



Pars plana vitrectomy for vitreoretinal complications in only seeing eyes after treatment for retinoblastoma

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ABSTRACT

Purpose: To report the outcomes of two only seeing eyes of two cases with retinoblastoma in which vitrectomy was performed to treat vitreous hemorrhage or rhegmatogenous retinal detachment after treatment for retinoblastoma.

Observations: Case 1 was an 8-month-old girl whose bilateral retinoblastoma (group D, OU) was treated by chemotherapy and focal ablation therapy. As the tumor size increased, enucleation was required in the right eye. At 4 years of age, about 1 year after the last treatment for retinoblastoma, lens-sparing vitrectomy was performed for dense, nonclearing vitreous hemorrhage, which had occurred 6 months previously. No recurrence of the tumor was found, and the patient's visual acuity improved to 0.9 postoperatively. Case 2 was a 4-month-old boy who was diagnosed with bilateral retinoblastoma (group D, OD; group C, OS) and underwent treatment, including systemic and local chemotherapy and proton beam therapy. Because large, regressed tumor masses were present in the posterior pole of the right eye, the left eye was the only seeing eye. At the age of 1 year 7 months, retinal detachment developed in the left eye 1 month after cryotherapy was performed for tumor recurrence. Although a scleral buckling procedure without drainage was performed, the retina was not reattached. The retina was reattached after vitrectomy with melphalan irrigation and silicone oil tamponade. However, recurrence was noted 6 months after the operation, and enucleation was required.

Conclusion and importance: Vitrectomy appears to be beneficial for the treatment of vision-threatening complications after retinoblastoma treatment. However, vitrectomy may be associated with the potential spread of tumor cells and/or tumor recurrence and therefore should be reserved as the last treatment modality for only seeing eyes. Careful postoperative follow-up is mandatory.

1. Introduction

Retinoblastoma is the most frequent pediatric intraocular malignant tumor, affecting approximately 1 in 15,000–18,000 live births each year.^{1–3} With recent advances in retinoblastoma treatments, such as external beam radiation, laser ablation, cryotherapy, and chemotherapy, the rate of salvaging the eye has been increasing. However, even if the tumor appears to be clinically stable and in regression, late vitreoretinal complications such as radiation-induced cataract, vitreous hemorrhage, and tractional and/or rhegmatogenous retinal

detachment^{4–7} can develop and threaten the patient's vision, sometimes of the only seeing eye. In general, because of the risk of extraocular tumor spreading, performing vitrectomy in eyes with retinoblastoma should be avoided. However, vitrectomy should be considered in the treatment of vision-threatening vitreoretinal complications, such as nonclearing vitreous hemorrhage or traction and/or rhegmatogenous retinal detachment, that have developed in the only seeing eyes after successful treatment of retinoblastoma.^{4–6}

Here, we report two such cases of retinoblastoma who underwent uneventful treatment with vitrectomy. The final prognosis of the two

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cases was dissimilar.

2. Case presentation

2.1. Case 1

An 8-month-old girl was referred to Osaka University Hospital for treatment of retinoblastoma in both eyes (class D; OU). Six cycles of chemotherapy (vincristine, etoposide, and carboplatin [VEC]) were administered followed by adjuvant treatment, including laser photocoagulation and cryotherapy. However, even after these treatments, the size of the tumor in the left eye increased, and enucleation was required. To treat the residual tumor in the right eye, intra-arterial (4.8 mg, 7.5 mg/m²) and intravitreal (0.024 mg) melphalan injections were administered twice and brachytherapy was performed at the National Cancer Center Hospital at the age of 3 years and 9 months to 4 years and 1 month. The tumor gradually regressed afterward, and the best-corrected visual acuity (BCVA) was 0.7. However, the patient developed dense vitreous hemorrhage at the age of 4 years 6 months, and the hemorrhage did not resolve for 6 months. She was subsequently referred to Kindai University Hospital for consultation of surgical treatment of vitreous hemorrhage. At the first visit, BCVA was hand movement (OD), and the intraocular pressure was 23 mmHg (noncontact tonometer). No abnormal findings were observed ophthalmoscopically in the anterior segment. Because of the presence of dense vitreous hemorrhage, the fundus was invisible. Because it had been more than 1 year since the last treatment of the tumor and there was no evidence of recurrence on ultrasonography, we considered vitrectomy as a treatment option. After we carefully explained to the parents the disease conditions and risks of surgery, especially with regard to the potential spread of tumor cells out of the eyeball, they agreed with and strongly wished for surgery.

We performed lens-sparing vitrectomy using a 27-gauge system (Fig. 1). During vitrectomy, we were careful to separate the hemorrhage adherent to the posterior surface of the lens using suction of the vitreous cutter, so as not to damage the lens. The hemorrhage was significantly dense and elastic and was difficult to distinguish from the potentially detached retina, if presented. Finally, we found that the retina was attached, and the two tumor masses became visible. We made no attempt to touch or dissect the tumor. The operation was completed without any complications. We securely sutured all scleral wounds,

taking into consideration the potential extraocular seeding of tumor cells. During the surgery, we used BSS to frequently rinse the ocular surface. Cytological examination of the vitreous humor collected from the vitrectomy machine's cassette was class 0. Postoperatively, the patient's BCVA improved to 0.9 OD. No postoperative complications or recurrence was noted during the 3-year follow-up period.

2.2. Case 2

A 4-month-old boy was diagnosed with bilateral retinoblastoma (class D, OD; class C, OS) and received chemotherapy (VEC, six cycles) at Osaka University Hospital. At the age of 9 months, he received an intra-arterial melphalan injection (2 mg, 5 mg/m²) twice at the National Cancer Center Hospital, followed by proton beam therapy for both eyes. Although regression of retinoblastoma was observed in both eyes, no useful vision could be obtained in the right eye due to multiple, large tumor masses in the posterior pole (Fig. 2). Therefore, the left eye was considered as his only seeing eye. Recurrence was noted in the left eye at the age of 1 year 6 months, which was treated by cryotherapy. One-month later, rhegmatogenous retinal detachment involving the macula and vitreous seeding were noted. Two retinal breaks were identified at 2 and 4 o'clock in the mid-peripheral retina. After the parents received an explanation of the disease conditions and risks, they opted for surgery.

We performed a scleral buckling procedure (SBP) with two segmental circumferential #503 sponges without subretinal fluid drainage and intravitreal melphalan injection (0.024 mg) without complications. Although the breaks appeared to be sealed after surgery, the retina remained detached, and therefore, we suspected the presence of an unidentified retinal break. Two months after surgery, we observed regression of vitreous seeding. Lens-sparing vitrectomy using a 25-gauge system with melphalan perfusion (5 µg/mL) was performed at Kindai University Hospital. During the surgery, the only retinal break identified was a macular hole. After we separated the posterior vitreous cortex from the retina, we attempted to peel the internal limiting membrane stained by brilliant blue G, but this was only partially possible. During fluid-air exchange, the subretinal fluid was aspirated through the macular hole using a back-flash needle, followed by silicone oil injection. We securely sutured all scleral wounds. We frequently rinsed the ocular surface during the surgery. The retina was noted to be reattached postoperatively (Fig. 3). Because of the young age of the patient, we

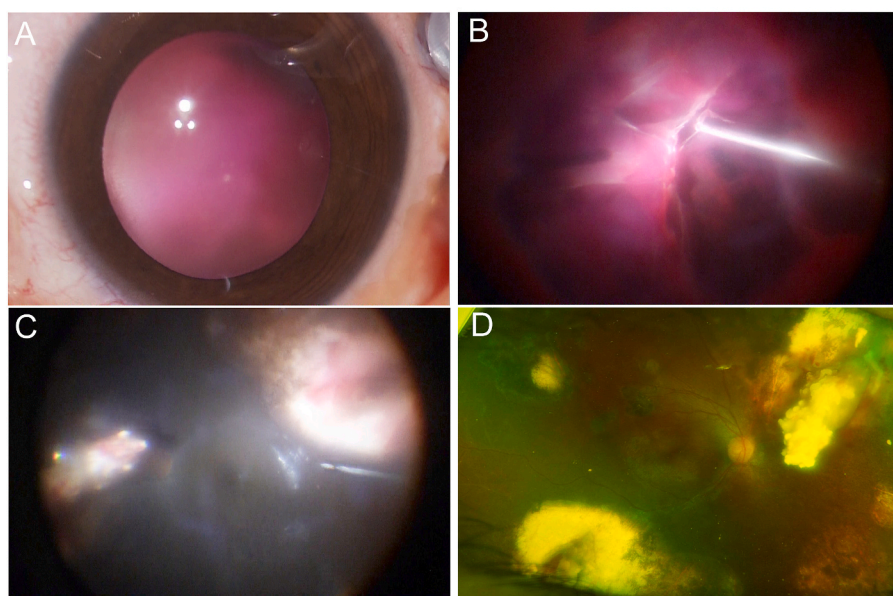


Fig. 1. Case 1. (A) Dense vitreous hemorrhage observed at the beginning of (A) and during vitrectomy. (B) After removal of vitreous hemorrhage, two regressed tumor masses are visible. (C) One-month postoperative fundus photograph. (D) Best-corrected visual acuity improved to 0.9.

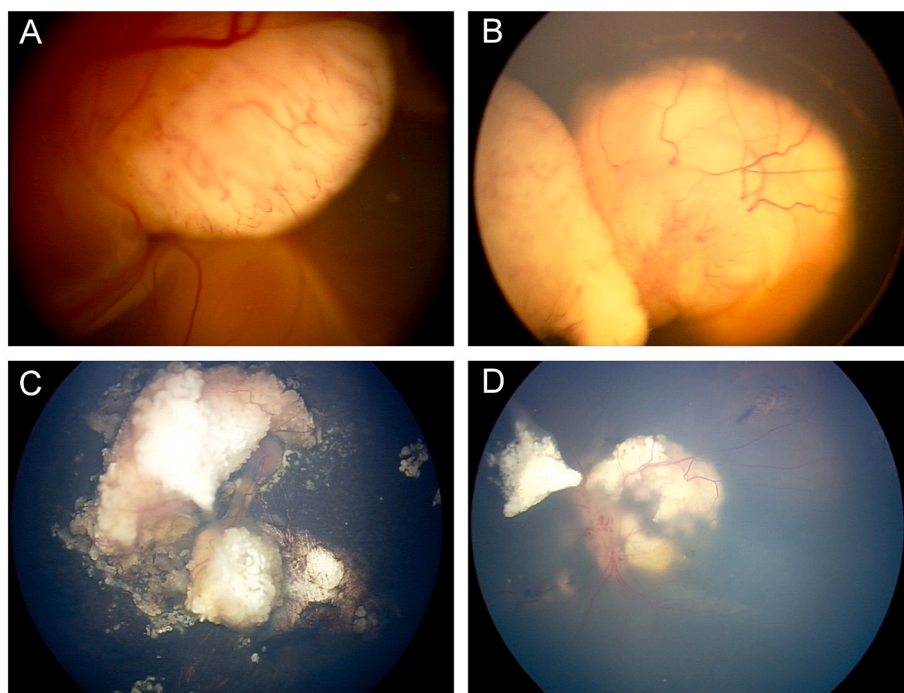


Fig. 2. Case 2. Fundus photographs at the first visit before treatment of retinoblastoma: (A) OD and (B) OS. Fundus photographs about 1 year 7 months from the first visit and after treatment for retinoblastoma, showing regressed large tumor masses present in the posterior retina (C) OD and macula-involving retinal detachment (D) OS.

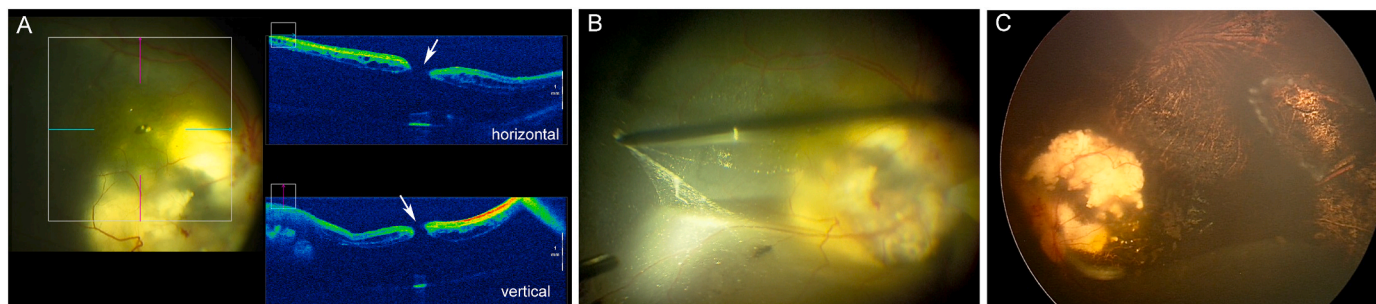


Fig. 3. Case 2. (A) Intraoperative optical coherence tomography clearly demonstrated the presence of macular hole, indicated by arrows. (B) Vitreous cortex is carefully removed from the posterior retina. (C) The retina was reattached with silicone oil 1 month postoperatively.

could not measure the BCVA. However, at 6 months postoperatively, seeding of tumor cells was detected in the anterior chamber, and enucleation of the left eye was required. During the pathological examination, we noted invasion of the tumor to the sclera but no sign of extraocular invasions and no tumor cells at the scleral wound. Chemotherapy (vincristine, endoxan, doxorubicin/carboplatin, and etoposide) was performed, and no sign of systemic metastasis was detected during the 3-month follow-up.

3. Discussion

We performed vitrectomy for late vitreoretinal complications, non-clearing vitreous hemorrhage in case 1 and rhegmatogenous retinal detachment in case 2, which occurred in the only seeing eyes after retinoblastoma treatment. As a result, postoperative BCVA improved in case 1 from hand movement to 0.9, with regressed tumor and no sign of recurrence during the 3-year postoperative follow-up. In case 2, although surgery was uneventful and the retina was reattached with silicone oil, we noted tumor recurrence 6 months after surgery, and enucleation was required. We speculate that one of the factors that

affected the postoperative clinical course was tumor activity at the time of vitrectomy. In case 1, the time interval between the last treatment for retinoblastoma and vitrectomy was approximately 1 year. The tumor seemed well regressed before the occurrence of vitreous hemorrhage, which was 6 months after the last treatment. Whereas, in case 2, only 1 month after the focal treatment (i.e., cryotherapy to the recurrent tumor mass), SBP in conjunction with intravitreal melphalan injection was required to treat the macula-involving rhegmatogenous retinal detachment with vitreous seeding.

We performed SBP without drainage first, considering that this method has a smaller chance of extraocular tumor spread as compared with vitrectomy. However, vitrectomy was necessary 2 months later, because we considered that there were unsealed retinal breaks; we could not expect the spontaneous absorption of subretinal fluid, and the prolonged macula-involving retinal detachment could cause serious damage to the visual function in the only seeing eye. In addition, the vitreous seeding decreased and was less inactive after intravitreal melphalan injection. However, tumor recurred 6 months after vitrectomy in case 2.

Intraocular surgery for eyes after treatment for retinoblastoma carries a potential risk for extraocular spread of tumor cells and

metastasis. Therefore, it is justified only in cases with clinically well-regressed retinoblastoma over a long period. To avoid intraocular manipulation, SBP without drainage of subretinal fluid has been chosen as a primary treatment option of rhegmatogenous retinal detachment in eyes with retinoblastoma. Boveri et al.⁵ reported five eyes with retinal detachment that had developed within 3 months after radiotherapy of retinoblastoma. SBP was successfully performed in two eyes; however, no surgery was performed for the remaining three eyes. Yousef et al.⁶ reported three eyes that underwent treatment by SBP without drainage. In two of the three eyes, the retinas were reattached, and no metastasis was detected in any of the eyes.

With regard to intraocular surgery for eyes with retinoblastoma, Madreperla et al.⁷ reported 4 out of more than 500 retinoblastoma eyes with retinal detachment that were treated by vitrectomy. The retinas were reattached in three eyes, and no enucleation or systemic metastasis was described. Honavar et al.⁴ reported that of 900 consecutive patients with retinoblastoma, intraocular surgery was performed in 45 eyes, including 12 eyes in which pars plana vitrectomy was performed. Indications for vitrectomy included vitreous hemorrhage in eight eyes and rhegmatogenous retinal detachment with proliferative vitreoretinopathy in two eyes. Those authors reported that continued clinical regression for at least 3 months was a prerequisite for consideration of intraocular surgery. Among the 12 eyes, recurrence of retinoblastoma, necessity of enucleation, and systemic metastasis were seen after vitrectomy in 5, 8, and 2 eyes, respectively. Those authors concluded that vitrectomy may be associated with a higher risk for recurrence, enucleation, and systemic metastasis.

Intravitreal injection of melphalan has been demonstrated to be safe and effective for the treatment of retinoblastoma, especially in eyes with vitreous seeding.^{8,9} During vitrectomy for case 2, to reduce the chance of recurrence and/or systemic metastasis, we used an irrigation of melphalan. In case 1, we judged the tumor activity to be reduced after vitrectomy; hence, we did not use melphalan irrigation. Yarovoy et al.¹⁰ reported successful vitrectomy with melphalan irrigation for vitreous hemorrhage in an eye with retinoblastoma in a 4-year-old boy. A similar attempt was reported for vitrectomy for retinal detachment.^{11,12} Because we did not observe any adverse event after surgery, we thought that melphalan irrigation is probably safe and can be a useful option. However, the efficacy of melphalan irrigation for the prevention of recurrence or tumor reduction is difficult to assess using data from only a small number of cases. Regarding postoperative prophylactic chemotherapy, we decided to forgo it in both cases because six cycles of VEC chemotherapy had already been administered and no active tumor was observed at vitrectomy.

With regard to preventing tumor spread during vitrectomy, we believe that the use of a small-gauge system with cannulas and closure valves, which minimize leakage of intraocular fluid out of the eye, securing the sutures of the scleral wounds, and frequent ocular surface rinsing during surgery are important. However, the efficacy of these methods is difficult to assess from our limited experience, and further studies are needed.

In conclusion, vitreoretinal complications after treatment of retinoblastoma, such as vitreous hemorrhage and rhegmatogenous retinal

detachment, are rare. Because vitrectomy may be associated with various consequences, such as recurrence of retinoblastoma, which may require enucleation and/or metastasis, clinicians should carefully consider the surgical indication. However, in only seeing eyes with regressed tumor and vision-disturbing vitreoretinal complications, vitrectomy should be considered a beneficial option. Careful postoperative follow-up is mandatory.

4. Patient consent

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

Authorship

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

Declaration of competing interest

The following authors have no financial disclosures: T.M., S.S., C.I., H.I., K.K., and S.K.

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