Author’s response to reviews

Title: Postoperative follow-up of a case of atypical morning glory syndrome associated with persistent fetal vasculature

Authors:

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Author’s response to reviews:

Dear Peiquan Zhao:

We sincerely appreciate for your comments on our manuscript. Your suggestions are greatly helpful to us. After careful consideration, our responses are as follows:

1. It is true that MGS is accompanied by central nervous system abnormalities sometimes. The girl had done brain MRI but there were no abnormal signals.

2. Apart from the postoperative fundus photos where the remnant white membrane on the surface of the optic disc showed, we found that a stalk arose from the optic disc and adhered to the peripheral retina and the vitreous proliferated along the Cloquet's canal during the surgery. Retinal folds and proliferative membrane were also found during the surgery. We removed the stalk and fibrous membrane. In addition, the preoperative ultrasound scan has shown the stalk and proliferative membrane arising from the optic disc (Figure 1). We have added some discussion about the diagnosis of PHPV.

Figure 1. The stalk and proliferative membrane arising from the optic disc in preoperative ultrasound scan.

According to the classification and manifestation of PHPV, we tend to hold that our case is more like posterior PHPV, which may manifest as a stalk from the optic nerve, retinal proliferative membrane, retinal fold, retinal detachment, or optic nerve hypoplasia.

3. Peripheral retina, not limited to supratemporal peripapillary retina, was reattached 4 months after the surgery when subretinal fluid was absorbed. Since there was some subretinal fluid right
after the surgery, we did OCT to see if the fluid will be absorbed later or not. And 4 months later, OCT revealed the complete absorption of the subretinal fluid (Figure 2A).

OCT from last November showed a little of subretinal fluid in supratemporal parapapillary retina. There was no obvious retinal detachment in the rest of the retina and the retinal hole we made in the surgery was surrounded by laser spots. We thought the fluid arose in part from MGS but the reason was unclear (Bartz-Schmidt and Heimann, 1995; Chang et al., 1984; Coll et al., 1995; Irvine et al., 1986; Lytvynchuk et al., 2017). Her parents refused the second surgery considering that the right eye was stable. And there was some emulsified silicone oil in the anterior chamber, but not much.

Figure 2. Both the posterior (2B) and peripheral retina (2A) were completely reattached 4 months after the surgery revealed by FFA and OCT.

4. As in some posterior or combined PHPV patients, retinal detachment, more specifically, tractional tent-like retinal detachment is the most common type. The primary vitreous proliferates and adheres to the retina, causing partial retinal traction and thus leading to tent-shaped retinal detachment. According to previous literature, in some cases, PHPV may also present as retina fold. The proliferation of the vitreous along the Cloquet's canal results in the formation of retina folds or even complete tractional retinal detachment. Moreover, MGS can cause retinal detachment due to unclear reason.

5. Yes, the retinal fold is not common in MGS. As mentioned above, according to previous literature, in some cases, PHPV may also present as retinal folds. The proliferation of the vitreous along the Cloquet's canal results in the formation of retina folds or even complete tractional retinal detachment.

Thank you again for your precious opinions, we would like to hear from you again.

Yours sincerely,
Jing Luo

Dear Lytvynchuk L M:

We sincerely appreciate for your comments on our manuscript. Your suggestions are greatly helpful to us. After careful consideration, our responses are as follows:
1. PPV was performed in order to relieve retinal detachment and prevent the exacerbation of vision loss and eyeball atrophy.

I understand it is a little bit confusing here. The fundus structures remained unrecognizable immediately after the surgery because there was still some subretinal fluid and the shape of the optic disc was not so clear to diagnose as MGS. But it became clearer over time. 1 week later, the subretinal fluid was absorbed mostly and the fundus was clear enough for the diagnosis of MGS with PFV. We have made it clear that the diagnosis was based on her follow-up visits.

2. The girl visited us last November after we submitted the paper. We will add more information for that.

3. Vitrectomy and lentectomy may be beneficial in the management of MGS and PFV if accompanied by retinal detachment or cataract in similar cases. Both MGS and PFV could be accompanied by retinal detachment. We will correct this misleading expression.

4. Thanks for your good advice.

5. We have considered that and corrected it in the revised manuscript. Thank you.

6. Before the surgery, the ultrasound scan and MRI showed the funnel-shaped depression of the optic disc which might be diagnosed as MGS. And retinal detachment was also revealed by ultrasound scan. We did the surgery in order to relief retinal detachment as well as to prevent the exacerbation of vision loss and the atrophy of the eyeball.

7. Thanks for the suggestion, we will do that.

8. Thanks for the suggestion, we will substitute "very similar" with "resembled". The ultrasound scan and what we found in the surgery serve as proofs for PFV. The ultrasound scan showed the funnel-shaped depression of the optic disc, retinal detachment, and vitreous proliferation before the surgery. And during the surgery, we found that a stalk arose from the optic disc and adhered to the peripheral retina and the vitreous proliferated along the Cloquet's canal. In addition, retinal folds were also found during the surgery.

"Persistent fatal vasculature could be divided into 3 categories based on the location of the vascular abnormalities—anterior, posterior, and combined PFV. Purely posterior PFV mainly involves the vitreous and the retina and accounts for 12% of PFV patients. It may manifest as a stalk from the optic nerve, retinal proliferative membrane, retinal fold, retinal detachment, or optic nerve hypoplasia." (Chen, C., H. Xiao, and X. Ding, Persistent Fetal Vasculature. Asia Pac J Ophthalmol (Phila), 2019. 8(1): p. 86-95.)

Considering the ultrasound scan and what we found during the surgery, we tend to hold that our case is more like posterior PFV.
9. The fluid was the result of preoperative RD.

10. Usually, patients with untreated retinal detachment will lose vision soon and suffer from the atrophy of eyeball. Before the surgery, the axial length of the surgery eye was only 19.69 mm compared to 21.20 mm in the fellow eye (Figure 1). For our patient, the vision acuity increased from hand motion to counting fingers after the surgery. When the girl visited us last November, the visual acuity was the same and the atrophy of eyeball hadn't deteriorated for two years and a half.

Figure 1. The axial length of the right eye (1A) and the left eye (1B) measured by preoperative ultrasound scan.

11. Optic nerve coloboma: Optic nerve colobomas will typically appear as a white excavation involving the inferior portion and extending to the choroid and retina.[1] Optic nerve colobomas also lack the central glial tuft and peripapillary pigmentation seen in morning glory disc anomalies.[2] It is important to differentiate from a morning glory disc anomaly because optic nerve colobomas can be associated with systemic syndromes such as CHARGE (coloboma of the eye, heart defects, choanal atresia, growth retardation, genitourinary abnormalities and ear abnormalities).[1]

Peripapillary staphyloma: Peripapillary staphyloma is another excavation of the optic disc where the optic disc is seen at the bottom of the excavation.[2] It can be differentiated from morning glory disc anomaly by the lack of central glial tuft and normal retinal vasculature.[2]

Optic pit: An optic pit is an oval or round depression in the optic disc that typically occurs temporally, although any portion of the disc may be affected. Pits may appear gray, white, or yellowish, and cilioretinal arteries emerge from the pit.[3] The pits usually are unilateral. The most common visual field defects are enlargement of the blind spot with connected paracentral arcuate scotoma.[4] Visual acuity usually is not affected by the pit unless associated serous macular detachments occur.

Bergmeister's papilla: Bergmeister's papilla consists of a small tuft of white, fibrous tissue that represents persistence a remnant of the fetal hyaloid artery. This tissue arises from the center of the optic disc and may overlay the disc or peripapillary retina in varying amounts. Visual function should be normal.


12. Will be added.

13. This was a case of MGS accompanied by PFV. According to the fundus, the OCT (2A), and the ultrasound scan (2B), the funnel-shaped depression of the optic disc was one of the characters of MGS. Other maldevelopments of the optic nerve doesn’t have such featured depression.

Figure 2. The funnel-shaped depression of the optic disc demonstrated by OCT from 4 months later (2A) and preoperative ultrasound scan (2B).

There are some references about the optic disc changes in MGS. In our case, the special part was the retina folds at the temporal side.

(1) "It is a congenital, funnel-shaped excavation of the posterior fundus that incorporates the optic disc, with a white tuft of glial tissue overlying the central portion of the disc and the increased number of blood vessels arising from the periphery of the disc." (Fei P, Zhang Q, Li J, Zhao P. Clinical characteristics and treatment of 22 eyes of morning glory syndrome associated with persistent hyperplastic primary vitreous. Br J Ophthalmol. 2013;97(10):1262-7.)

(2) "The appearance of MGDA is very characteristic with a central glial tuft, retinal vessels that exit in a radial fashion from the enlarged posterior scleral opening where the optic nerve tissue exits the globe, and a variable degree of peripapillary pigmentation." (Lee BJ, Traboulsi EI. Update on the morning glory disc anomaly. Ophthalmic Genet. 2008;29(2):47-52.)

(3) Figure 3. Cao XG, Li XX, Bao YZ. Morning glory syndrome associated with posterior lenticonus. Open Neurol J. 2009;3:45-7


(4) Figure 5. Our case: MGS with temporal retina folds.

Thank you again for your precious opinions, we would like to hear from you again.

Yours sincerely,

Jing Luo
Dear Hitoshi Tabuchi:

We sincerely appreciate for your comments on our manuscript. Your suggestions are greatly helpful to us. After careful consideration, our responses are as follows:

1. Indeed, the co-existence of PHPV, and other deformities are found in many MGS patients. In some situations, there might be a universal genetic mutation that leads to the multiple malformations. Given this, we may have a better understanding of the underlying mechanism among them.

2. Thank you for advising this. The vision acuity was hand motion before the surgery, counting fingers after the surgery and couldn't be corrected with glasses. We will put more details about postoperative visual acuity in the revised edition.

3. Usually, the untreated MGS and PHPV patients with retinal detachment might lose vision soon and suffer from atrophy of eyeball. That’s why surgery is recommended for complicated retinal detachment in many studies. For our patient, the vision acuity increased from hand motion to counting fingers after the surgery. When the girl visited us last November, the vision acuity was the same and there was no obvious atrophy of the eyeball after two and a half years. But OCT showed a little of subretinal fluid in supratemporal parapapillary retina. There was no obvious retinal detachment in the rest of the retina We thought the fluid might arose in part from MGS but the reason was unclear (Bartz-Schmidt and Heimann, 1995; Chang et al., 1984; Coll et al., 1995; Irvine et al., 1986; Lytvynchuk et al., 2017). Her parents refused the second surgery considering the right eye was stable. And there was some emulsified silicone oil in the anterior chamber, but not much.

4. We will update further details about her visits in the following two years.

Thank you again for your precious opinions, we would like to hear from you again.

Yours sincerely,

Jing Luo
Dear Funmi Ogun:

We sincerely appreciate for your comments on our manuscript. Your suggestions are greatly helpful to us. After careful consideration, our responses are as follows:

1. Thank you for your suggestion. We rephrased the sentence as "B-ultrasound and magnetic resonance imaging scans suggested that it could be a congenital dysplasia of the right eye".

2. We have corrected the manuscript with past tense.

3. We tried to put any details that either support the subject directly or can act as proofs for differential diagnosis into the manuscript.

It is true that MGS is accompanied by central nervous system abnormalities sometimes. The girl had done brain MRI but there were no abnormal signals. Her head size was normal and there was no facial dysmorphism.

4. We will add elaboration on the association between MGS and PHPV and the frequency of atypical MGS.

Thank you again for your precious opinions, we would like to hear from you again.

Yours sincerely,

Jing Luo