ITP was replaced with possible ITP
Line 52: add date following "On admission" → the date was added.
Line 55: add outpatient visit date → the date was added.
Line 65 and 69: change dates format → the date format was changed to "month day, year"
Line 71: replace this part: "In the evening of the same day (May 28th)," with "On May 28, 2020" → it was replaced with "On May 28, 2020"
Line 78 (Table 1): add the date of the first admission "day 0" in the first column.--> the date was added
Line 80: change date format → the date format was changed to "month day, year"
Line 89: "Anti-CMV IgM and anti-EBV IgM" is correct.--> it was corrected.
Line 96: add PCR and serology dates → the dates were added.
Line 97: "Anti-SARS-CoV-2 IgM and IgG both were in negative range" is correct.--> it was corrected.
Line 99 and 103: change dates format → the date format was changed to "month day, year"
Line 108: Why did the author treat an asymptomatic COVID-19 case with an antiviral? It seems that the patient readmitted after at least 10 days (even more) after first clinical signs and symptoms (which non of the are COVID related). On the other hand, SARS-CoV-2 induce ITP is an immune-mediated process. What is the common time-interval between COVID infection and occurrence of ITP. Is there any evidence to support antiviral treatment for such immune-mediated phenomenons?--> Given the unresponsiveness of the patient to the primary treatment

(IVIG and prednisolone), repetitive platelet reduction, and the possible activity of SARS-CoV-2, we decided to administer antivirals for the patients

Line 111 and 119: change dates format→ the date format was changed to “month day, year”

Line 121: what is the results of "CBC and SARS-CoV-2 on RT-PCR testing"?--> we did not have the results of the follow-up CBC and SARS-CoV-2

Line 123 (Table 2): add the date of the second admission "day 0" in the first column. .--> the date was added

Line 142: "SARS-CoV-2 induce ITP" are better words for the patient and "possible SARS-CoV-2 induce ITP" for his father.-->these phrases were replaced with the suggested phrases.

Remove lines 147 to 154.--> these lines were removed.

Line 156: remove "hydroxychloroquine and"→ it was removed.

Line 168 to 172: remove newly added highlighted parts.--> the new highlighted parts were removed.

Line 178 to 184: remove all statement regarding "hydroxychloroquine"→ all statements about hydroxychloroquine were removed.

Line 186: remove "viral load". No specific information is provided regarding viral load in this report. "using antiviral agents to decrease the viral load" this is not a true conclusion.--> viral load was removed.

Line 189: replace "one of which may be thrombocytopenia" with "such as SARS-CoV-2 induce ITP"→ “one of which may be thrombocytopenia” was replaced with “SARS-CoV-2-induced ITP”

Finally, the discussion section should be improved with more comprehensive and up-to-date information regarding "SARS-CoV-2 induce ITP". The more recent article published by Sukrita Bhattacharjee et al. is suggested (available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7501509/). The following points should be discussed:

-common affected age→ In a recent systematic review, the median age of patients with SARS-CoV-2-induced ITP was 62 years and only 7% were in the pediatric age group (lines 148-150).

-common COVID-19 phenotypes which are more complicated with "SARS-CoV-2 induce ITP" (moderate-to-severe COVID-19)→ it appears that some COVID-19 phenotypes are more prone to SARS-CoV-2-induced ITP as demonstrated by Bhattacharjee and Banerjee (11). They showed that 75% of patients with SARS-CoV-2-induced ITP had moderate-to-severe COVID-19. Mild COVID-19 patients were reported in 18% and 7% did not give any history of fever or other typical flu-like symptoms; therefore, patients with moderate-to-sever COVID-19 appear to be more susceptible to SARS-CoV-2-induced ITP compared to others (lines 185-191)

-common reported interval between "SARS-CoV-2 induce ITP" after initial COVID-19 symptoms→ The median time between the onset of COVID-19 symptoms and the diagnosis of SARS-CoV-2-induced ITP has been reported to be 13 days, with the majority of cases occurring in during the second and third week of COVID-19 onset of symptoms (lines 157-160)

-The rate of bleeding tendency in affected patients→ Furthermore, it has been reported in a recent study that 69% of patients with SARS-CoV-2-induced ITP had bleeding tendency: cutaneous manifestations in the form of petechiae, purpura, and ecchymosis were observed in 51% of the patients, while among other forms of bleeding, epistaxis was the most common. In addition, intracranial hemorrhage (ICH) was found in 4 patients (7.8%) as well as small intraventricular hemorrhage and subarachnoid hemorrhage in 4% (lines141-146)

-the need for COVID-19 testing in newly diagnosed patients with ITP irrespective of COVID-19 symptoms during the pandemic → Nonetheless, reports of ITP in asymptomatic COVID-19

patients underscores the need for COVID-19 testing in newly diagnosed ITP patients amid this pandemic (lines 160-161)
-mortality of this phenomenon and its causes → Hemorrhage in terms of ICH can lead to mortality in SARS-CoV-2-induced ITP as one of the 4 patients with ICH had died (lines 146-147)
-diagnostic and treatment approach → diagnostic and treatment approach has already been discussed.

Our response: All the issues mentions by line have been corrected and highlighted. The stated points were extracted from the suggested article and have been added to the manuscript discussion in the appropriate sections.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Ali Amanati: Associate Editor | **Revision** (2) 27 Apr 2021

Dear EIC,
I read the revised manuscript.
I have no further comments to add. I thank the authors for their very detailed replies to my comments.
Regards

REFEREE: EIC | **Revision** (2) 29 Apr 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.