Spotlight on retinoblastoma-related cataracts: A case series

Asma Abdul Razak, MBBS (USIM)[1], Chan Li Yen, MBBS (IMU), MOphthal (UM)[1], Evelyn Tai Li Min, MD (USM), MMed Ophthalmology (USM)[2], Jamalia Rahmat, MBBS (UM), MOphthal (UM)[1]

[1]Department of Ophthalmology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, [2]Department of Ophthalmology and Visual Science, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

SUMMARY

Retinoblastoma is the most common primary intraocular malignancy in children, accounting for approximately 4% of all childhood cancers. While cataracts may rarely present as a direct manifestation of advanced disease, they are more frequently associated with treatment-related factors. Historically, cataract formation has been reported after external beam radiotherapy. However, cataracts continue to be reported with modern targeted chemotherapy. This case series describes three pediatric patients with bilateral retinoblastoma complicated by cataract formation. These cases illustrate the diverse mechanisms of cataract development and highlight the challenges posed by the timing of cataract surgery, tumor surveillance, and long-term visual outcomes.

INTRODUCTION

Retinoblastoma (RB) is the most common primary intraocular malignancy in children.[1] Recent advances in RB management have shifted treatment towards globe-salvaging approaches, including systemic, intra-arterial, and intravitreal chemotherapy.[2] Despite these advances, cataract formation may occur either as a manifestation of advanced disease or as a treatment-related complication, complicating tumor surveillance and visual rehabilitation.[3] This case series describes three pediatric patients with retinoblastoma complicated by cataract formation arising from distinct mechanisms.

METHODS

This retrospective case series included three pediatric patients with retinoblastoma and associated cataracts who were managed at Hospital Kuala Lumpur between 2010 and 2016. Clinical data were obtained through a retrospective review of medical records and follow-up examinations. Information on demographic and tumor characteristics, treatment history, surgical outcomes, visual acuity, and postoperative complications was collected, with follow-up data available up to 2025.

CASE PRESENTATION

The following cases demonstrate cataract formation in RB resulting from distinct mechanisms, including tumor-related factors and treatment-associated complications in the context of targeted chemotherapy.

Case 1

Bilateral RB was diagnosed at 18 months of age. According to the International Intraocular Retinoblastoma Classification (IIRC), the right eye (RE) was classified as Group E and the left eye (LE) as Group D. At presentation, a central lens opacity was observed in the LE. The RE underwent primary enucleation. The LE received focal therapy, including laser photocoagulation and cryotherapy; seven sessions of intra-arterial chemotherapy (IAC) with melphalan; and six cycles of systemic chemotherapy with carboplatin, vincristine, and etoposide (JOE regimen) administered at three-week intervals. During treatment, the cataract in the LE progressed to a white cataract, which prevented adequate tumor surveillance. Formal visual acuity (VA) assessment was not feasible due to the patient's age; the LE exhibited only light perception, poor visual behavior, absence of object fixation, and no red reflex. Intravitreal chemotherapy (IVitC) with melphalan (20 µg/0.1 mL) was administered to control the tumor seeds. Lens aspiration with intraocular lens (IOL) implantation was performed three weeks after the initial IVitC melphalan injection. Six additional postoperative IVitC melphalan injections (20 µg/0.1 mL) were administered at two-to three-week intervals to minimize the risk of tumor dissemination. Following surgery, visual behavior improved, with the child able to fixate and follow light, demonstrate object-directed visual responses, and exhibit a faint red reflex. Despite further laser photocoagulation, cryotherapy, three additional cycles of JOE chemotherapy, and external beam radiotherapy (EBRT) (40 Gy in 20 fractions), the progressive disease persisted. Enucleation of the LE was performed 10 months after the cataract surgery. The patient remained clinically stable, with no evidence of systemic disease.

Case 2

Case 2 was diagnosed with bilateral RB at 3 months of age, with Group B disease in the RE and Group C disease in the LE. She underwent six cycles of systemic chemotherapy (JOE regimen) at three-week intervals, together with focal therapy, comprising laser photocoagulation and cryotherapy. Despite initial tumor regression, new lesions developed in the LE, resulting in progression to Group E disease. As the parents declined enucleation, additional treatment was administered over subsequent visits and examination under anesthesia

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Corresponding Author: Evelyn Tai Li Min
Email: evelyn@usm.my

Table I: Clinical Characteristics and Treatment Overview.

Patient	Age at RB Diagnosis	RB Group	Interval of cataract diagnosis from RB diagnosis	Interval of cataract onset from last treatment	Interval of cataract surgery from last treatment	Systemic chemo-therapy (Y/N)	IAC Melphalan (Y/N)	IVitC Melphalan (Y/N)	VA (Pre-cataract operation)	VA (Post-cataract operation)	Proposed mechanism of cataract formation
1	17 months	D	-	-	3 weeks	Y	Y	Y	PL (No object fixation)	(Able to fixate and follow light, object-directed visual response)	Tumour-associated cataract (present at diagnosis)
2	3 months	C	42 months	15 months	19 months	Y	Y	Y	PL	2/60	Treatment-associated cataract (following prolonged multimodal globe-sparing therapy)
3	7 months	D	67 months	7 months	3 weeks	Y	Y	Y	6/120	6/76	Treatment-associated cataract (following prolonged multimodal globe-sparing therapy, possible iatrogenic lens injury)

Fig. 1: (A) Case 1: Cataract obstructing the fundus view in the LE. (B) Case 1: Clearer fundus view following lens aspiration. (C) Case 2: Central lens opacification in the LE, which progressed to a white cataract

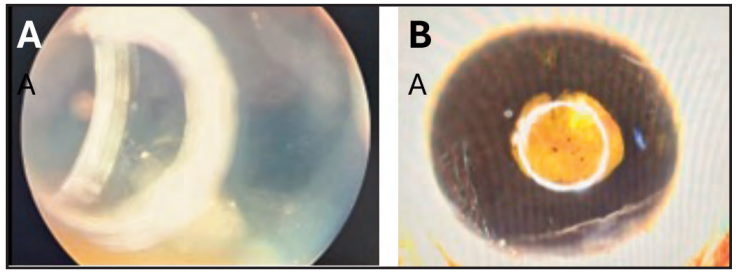

Fig. 2: (Case 3) (A) Cataract obscuring posterior segment view. (B) Progression to white cataract obstructing fundus view

(EUA) sessions, including three further cycles of JOE chemotherapy. Globe-salvage treatment for LE comprised two sessions of IAC melphalan (5 mg/30 mL), intracameral topotecan (7.5 µg/0.015 mL), and one IVitC melphalan injection (20 µg/0.1 mL). The LE remained free of tumor recurrence on surveillance; however, a mild cataract developed approximately 15 months after the last intravitreal injection and subsequently progressed to a mature white cataract, limiting fundus examination. Preoperative VA was perception of light in the LE and 6/38 in the RE. Lens aspiration with IOL implantation improved LE vision to 2/60. Two years later, vision declined to counting fingers (CF) due to posterior capsular opacification (PCO), and surgical capsulotomy was performed. Final VA remained 2/60, with no evidence of tumor recurrence 5 years after cataract surgery.

Case 3

Case 3 was diagnosed with bilateral RB at 7 months of age, with Group E disease in the RE and Group D disease in the LE. The RE underwent primary enucleation, whereas the LE was managed with globe-sparing therapies. The patient completed nine cycles of the JOE chemotherapy regimen, together with focal therapy comprising laser photocoagulation and cryotherapy. Recurrent vitreous seeding in the LE was treated over multiple sessions with 14 IVitC melphalan injections (20 µg/0.1 mL) and one IAC melphalan injection. Six years after diagnosis, five years after completion of systemic chemotherapy, and seven months after the final IVitC melphalan injection, the patient developed a LE cataract. Examination revealed a posterior subcapsular opacity with cortical wedge opacity and anterior capsular wrinkling, raising the possibility of an iatrogenic lens injury from repeated intravitreal injections. Progressive cataract formation necessitated lens aspiration with intraocular lens implantation to allow tumor surveillance; two IVitC melphalan injections (20 µg/0.1 mL) were administered before surgery for ocular priming. Postoperatively, the best-corrected VA improved from 6/120 to 6/76. Four years later, vision declined to CF due to dense PCO and was successfully treated with Nd:YAG capsulotomy, resulting in an improvement in VA to 2/60, which remained stable for several years after. During subsequent follow-ups, VA progressively deteriorated to CF due to treatment-related posterior segment changes. Fundus examination revealed mixed calcific regression and scarring, with no evidence of tumor recurrence.

DISCUSSION

Cataract formation in patients with RB is a multifactorial complication that may occur as a direct manifestation of advanced intraocular disease, reported in approximately 0.25% of cases, or as a delayed consequence of treatment.[3] Although cataracts have historically been most associated with EBRT, the increasing use of globe-sparing modalities such as systemic chemotherapy, IAC, and IVitC has altered patterns of cataract development. This case series presents three distinct mechanisms of cataract formation in RB and highlights the complexity of management decisions regarding the timing of cataract surgery, tumor surveillance, and long-term visual outcomes.

Historically, cataracts have been a well-recognized late complication of EBRT for RB, with a reported incidence as high as 71.7%, particularly with higher radiation doses and younger age at exposure.[3] Radiation-induced cataracts are typically posterior subcapsular in morphology and may progress gradually over time. With the decline in EBRT use following the advent of chemoreduction and targeted chemotherapy delivery, radiotherapy-related cataracts have become less frequent in recent years. However, as demonstrated in this series, cataract formation remains a clinically relevant issue in the modern treatment era, occurring in approximately 16.8% of eyes undergoing eye-preservation therapy, even in the absence of or before radiotherapy.[4]

In Case 1, cataracts were present at diagnosis and progressed rapidly during treatment. Cataracts as a presenting feature of RB are rare and typically associated with advanced disease.[3-4] Proposed mechanisms include tumor-related inflammation, exudation, ischemia, or direct invasion of adjacent ocular structures, all of which may disrupt lens metabolism.[3] In this case, early cataract progression significantly limited tumor visualization, complicating surveillance and treatment assessment. Although cataract extraction was performed to restore fundus visualization, the disease continued to progress despite aggressive multimodal therapy, ultimately necessitating enucleation. This case demonstrates the challenge of managing cataracts in eyes with an active, advanced intraocular tumor burden, where surgical intervention may be required primarily for diagnostic or surveillance purposes rather than for visual rehabilitation.

Cases 2 and 3 demonstrate cataract development as a delayed complication of RB treatment. Both patients received prolonged globe-sparing therapy involving systemic chemotherapy, IAC, and IVitC, with cataracts developing months to years after the completion of active treatment. Although systemic chemotherapy alone has not been strongly implicated in cataractogenesis, repeated intraocular interventions and local drug toxicity may contribute to lens changes.[4] IVitC melphalan has been associated with anterior segment toxicity, including iris atrophy, hypotony, and cataract formation.[2] Mechanical lens injury during intravitreal injection is also a recognized risk.[2] Previous studies have identified a greater number of IVitC cycles as a risk factor for cataract formation following retinoblastoma treatment.[4] These findings are consistent with those of Cases 2 and 3, in which cataracts developed following prolonged treatment incorporating IVitC.

In Case 3, clinical examination identified a posterior subcapsular cataract with associated cortical wedge opacity and anterior capsular wrinkling; findings that suggested iatrogenic lens trauma from repeated intravitreal injections. This observation supports the hypothesis that both mechanical injury and cumulative drug toxicity contribute to cataract development following IVitC.[2,4] The cataract developed several years after the initial diagnosis and months after the final intravitreal injection, indicating delayed presentation. This latency highlights the importance of long-term surveillance for anterior segment complications in RB survivors. The morphological features observed in Case 3 were consistent with previous reports of injection-related

lens injury, further supporting the role of injection in cataract formation.

The timing of cataract surgery in eyes previously treated for retinoblastoma (RB) remains a subject of debate. Historically, cataract extraction was avoided because of concerns regarding tumor dissemination and metastatic risk. However, recent evidence indicates that cataract surgery can be performed safely in selected cases, provided the tumor has remained inactive for an adequate interval and appropriate precautions are implemented.[9] Even in eyes with documented tumor regression, a minimum observation interval of six months prior to intraocular surgery has been recommended.[5] In this series, cataract surgery was undertaken primarily to restore tumor surveillance rather than to optimize VA. Preoperative IVitC was administered in cases 1 and 3 to prime the eye and reduce the theoretical risk of tumor dissemination, a strategy increasingly accepted in current practice.[7]

Although cataract surgery was technically successful, the visual outcomes in this series were limited. In Case 2, visual improvement was modest and subsequently compromised by PCO, a common complication of pediatric cataract surgery. Similarly, Case 3 developed dense PCO several years postoperatively, necessitating Nd: YAG capsulotomy. These findings reflect the cumulative effects of amblyopia, retinal damage from the tumor and treatment, and anterior segment complications on visual prognosis.[9] Visual outcomes should be interpreted with caution in RB survivors, as preservation of life and globe frequently takes precedence over visual rehabilitation.

From an oncological perspective, none of the eyes that underwent cataract surgery for tumor surveillance demonstrated recurrence attributable to surgical intervention. This observation supports the accumulating evidence that cataract extraction, when carefully timed and performed in controlled settings, does not increase the risk of tumor recurrence. Stringent patient selection, multidisciplinary decision-making, and long-term follow-up are essential.

This case series was limited by its retrospective design and small sample size. Nevertheless, it provides valuable insights into the heterogeneous pathways leading to cataract formation in RB and highlights practical considerations for management. The variability in etiology, timing of presentation, and outcomes underscores the importance of individualized care and long-term surveillance in this population.

In conclusion, cataract formation in RB may result from tumor-related factors, treatment toxicity, or iatrogenic injury. Despite advances in targeted chemotherapy, cataracts remain a significant complication that can impair tumor surveillance and visual outcomes. Cataract surgery can be safely performed in selected cases with appropriate precautions, primarily to facilitate ongoing monitoring. Awareness of the diverse mechanisms and long-term implications of cataract development is essential for optimizing care in children with RB.

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