Author’s response to reviews

Title: Regression of Fetal Vasculature and Visual Improvement in Nonsurgical Persistent Hyperplastic Primary Vitreous: A Case Report

Authors:

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Author’s response to reviews:

Dear Editor,

BMC Ophthalmology

Re: (BOPH-D-18-00778) titled “Regression of Fetal Vasculature and Visual Improvement in Nonsurgical Persistent Hyperplastic Primary Vitreous: A Case Report” by Jianqing Li, Jiaju Zhang, Peirong Lu.

We appreciate you for your thoughtful comments on our above-mentioned manuscript. We thoroughly read the comments and revised the manuscript in accordance with the reviewer’s comments as follows. In the revised manuscript, we highlight the modified points in red.

Reviewer #1:

Okonkwo Ogugua (Reviewer 1): She had been diagnosed to have cataract previously, but what symptoms did she present with?

Re: Thank you for your valuable question. Actually, the patient had no complaint and was found to have amblyopia in the left eye in the kindergarten admission physical examination. Then she was taken to other hospitals and was diagnosed with congenital cataract. We have added this information in Line 32-33.

Page 4, line 32: intervention should replace interventions. Remove the "s".

Re: Thank you for the careful correction. We have made the amendment in Line 34.
Page 5, line 45: ophthalmoscopy should replace ophthalmoscope.

Re: Thank you for the careful correction. We have made the amendment in Line 45.

Page 5, line 48: made should replace determined.

Re: Thank you for the careful correction. The amendment has been made in Line 48.

Page 5, line 54: Give details of how the amblyopia treatment was done. How many hours of contralateral eye patching were done and how was this monitored?

Re: Thank you for your significant question. At the initial treatment, 6 hours of daily patching the fellow eye was prescribed. The vision acuity of the affected eye improved from 20/100 to 20/50 after 19 months, thus 2 hours of daily patching was then prescribed. Patching was conducted by applying an opaque patch to the contralateral eye and was closely monitored by her parents at home. We have added this information in Line 51-55 and Line 70.

Page 5, Line 57: What does stationary mean? Perhaps this represents the clinical state of the eye. Please clarify.

Re: We feel sorry for the improper wording. We meant to say that no changes were noted in the eye on follow-up examinations. Corrections have been made in Line 59. Thank you for your help in the improvement of the manuscript.

Page 6, line 63: 100 should be replaced with the appropriate number which I suspect is 1.00.

Re: Thank you for the correction. We have made the amendment in Line 65.

Page 6, line 73: associated with, should replace distinctive for the.

Re: Thank you for the careful correction. We are sorry for the improper wording. The amendment has been made in Line 76.

Page 6, line 88: insert be before performed.

Re: Thank you for the careful correction. We have made the amendment in Line 93.

Page 7, line 89: case should replace cases (remove s).
Re: Thank you for the careful correction. We have made the amendment in Line 98.

Page 7, line 91: firstly instead of first of all.

Re: Thank you for the careful correction. The amendment has been made in Line 100.

Page 7, line 96: perfused should replace perfusion.

Re: Thank you for the careful correction. We have made the amendment in Line 105.

Page 7, line 100: This case was not closely follow up in my mind if indeed she was seen at 2 months, 7 months and then 19 months (ie. 1 year in between the 2 and 3 visits. Except the authors have not indicated other follow up visits which the child may have had). The authors only saw the eye 3 times within the 19 months study period. This may not represent a close follow up as indicated by the authors.

Re: Thank you for the significant question. Actually, the child was followed up approximately bimonthly but we only presented the significant data in the manuscript. We feel sorry that we did not indicate this information clearly. Amendments have been made in Line 55-58. Thank you very much for your help in the improvement of the manuscript.

Page 8, line 108-109: The authors should include popular search engines e.g. Pubmed, Google used in their search before the conclusion that this is the first case of post natal regression of persistent fetal hyalodal vessels.

Re: Thank you for the valuable suggestion. We have searched Google, Pubmed, Embase and the Cochrane Library in English and Chinese and we believe that this is the first clinical description of post natal regression of persistent fetal hyalodal vessels to the best of our knowledge. We have added these search engines and made some amendments in Line 117-120. We feel sorry to bother you, but if you have seen any such publications please relate us.

The discussion in this manuscript should be more detailed. There should be a discussion on the mechanism of the post natal regression of the fetal hyaloid artery. What theories could have been responsible for this delay in fetal vasculature regression?

Re: Thank you for the significant suggestion. We have tried to search for the mechanism of the postnatal spontaneous regression of the hyaloid vascular system in human but so far, no publications have been found, because the hyaloid vessels tend to regress in utero. However, the involution occurs in the early postnatal period in mice and several works have been focused on this and found that macrophages may play a central role in the regression of hyaloid vasculature involving the blocking of blood flow, the induction of apoptosis and the clearance of atrophic
vessels. Besides, Arf tumor suppressor gene, Norrie gene product and some proapoptotic factors Bax, Bak and Bim have been discovered to be involved with postnatal fetal vasculature regression. What is more, a progressive decrease in blood velocity in the hyaloid vessels as well as neurons have been considered to be the triggering factors of the vessel regression. In this case report, we could not rule out the possibility that Arf tumor suppressor gene might play a role in the delay of fetal vasculature regression because the child’s mother was diagnosed with thyroid cancer 5 months after delivery, she was likely to suffer from the cancer during her pregnancy which might influence the Arf tumor suppressor gene of the child. In addition, the other above-mentioned mechanisms might also be of significance in the regression of hyaloid vasculature in the present case. We have added these potential mechanisms in the Discussion Section (Line 120-138).

A comparism of the visual outcome of this case with other similar cases reported to have had surgical and non-surgical management should be provided. This can be done and presented using a tabular pattern.

Re: Thank you for the valuable suggestion. We have tried our best to compare the visual outcome of this case with other similar cases managed surgically and conservatively. However, the vision acuity of each patient at the final visit varied largely from light perception to mild vision impairment (≥ 20/63 according to the World Health Organization classification method) in both surgical and nonsurgical treatment groups. Therefore, we feel very sorry that it is unable for us to present the visual comparison in a tabular pattern. Nevertheless, this comparison makes us more aware of the individual differences thus we are more convinced that the optimal management for PHPV depends on the individual case. The comparison has been added in the Discussion Section (Line 94-97), but we feel sorry that it was not presented using a tabular pattern.

This manuscript requires considerable review of its English language. Several sentences require reconstruction to provide clarity.

Re: Thank you for the valuable and significant suggestion. We feel very sorry for the language problems. We have got professional help in revising this manuscript to improve English language.

We have revised the related paragraph according to your meaningful recommendation. We hope that we have fully understood your comments. If there is any problem, please no hesitate to relate us. Thank you very much for your kindness.

Parul Chawla Gupta (Reviewer 2): Comments:
This is a nice report documented by the authors, though its results can be validated with randomised controlled trails including more number of patients with a larger follow up. As shown in the Infant Aphakia Treatment Study, surgeons should be aware of the relatively higher likelihood of postoperative adverse events in aphakic eyes with anterior PFV. Conservative treatment with part time occlusion therapy in patients with relatively clear visual axis can save these children from these adverse events.

Re: Thank you very much for your kind comments and valuable suggestions. We feel sorry that it is difficult for us to include more patients with persistent hyperplastic primary vitreous because this is our first case. In the Discussion Section (Line 85-87), we have cited the relevant results of the Infant Aphakia Treatment Study, which are in support of our view point. Thank you again for your help in the improvement of our manuscript.

We hope that we have fully responded to the comments and we would be very glade if you could consider this manuscript for the publication in the Journal, and please no hesitate to relate me if there is any problem.

We thank you in advance for your great kindness and look forward to your good reply.

Yours sincerely,

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