



Recurrent proliferative vitreoretinopathy in a patient with morning glory syndrome and intellectual disability

Tomoko Sato^a, Kazuki Kuniyoshi^a, Tatsuo Kodama^b, Shunji Kusaka^{a,*}

^a Department of Ophthalmology, Kindai University Faculty of Medicine 377-2 Ohno-higashi, Osakasayama, Osaka, 589-8511, Japan

^b Department of Ophthalmology, Shimane University 89-1 Enya, Izumo, Shimane, 693-8501, Japan

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ABSTRACT

Purpose: To report a case of morning glory syndrome (MGS) with retinal detachment, in whom unusually severe proliferative vitreoretinopathy (PVR) developed after surgery.

Observations: A 6-year-old boy with intellectual disability underwent vitrectomy for retinal detachment associated with MGS in the left eye. Vitrectomy was performed five times. C₃F₈ gas tamponade was used for the first and second surgeries. However, the retina developed PVR with a nearly 360-degree giant retinal tear after the second surgery. The third surgery required 360-degree retinotomy, followed by short-term perfluoro-*n*-octane (PFO) tamponade, which was removed ten days later. During the fourth surgery, the retina was found to be flipped over in a funnel-shape on the retinal pigment epithelium under the PFO. Silicone oil (SO) tamponade was used. During the fifth surgery, the retina was flipped over under the SO again. We found that the patient shook his head rapidly and vigorously while crying.

Conclusions and importance: We speculate that excessive head shaking associated with the patient's intellectual disability induced an unusual shape of the retina under PFO or SO. Although difficult to achieve, postoperative resting seems important in preventing such complications in intellectually disabled patients with retinal detachment.

1. Introduction

Morning glory syndrome (MGS), first described by Kindler in 1970,¹ is a congenital anomaly characterized by optic disc enlargement, depression with or without prepapillary white tissue, and peripapillary pigmentation. Regarding its pathogenesis, although not fully understood, incomplete closure of the embryonic fissure of the globe or abnormal differentiation of mesoblasts have been suggested.^{2,3} In approximately 80% of patients, MGS coexists with other ocular abnormalities, such as cataract, corneal opacity, and retinal detachment (RD).^{4,5} RD has been reported to occur in approximately 30% of eyes with MGS,^{1,5-7} and the possible causes include exudation from the vessels,¹ vitreous traction,^{7,8} retinal breaks,⁸⁻¹² or migration of the cerebrospinal fluid from the subarachnoid space,^{6,13} although its precise pathogenesis remains unclear. RD associated with MGS without retinal breaks may resolve spontaneously, while that with retinal breaks requires surgical treatment.¹⁴ However, the surgical results of RD associated with MGS seem to be far from satisfactory, especially in young children.¹⁴

We encountered a pediatric patient with intellectual disability and RD associated with MGS who exhibited unusually severe recurrent proliferative vitreoretinopathy (PVR) after primary vitrectomy.

2. Case report

A 6-year-old Japanese boy was referred to our hospital for treatment of RD associated with MGS in his left eye. The patient was unable to sit still even for the short duration when ophthalmoscopic examinations were performed due to intellectual disability. The best-corrected visual acuities were 1.2 OD and 0.03 OS. The intraocular pressure was 15 mmHg OD and 6 mmHg OS. The patient's right eye was normal. No abnormal findings were observed in the anterior segment on slit-lamp examination. Fundus examination revealed an enlarged optic disc depression and RD in the left eye (Fig. 1A and B). A retinal break could not be detected by ophthalmoscopy.

The patient underwent lens-sparing vitrectomy using a 25-gauge system. During surgery, a small break was found on the temporal side within the excavated peripapillary area (Fig. 1C). After creation of a

* Corresponding author.

E-mail address: skusaka@gmail.com (S. Kusaka).

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posterior vitreous separation, subretinal fluid was aspirated from the break, followed by laser ablation of the retina around the excavation (Fig. 1D). Posterior vitreous separation was not easy, as in most pediatric cases, but was not as evidently tighter compared to that in other MGS cases. Finally, 10% C₃F₈ gas was injected into the eye.

Three weeks after the first surgery, the patient visited our clinic, and the retina was found to be totally detached with the development of proliferative vitreoretinopathy (PVR) (Fig. 1E) and cataract. The patient underwent a second surgery, which included vitrectomy, lensectomy, and implantation of the intraocular lens (IOL). During surgery, a newly developed retinal break was found in the temporal peripheral retina, probably created by shrinkage of the retina due to the proliferative membranes. Removal of the proliferative membranes and subretinal strands in the mid-peripheral retina (Fig. 1E, arrows), which seemed to hinder the retinal reattachment without tension, was performed, followed by laser ablation around the excavated peripapillary area and all retinal breaks, and 14% C₃F₈ gas tamponade (Fig. 1F).

Two months after the second surgery, the patient developed severe PVR with a nearly 360-degree giant retinal tear (Fig. 2A). A third surgery was performed in which peripheral retinotomy and peeling of the proliferative membrane under perfluoro-*n*-octane (PFO) were followed by laser ablation on the peripheral retina to avoid the recurrent RD (Fig. 2B). PFO was retained to achieve better apposition of the retina and underlying RPE without maintaining face-down position.¹⁵ IOL was

removed in the third surgery because of the severe PVR and fibrin formation on both anterior and posterior surfaces of the IOL.

Ten days later, fourth surgery was performed to remove PFO, and it was observed that the retina was flipped over toward the superior direction in a funnel-shaped under the PFO (Fig. 2C). Proliferative membranes were minimal on and beneath the retina, and the retina could be opened and re-flattened easily under PFO and directly exchanged with silicone oil (SO) (Fig. 2D). Two weeks after the fourth surgery, SO was also emulsified in the eye, and a fifth surgery was planned to remove the SO (Fig. 2E). However, the patient refused to go to the operation room, although the mother and our medical staff tried to persuade him. In the ward, we noted that the patient was shaking his head rapidly and vigorously while crying. His mother informed us that the patient demonstrates this behavior whenever he cries.

Finally, SO was removed 5 months after the fourth surgery. Before SO removal, we found the retina was again flipped over toward the nasal direction under SO (Fig. 2F). SO was removed, but no attempt was made to open and flatten the retina, as we considered retinal reattachment was impossible. The final visual acuity was light perception.

3. Discussion

We treated a patient with intellectual disability and RD associated with MGS. We performed multiple surgeries, including heavy liquid

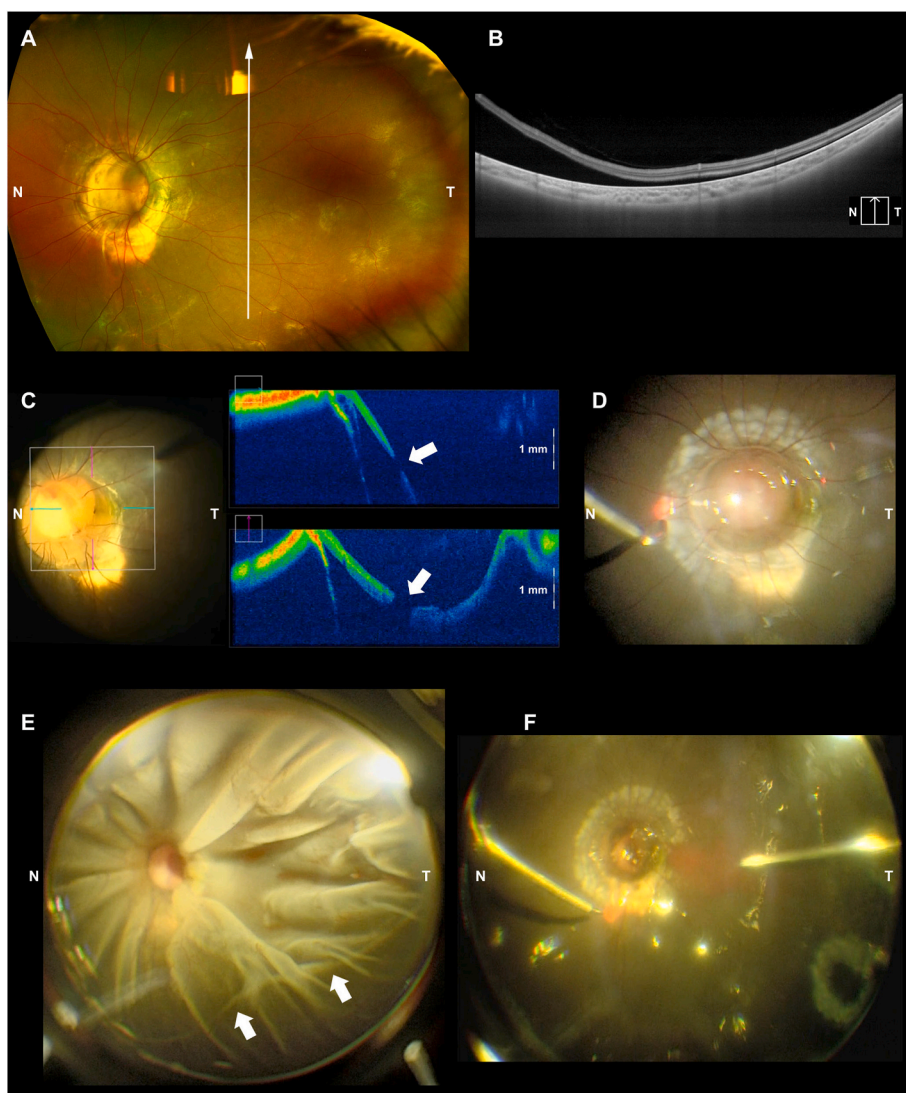


Fig. 1. Fundus photographs (A, D, E, F), optical coherence tomography (OCT) images (B and C) of the left eye. T; temporal, N; nasal

A) Fundus photograph of the left eye at the initial visit. B) OCT image of the left eye at the initial visit. C) Intraoperative OCT images of the disc area in the left eye at the beginning of the first surgery, demonstrating a small break present in the temporal side of the disc within the excavated peripapillary area (arrows). D) Fundus view during the first surgery showing laser ablation on the retina around the optic disc. E) Fundus view at the beginning of the second surgery, showing a proliferative vitreoretinopathy with subretinal strands (arrows). F) Fundus view under air irrigation during the second surgery. Photocoagulation was performed around the excavated peripapillary area and all retinal breaks, including intentional holes through which the subretinal strands had been removed.

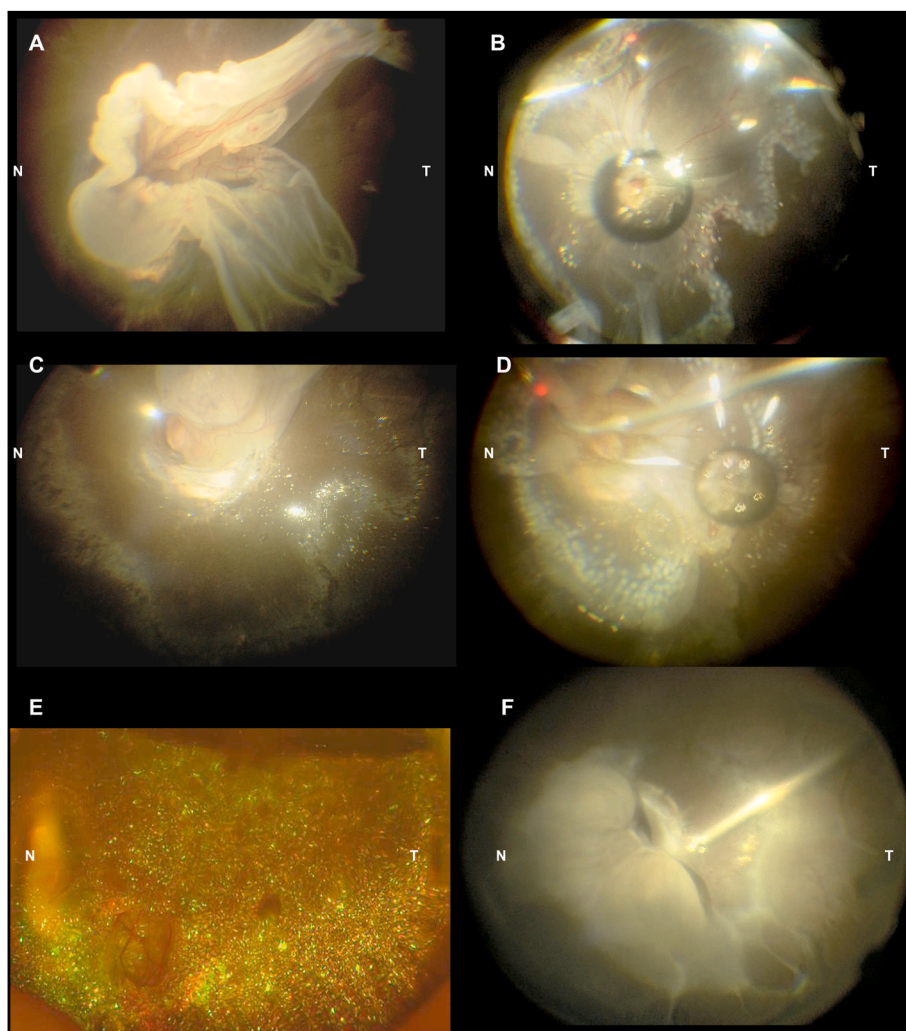


Fig. 2. Fundus views of the patient during surgeries of the left eye. T; temporal, N; nasal
 A) Fundus view at the beginning of the third surgery, showing total retinal detachment with nearly-360-degree giant retinal tear. B) Fundus view after per-fluoro-*n*-octane (PFO) tamponade in the third surgery. The retina is reattached under PFO. C) Fundus view at the beginning of the fourth surgery, showing a flipped over, funnel-shaped retina in the superior direction. D) Fundus view after silicone oil (SO) tamponade in the fourth surgery. The retina is reattached under SO. E) Fundus photograph taken 2 months after the fourth surgery showing massive, emulsified SO bubbles in the eye. F) Fundus view at the beginning of the fifth surgery. The retina was flipped over to the nasal direction under SO.

tamponade. However, unusually severe PVR with the flipped over retina developed twice, and unfortunately, final anatomical success was not obtained.

We speculated that the unusual form of PVR developed because of unfavorable factors, namely, MGS, the patient's young age, intellectual disability, and his habit of excessive head shaking during crying.

In the present patient, a retinal break was initially found within the excavated peripapillary area, which is often observed in the eyes with RD associated with MGS. In such cases, RD is usually treated with the procedure, as performed in the first surgery, that is, vitrectomy, creation of posterior vitreous separation, and aspiration of the subretinal fluid from the break, followed by laser ablation of the retina around the optic disc.

The first and second surgeries failed and severe PVR with a nearly 360-degree giant retinal tear developed. The third and fourth surgeries also failed even when we filled heavy liquids, that is, SO or PFO, into the vitreous cavity to avoid more PVR. Surprisingly, severe PVR developed repeatedly and the retina was flipped over even beneath the heavy liquid. We have never seen such a PVR in the eyes with heavy liquid tamponade, although the surgeon (S.K.) has treated more than 800 pediatric RDs, including intellectually disabled patients.

RD associated with MGS is difficult to treat¹⁴ although several clinicians have reported successful surgical treatment of MGS-RD.¹⁰⁻¹³

von Fricken et al. were the first to report successful treatment of RD associated with MGS.¹⁰ They applied laser photocoagulation around the optic disc after vitrectomy and fluid-gas exchange, which are essentially

the same techniques we performed for our patient. Several other papers reported successful surgery for RD associated with MGS using similar techniques.¹¹⁻¹³

Thus, it appears that vitrectomy, induction of posterior vitreous separation, and laser photocoagulation around the optic disc are effective in achieving retinal reattachment in the eyes with RD associated with MGS with a break within the excavated peripapillary area.

RD associated with MGS often develops PVR when the initial treatment fails. PVR is a clinical syndrome associated with RD due to the growth and contraction of cellular membranes on both sides of the retinal surface.¹⁶ Risk factors for PVR include prolonged intraocular inflammation, lower intraocular pressure with choroidal detachment, vitreous hemorrhage, multiple and/or giant retinal breaks, multiple surgical procedures, and persistent traction on retinal breaks.¹⁶

Intellectual disability seems to have an influence on the treatment outcomes and/or development of RD in pediatric patients. Agarkar et al.¹⁷ reported that intellectual disability was a risk factor for the development of RD following pediatric cataract surgery. Kuwabara et al.¹⁸ reported that approximately 46% of eyes developed PVR after RD surgery in patients with intellectual disability. Oono et al.¹⁹ also suggested that higher intraocular cellular activity and difficulty in maintaining postoperative rest and prone positioning are risk factors for recurrent RD in children with intellectual disability. AlAhmadi et al.²⁰ suggested that the poor prognosis of RD in patients with Down syndrome may be related to the difficulty in compliance with postoperative instructions. In an international multicenter study, Rossin et al.²¹ reported

that the surgical success rates for RD associated with self-injury were the lowest in the recent RD literature.

SO tamponade is useful for the treatment of RD in patients who have difficulty in resting after surgery, such as infants, children, and intellectually disabled patients. However, SO tamponade should be carefully applied for RD with MGS because migration of SO from the vitreous cavity into the subretinal space or subarachnoid space has been reported after surgery for RD associated with optic disc anomalies, including MGS.^{22,23}

The most unique and surprising phenomenon in the treatment of this patient was the flipped over retina on the RPE, which was observed twice, i.e., first, during the fourth vitrectomy performed 10 days after the third vitrectomy even under PFO (Fig. 2C) and second, during the fifth vitrectomy (SO removal) performed 5 months after the fourth vitrectomy (Fig. 2F). We have never seen this unique configuration of the retina in over 800 vitreoretinal surgeries for pediatric RD performed at our center in the last 20 years. We believe that this phenomenon cannot be explained only by the strong proliferative response in pediatric eyes. In fact, the first occurrence of the funnel-shaped, flipped over retina was noted only 10 days after the third surgery. In addition, we observed only thin and localized proliferative membranes during the fourth surgery, in which removal of PFO, re-flattening the retina, and SO tamponade were performed. Furthermore, massive emulsification of PFO and SO (Fig. 2E) was observed 9 days after the third surgery and 2 months after SO tamponade, respectively, which might have been caused by excessive head shaking.

Therefore, we believe that this patient's excessive head shaking, probably associated with his intellectual disability, was the main cause of the unique configuration of the retina as shown in Fig. 2C and F.

However, we have no direct evidence that proves the pathogenesis of the unique configuration of the retina seen in this patient. Further studies, including development of an animal model, are necessary to clarify the association between excessive head shaking and the unique retinal configuration and severe PVR seen in our patient.

4. Conclusions

The treatment of pediatric RD associated with MGS and intellectual disability is still challenging. Attention should be paid not only to the surgical techniques but also to the patients' characteristics and other conditions, such as postoperative rest, in patients with intellectual disability.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

CRedit authorship contribution statement

Tomoko Sato: Writing – original draft, Visualization, Resources. **Kazuki Kuniyoshi:** Writing – review & editing, Visualization. **Tatsuo Kodama:** Resources, Writing – review & editing. **Shunji Kusaka:** Conceptualization, Writing – review & editing, Management and

coordination responsibility for the research activity planning and execution, Supervision.

Declaration of competing interest

None of the authors have financial disclosures relevant to this article: (T.S., K.K., T.K., and S.K.)

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