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CASE REPORT

Subconjunctival Hemorrhage as a Sign of Intraocular Retinoblastoma Progression to Orbital Retinoblastoma

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Abstract

Introduction: Retinoblastoma is the most common intraocular malignancy of childhood. While treatable when detected early, a delayed diagnosis can lead to orbital extension, which significantly worsens the prognosis. We report an unusual case in which a subconjunctival hemorrhage signaled the progression of intraocular retinoblastoma to orbital involvement. **Case Presentation:** A 2-year-4-month-old child presented with a one-month history of left-eye leukocoria. Ocular ultrasound and computed tomography (CT) confirmed features of an intraocular retinoblastoma (Group E), and urgent enucleation was planned. The surgery was delayed by two months; shortly before the operation, the child developed an inferonasal subconjunctival hemorrhage that rapidly expanded. During enucleation, a reddish-brown extrascleral tumor was discovered beneath the hemorrhage, indicating orbital extension. Histopathology revealed Grade 3 retinoblastoma with optic nerve invasion (resection margin free of tumor). Adjuvant chemotherapy was initiated postoperatively. **Conclusion:** Subconjunctival hemorrhage can be an unusual warning sign of orbital tumor extension in retinoblastoma. This case highlights the importance of raising awareness and reducing diagnostic delays, particularly in resource-constrained settings.

Keywords: orbital retinoblastoma; subconjunctival hemorrhage; progression

Introduction

Retinoblastoma is the most common malignant intraocular tumor of childhood, with an incidence of approximately one in 14,000–20,000 live births worldwide.[1],[2] Approximately 7,500–8,000 new cases are diagnosed each year, and roughly 90% of cases present before the age of three.[1],[2] The disease affects both genders equally and is bilateral in about one-third of patients. Retinoblastoma is highly curable when confined to the globe; however, delayed diagnosis or inadequate treatment can allow the tumor to extend beyond the eye, greatly complicating management. Orbital extension of retinoblastoma (extraocular disease) is uncommon in high-income countries (historical incidence ~6–8%), however, remains a significant problem in low- and middle-income regions.[1],[2] Reports from Asia and other developing regions have documented orbital involvement in 18–40% of retinoblastoma cases, which is far higher than in the West.[1],[2] This disparity is mainly due to delayed presentation and limited access to specialized care.[1],[2]

Once retinoblastoma breaches the globe via scleral or optic nerve invasion, the prognosis worsens considerably. Orbital involvement carries a 10 to 27-fold higher risk of metastatic spread compared to intraocular disease.[1],[3] Metastatic retinoblastoma involving sites such as the bone marrow, central nervous system (CNS), and others, occurs in approximately 5–10% of all cases, often arising from advanced orbital disease.[1],[3] Five-year survival rates for retinoblastoma with orbital extension ranges from approximately 88% to 93% in developed countries to 10% to 50% in many developing countries.[1],[3] This outcome gap reflects socioeconomic and healthcare disparities: survival rates exceed 95% in wealthy nations, however, fall to nearly 30% in low-income regions.[1],[3] Late diagnosis, treatment refusal or abandonment, and limited therapy options contribute to higher mortality where resources are scarce.[1],[3]

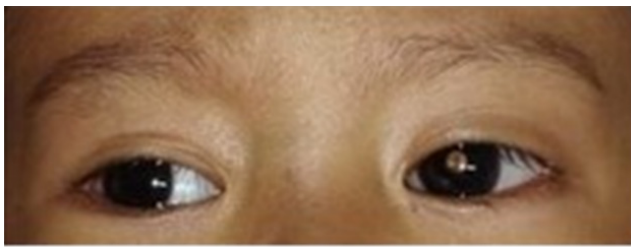

Figure 1. Anterior segment examination showed leukocoria in the left eye.

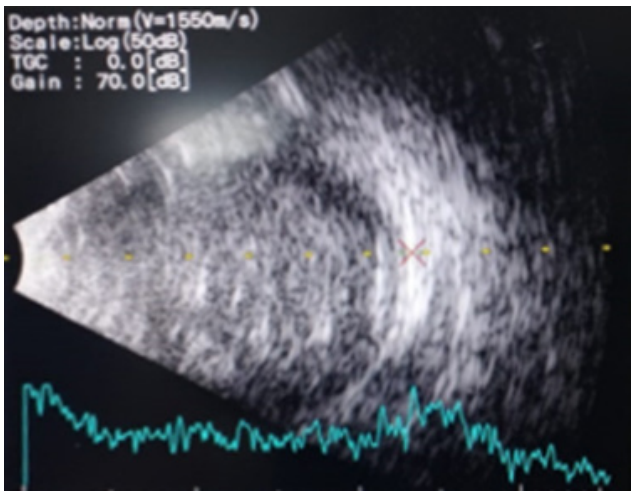

Figure 2. Ocular Ultrasound of the left eye revealed a mass with calcification.

While leukocoria (white pupil) is the classic presenting sign of intraocular retinoblastoma, our case is notable for an unusual clinical clue to extraocular progression. We describe a child in whom a subconjunctival hemorrhage—an atypical finding in retinoblastoma—marked the escalation from intraocular tumor to overt orbital disease. To our knowledge, subconjunctival hemorrhage is rarely reported as a sentinel sign of orbital retinoblastoma. This case underlines the need for heightened awareness and thorough evaluation when any new ocular changes occur in a child with retinoblastoma, as such changes may signal tumor extension.

Case presentation

A 2-year-old and a 4-month-old child were brought to the ophthalmology clinic by their parents due to the appearance of a white reflex in the left eye when exposed to light, resembling a cat's eye, which had been present for one month. There were no complaints of strabismus, eye redness, or ocular pain. The patient was still responsive when given toys. There was no family history of malignancy. On ocular examination, leukocoria was noted in the left eye (Figure 1). Ocular ultrasound of the left eye revealed an echogenic lesion involving 80-100% of the retinal-choroid-scleral (RCS) complex, suggestive of a mass with calcification, low mobility, and an axial length of 22.32 mm (Figure 2). The patient was diagnosed with a left intraocular tumor with a differential diagnosis of retinoblastoma.

The patient was scheduled for a head computed tomography (CT) scan focused on the orbits, with the appointment set for two months from the initial visit. The CT scan results revealed a solid lesion (31 HU) with calcified components (163 HU) measuring approximately 2.0 x 1.7 x 1.9 cm in the left retrolental region, predominantly on the medial side, extending into the left vitreous body (Figure 3). Contrast administration showed contrast enhancement (72 HU), with no involvement of the left optic nerve. These findings support the diagnosis of left retinoblastoma with extension into the vitreous body. No evidence of infarction, hemorrhage, masses or metastatic processes, or infectious processes was observed in the brain parenchyma. The patient was diagnosed with left intraocular retinoblastoma, Group E. The patient is scheduled for an urgent left eye primary enucleation under general anesthesia.

The patient opted to proceed with surgery two months after the surgical advice was given. One day before the scheduled operation, a subconjunctival hemorrhage appeared in the inferonasal area, measuring 3 x 5 mm (Figure 4). The hemorrhage expanded to involve the entire inferonasal region on the day of surgery (Figure 5). The patient underwent primary enucleation of the left eye using a myoconjunctival technique.

During the surgery, an extrascleral mass, reddish-brown in color, was found in the inferonasal orbital region, directly beneath the subconjunctival hemorrhage, with a firm, elastic consistency. The optic nerve measured 18 mm in length, with a base width of 6 mm at the globe, and was non-pliable, suggesting infiltration up to 10 mm (Figure 6). The patient was diagnosed with left eye overt orbital retinoblastoma.

Histopathological examination revealed grade 3 retinoblastoma. The tumor measured 11 x 9 x 7 mm. There was no evidence of lymphovascular invasion or perineural invasion. The tumor extended through the posterior aspect of the globe. Tumor cell infiltration was observed in the optic nerve, but the optic nerve resection margins were free of tumor cells. The patient underwent adjuvant chemotherapy.

Discussion and conclusions

Retinoblastoma is often curable when detected early, however, orbital retinoblastoma defined as tumor extension into the orbit, represents an advanced stage associated with significantly higher morbidity and mortality. Orbital retinoblastoma can arise in various contexts, and understanding these contexts is crucial for effective prevention and management.[2] Honavar et al.[4] categorize orbital retinoblastoma into primary, secondary, accidental, overt, and microscopic forms.

Our patient's scenario falls under overt orbital retinoblastoma, which is a recognized presentation,

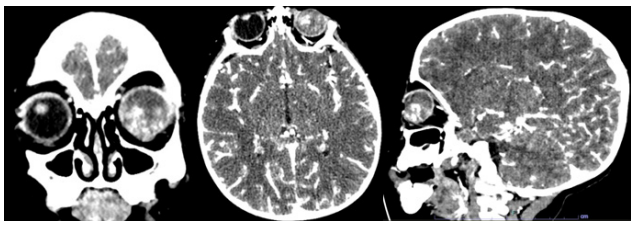

Figure 3. CT Scan findings support the diagnosis of left retinoblastoma with extension into the vitreous body.

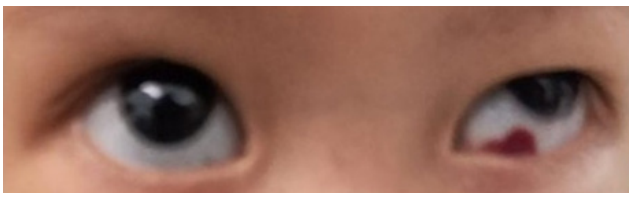

Figure 4. A subconjunctival hemorrhage appeared in the inferonasal area, measuring 3 x 5 mm, one day before surgery.

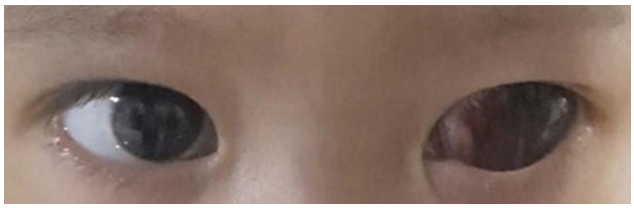

Figure 5. Subconjunctival hemorrhage expanded to involve the entire inferonasal region on the day of surgery.

however, not very common. What makes this case remarkable is how the orbital extension manifested: as a subconjunctival hemorrhage. Clinically, orbital retinoblastoma usually presents with more dramatic signs. Proptosis (forward displacement of the eye) is the most frequent presenting symptom in orbital disease, reported in about 70–80% of cases in various series. For instance, Menon et al.[5] observed proptosis in 83% of their extraocular cases, and other studies[6] have similarly found proptosis to be the leading sign of orbital involvement. Signs of inflammation, such as redness, swelling, or a fungating orbital mass on the eye surface, can also occur in advanced cases. Interestingly, leukocoria is typically a sign of intraocular tumor, can still be a presenting feature in extraocular retinoblastoma; one study from Brazil noted leukocoria as the initial symptom in 68% of children who ultimately were found to have extraocular spread. Our patient indeed presented with leukocoria, which led to the initial diagnosis. He did not develop classic proptosis or a visible orbital mass before enucleation; instead, the rapid subconjunctival bleeding was the clue to something amiss. We suspect that the growing extrascleral tumor nodule ruptured small conjunctival vessels or caused sufficient irritation to produce the hemorrhage. This atypical sign should alert clinicians: in a known retinoblastoma eye, any new redness, localized hemorrhage, or conjunctival swelling warrants immediate evaluation for possible extraocular extension.[5],[6]

The long posterior ciliary arteries travel in the suprachoroidal space, where they terminate at the major arterial circle of the iris. The anterior ciliary arteries emerge from the surface of the rectus muscles to penetrate the sclera and join the posterior ciliary arteries at the major arterial circle of the iris. The episcleral arterial circle runs on the surface of the sclera, connecting the anterior ciliary arteries. In this case, the tumor penetrates through Bruch's membrane, invading the choroid and extending to the sclera. The extrascleral mass compresses the posterior ciliary arteries, which anastomose with the anterior ciliary artery and the episcleral arterial circle.[7] Consequently, the rupture of the episcleral arterial circle leads to the development of subconjunctival hemorrhage.[7]

This case highlights the crucial importance of thorough pre-operative assessment in retinoblastoma, particularly when there is any indication of advanced disease. According to the Indonesian National Clinical Practice Guidelines[8], if clinical signs suggest possible extraocular extension (such as proptosis, orbital cellulitis-like inflammation, or buphthalmos), the child should undergo complete staging work-up before definitive surgery. Key elements include neuroimaging and systemic metastatic evaluation. Magnetic resonance imaging (MRI) of the orbits and brain with contrast is the preferred modality to assess optic nerve involvement and extrascleral extension.[4],[8],[9] MRI provides superior soft tissue detail and reduces exposure to ionizing radiation. (Notably, heritable retinoblastoma patients have a predisposition to second malignancies; hence, minimizing radiation from CT scans or X-rays is advised whenever possible.) In centers where MRI is not immediately available, a contrast-enhanced CT scan can be used; however, MRI is generally recommended for its superior resolution of the optic nerve and meningeal enhancement. In our patient, an MRI was not performed prior to enucleation – a CT was done two months earlier and showed no orbital tumor at that time. In hindsight, given the interval and the appearance of the subconjunctival hemorrhage, an urgent MRI just before surgery might have delineated the extrascleral extension. However, the outcome in this case was not compromised, as the orbital disease was discovered and removed during surgery.[4],[8],[9]

The management of orbital retinoblastoma requires a multimodal approach. Simply removing the eye is not sufficient when extraocular extension exists, due to the high risk of microscopic residual disease and metastasis. Historically, treatment for orbital retinoblastoma often entailed aggressive surgery such as orbital exenteration (removal of the entire contents of the orbit) and external beam radiotherapy, yet outcomes were poor, with survival rates often <50%. Over the past few decades, outcomes have improved significantly with

the introduction of effective systemic chemotherapy and tailored radiotherapy. Chemoreduction can sterilize microscopic disease and, in many cases, has reduced the need for radical exenteration.[10],[11] A study by Goble et al.[12] in 1990 was the first to demonstrate that combined therapy (surgery, radiotherapy, and chemotherapy) could successfully treat orbital recurrence of retinoblastoma. Subsequent series have demonstrated markedly improved survival with a combination of high-dose multi-agent chemotherapy, surgery, and adjuvant radiotherapy, when indicated. For instance, in one report, among 30 patients with orbital retinoblastoma treated with chemotherapy, surgery, and radiation, only two (6.7%) developed systemic metastases, a dramatic improvement over historical controls.[10],[11],[12]

Our patient's outcome so far has been positive: at one-year follow-up, he shows no evidence of disease. His case highlights several key points regarding the management of orbital retinoblastoma. First, early detection and treatment are paramount. Had the family not delayed the initial enucleation by two months, it is possible the tumor might have been removed before breaching the sclera. Treatment delays are a well-known risk factor for extraocular spread and worse outcomes. It is why public health efforts in retinoblastoma focus on educating caregivers to recognize leukocoria early and on improving referral pathways. Second, meticulous clinical examination can save lives. In this case, noticing the subconjunctival hemorrhage and recognizing it as an ominous sign prompted swift surgical intervention. Any child on observation or awaiting treatment for retinoblastoma who develops new signs (red eye, glaucoma, proptosis, orbital redness or swelling) should be re-evaluated immediately. Third, adherence to guidelines and protocols such as the Indonesian National Clinical Practice Guidelines[8] ensures that nothing is overlooked from imaging to systemic work-up, thereby optimizing treatment planning. We followed the guidelines by performing appropriate imaging and involving a pediatric oncologist for staging and chemotherapy, which undoubtedly contributed to the favorable outcome.[3],[4],[8]

Finally, this case highlights the significant progress made in retinoblastoma care and the substantial gap that remains globally. In the early 20th century, retinoblastoma was almost invariably fatal, with over 95% mortality. Today, in centers like ours with access to modern therapies, survival rates for intraocular cases are above 95%, and even orbital cases can often be cured. However, in many parts of the world, half of the affected children still die due to late presentation and lack of resources. Continued improvements in treatment (such as intra-arterial and intravitreal chemotherapy for eye salvage) and better healthcare access are expected to improve outcomes further. Equally important is

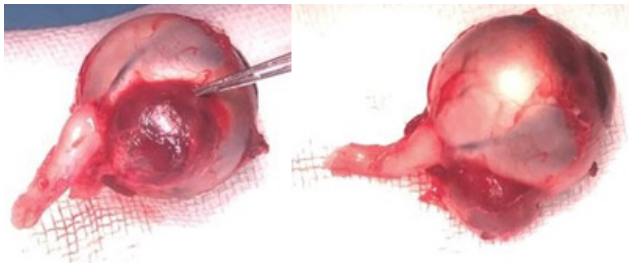

Figure 6. An extrascleral mass, reddish-brown in color, was found.

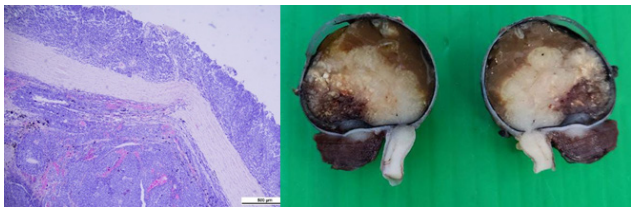

Figure 7. Histopathological examination revealed grade 3 retinoblastoma; the tumor measured 11 x 9 x 7 mm.

strengthening awareness and screening so that fewer children reach the orbital stage of the disease.[9],[13],[14],[16]

In summary, we report a unique case of retinoblastoma in which a subconjunctival hemorrhage was the harbinger of orbital tumor extension. Orbital retinoblastoma, once a uniformly fatal condition, can now often be successfully managed with a combination of surgery, chemotherapy, and radiotherapy, yielding greatly improved survival. However, the foundation of a good outcome is early diagnosis and complete initial treatment. This case underscores the importance of adhering to clinical guidelines for retinoblastoma: thorough pre-operative evaluation (including appropriate imaging and staging studies) should be performed to detect extraocular spread before surgery whenever possible. Even atypical signs like subconjunctival hemorrhage in a child with known retinoblastoma should prompt urgent reassessment, as timely intervention can be vision- and life-saving.

Multidisciplinary care is crucial, ophthalmologists, pediatric oncologists, radiologists, and pathologists must collaborate to ensure that the necessary adjuvant therapies complement surgery effectively. In our resource limited context, we also emphasize the importance of increased awareness to ensure children present early, and for healthcare systems to facilitate prompt referrals and treatment. By combining early detection, evidence-based multimodal treatment, and attention to social determinants of health, we can continue to close the outcome gap and give every child with retinoblastoma the best chance at a long-term cure and a high quality of life.

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