Author’s response to reviews

Title: Peripheral Retinal Neovascularization Secondary to Highly Myopic Superficial Retinoschisis: A Case Report

Authors:

Mingyue Luo (luomingyue1992@qq.com)

Hong Du (duhong666@163.com)

Hua Ding (422403167@qq.com)

Dai Rongping (derricka@sina.com)

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Author’s response to reviews:

Dear editors,

Firstly, we would like to express our sincere gratitude to all the editors and reviewers in your effort to improve this case report.

Listed are our replies to reviewers’ comments.

Reviewer 1.

Comment 1. “Pars planitis is a differential diagnosis because this disorder is sometimes complicated by vitreous hemorrhage and traction-induced retinoschisis. Pars planitis usually affects children and adults less than 50 years old. Please discuss in your paper.”

Thank you very much for this advice. This is a very important differential diagnosis. There was only mild hemorrhage in the bottom of the vitreous, and no sign of inflammatory opacities, snowball or snowbank, so it is likely the retinoschisis is secondary to high myopia. We added these negative slit lamp findings to the manuscript. (line 62-63)

Comment 2. In the discussion, the author suggested that is more prominent in superficial retinoschisis (line 86-87). However, they affirmed that the location of schisis doesn't seem like a significant contributory factor, since retinal neovascularization secondary to superficial retinoschisis was reported both at macula and nasal quadrant. The concept that the author wants to give is not clear.
We have reorganized our language to illustrate our concept (line 105-106). Originally, we tried to emphasize it is the layer of schisis rather than the location (at the retina) that matters more in initiating neovascularization.

Comment 3. The schisis classification at the beginning (of the discussion) seems pointless, it does not support a thesis discussed by the authors.

As illustrated in the previous reply, originally, we would like to stress the role of superficial retinoschisis in initiating retinal neovascularization. Since this classification is not a consensus and lacking enough supporting evidence, we have reorganized our language.

Comment 4. Please add to the figure an early and later fluorescein angiograms to better show the neovascular abnormalities.

FFA was performed in her local hospital in Shanxi with Dr. Hua Ding’s prescription (Author3). Corresponding author Rongping Dai paid a visit to Datong Coal Mine Group Hospital in Shanxi to review all her FFA images, but we decided the quality of other images wasn’t fit for publication.

Comment 5. Why should myopia be an important factor?

We think the layer or depth of retinoschisis matters more in initiating retinoschisis. The reason for retinoschisis (senile, X-linked, myopic) may not be the main driver.

Reviewer 2.

Comment 1. In the background section of the abstract, the authors say that the occurrence of neovascularization is "rarely reported" in high myopia. This implies that there has been at least 1 report. This statement is not the same as in the background of the case report. Can you please give more background that summarizes existing literature for those who are not familiar with myopia associated with peripheral retinoschisis and neovascularization?

There are some cases reported as retinal microvascular abnormalities (Reference 2 and 3) in myopic retinoschisis, but there are some disagreements between the authors, which are discussed in the discussion section.

Comment 2 In the case presentation, there was no mention of the patient's medical history. Was there any relevant medical history?

There was no relevant medical history reported by the patient, which was added in line 58.
Comment 3 In the Discussion, the authors say that myopic neovascularization associated with retinoschisis occurs in the RNFL. The language implies that there were no other affected layers. Reference 1 shows a single OCT scan where there are schisis cavities in both the RNFL and the ONL. The 2nd reference also shows images with cavities in multiple layers (ONL, RNFL, and between the IPL and GCL). I was unable to access reference 3. Reference 4 shows schisis in the GCL, INL, and OPL but not in the RNFL. Please reword or clarify the statement.

Thank you so much for confirming the OCT images. We have reworded and clarified our statement (line 111-113). We really appreciate your time and effort in making the statement more accurate.

Comment 4. Line 86, I think the term "inaccurate" is an inappropriate thing to write.

This is a really great reminder. We have reorganized our discussion structure, and won’t stress our classification of retinoschisis. We will keep this advice in mind in future articles. Thank you so much for reminding.

Comment 5. Line 90 mentions VEGF. Can you comment on your chosen treatment option instead of an administering an anti-VEGF treatment?

We chose laser because we believed with enough photocoagulation, her retina would stabilize, and most abnormal vessels (which we believe to be retinal neovascularization) would regress. We consider it to be similar to the logic in using pan-retinal photocoagulation to treat proliferative diabetic retinopathy. In fact, we did observe shrinkage of vascular network in her follow-up visit. Although there was recurrent vitreous hemorrhage, we still consider supplementing laser as a good option. Another consideration is the cost for anti-VEGF treatment. We have Ranibizumab, Combercept and Eylea. Avastin is not allowed in public hospitals in Beijing. These will cost over 1,000 USD, roughly one month’s salary for our patient.

Comment 5. Can you put the images in order as addressed in the text?

Figure 1C and Figure 2B were placed to compare with Figure 1A~B and Figure 2A respectively. We think it more convenient to compare pre- and post- laser images.

Comment 6. Please add arrows for reference in pictures that were described in the text.

We have added arrows and illustrated them in figure legends.

Reviewer 3

Comment 1. Please define PVD at first mentioned.

We reorganized our discussion, and no longer discuss the cause of retinoschisis.
Comment 2. Please include vitreous hemorrhage images at first visit and follow-up visits.

We agreed adding these images would better present the case, but unfortunately, back then we mainly paid attention to the lesion, so there were no high-quality images for vitreous hemorrhage. We will pay attention in our future work. Thank you for reminding.

Comment 3. What was the visual acuity during follow-ups?

We added her corrected visual acuity during follow-ups in line 76 and 77.

Comment 4. Add a reference for the statement "The location of schisis doesn't seem like a significant contributory factor, since retinal neovascularization secondary to superficial retinoschisis was reported both at macula and nasal quadrant".

We reorganized our discussion structure, and no longer stress this point.

Comment 5. Please update the reference 5 and write it in journal's reference style.

Thank you for correction. We have updated the discussion, and discussed the nature of these microvascular abnormalities (neovascularization VS remodeling), so we no longer cite this reference.

Once again, we want to thank all the editors and reviewers in your effort. Should there be any modifications, please contact us any time. Looking forward to your kind reply.