Author’s response to reviews

Title: Case report of severe myocarditis in an immunocompromised child with Respiratory Syncytial Virus infection

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Author’s response to reviews:

June 19, 2017

Dear Dr. Nawsheen Boodhun

I would like to express our appreciation to you and the reviewers for the thorough review of our paper entitled “Manuscript ID BPED-D-17-00037R1 entitled "Case report of severe myocarditis in an immunocompromised child with Respiratory Syncytial Virus infection". I am now returning our revised manuscript to you. I heeded suggestions and comments by you and the reviewers. Followings are replies to the questions and the comments. Our comments are shown as bold.

1. Please represent authors' names using their full initials, not their full name, in the Authors’ contribution section. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors.

Thank you for your comment. The authors’ names were corrected in the revised manuscript.

Reviewer reports:
Bernhard Resch (Reviewer 1): Review

Manuscript Number: BPED-D-17-00037

Title: Case report of severe myocarditis in an immunocompromised child with Respiratory Syncytial Virus infection

The authors report on a 4-year-old Japanese girl with ALL who suffered from severe myocarditis caused by RSV infection during maintenance treatment. RSV type B RNA was detected in both tracheal aspirates and serum samples during the acute phase of the disease.

This is an interesting case report.

Major comments: none

Minor comments:

P. 7:

① marked increase in myocardial markers were noted,… Change to …was noted

Thank you for your comment. These descriptions were corrected (page 10, line 4).

② …her catecholamine levels tapered off. Please rewrite e.g. inotropic support was gradually reduced o suffered froby day x

This sentence was corrected as suggested by reviewer (page 10, line 8).

③ ventricular function was gradually improved, - Delete “was”

The grammatical mistake was corrected (page 10, line 10).

④ Give details to the neutralizing antibody test (company, test sensitivity, etc.)

We added name of the commercial laboratory (SRL) that is the largest commercial laboratory in our country (page 10, line 18).

P. 9: Conclusion = Discussion, please correct

This was corrected (page 12, line 1).

⑤ It is important to note, high amounts of RSV RNA were detected…
Please reword, meaning of the sentence is unclear.

Thank you for your comment. The most important point is detection of RSV RNA in serum. So, that sentence was modified for better understanding for readers (page 12, line 16).

P. 10: the detection of viral RNA in serum samples were significantly … Change to …was significantly

It was corrected (page 13, line 2).

Furthermore, the presence of viral RNA in our patient may support the notion of direct invasion of RSV into myocardial tissues. Meaning is unclear, please rewrite.

Thank you for your suggestion. As described in the revised manuscript, serum RNAemia suggests systemic viral infection, which is considered to be first step for direct viral invasion into myocardial tissue. Therefore, we modified the sentence in the revised manuscript (page 13, line 5).

P. 11: Herein, we reported on a 4-year-old Japanese girl… Please insert "Conclusions" at the beginning of this para.

As suggested by reviewer, the sentence was corrected (page 14, line 7).

Ian Mitchell (Reviewer 2): should indicate when clinicians might suspect myocarditis, and when to investigate.

manuscript could be more concise

Thank you for your comment. As we suspected myocarditis at the time of admission of the patient into ICU, so that information was added in the revised manuscript (page 9, line 17).

Imad Kassis (Reviewer 3): BMC Pediatrics,

Here are my comments

I The main draw back in the article is the absence of a tissue sample (heart muscle biopsy) that confirms the causal relationship between RSV respiratory infection and viremia. Many reasons may affect myocardial performance in a child with leukemia on chemotherapy and it is not always possible to know exactly the co-effect of each reason. I am aware as a pediatrician that such an intervention is rarely performed in most cases of pediatric myocarditis especially when the child improves, so the prerequisite of tissue diagnosis is rarely available.

I suggest that this point be clarified and discussed in the "discussion section".
Thank you for your comment. I agree with reviewer’s comment. Various factors may be involved in myocardial tissue damage in this patient. So, I think that lack of myocardial biopsy is limitation of this study. So, discussion in terms of this issue was modified in the revised manuscript (page 13, line 5).

2 Abstract: in the background it is stated "It is well known that RSV is associated with extra pulmonary complications such as myocardial involvement. ….there has been no known cases of RSV associated myocarditis.

I think this sentence does not reflect the situation. I think this sentence should be reformed stressing that RSV infection is common and may be severe among patients with preexisting cardiac anomalies, but direct involvement is not common and as the article states it jabs not well been described among immune compromised children.

Thank you for your comment. Background was modified as suggested by reviewer (page 6, line 3).

3 In the conclusion sentence may "cause" as I stated causality was not proofed by biopsy and staining so better to say associated as written in the background paragraph.

I agree with reviewer’s comment. So, the sentence was modified (page 6, line 17).

4 Again background Line 4 are at high risk for RSV infection. This is true for all infants and children. Children with leukemia may be at high risk for more severe and complicated RSV infection than previously healthy children without risk factors.

I agree with reviewer’s comment. So, the sentence was modified (page 8, line 5).

4 Case presentation

Tei index may not be clear to many pediatritians who may be target readers, better to clarify.

Explanation for Tei index was added in the revised manuscript (page 10, line 1).

5 case presentation page 2

"Continuous hemofiltration" is this what we call ECMO or CVVH? Not sure should be clarified It’s information was added in the revised manuscript (page 9, line 16).

Sincerely yours,
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