Orbital rhabdomyosarcoma presenting as optic nerve glioma in a child

Nasyitah Yakub, MD[1,2], Siti Nor Zalehawati Sepian, MSurg (Ophthal)[3], Julieana Muhammed, MMed(Ophthal)[1,2]

[1]Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, [2]Hospital Pakar Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, [3]Department of Ophthalmology, Hospital Sultanah Nur Zahirah,Jalan Sultan Mahmud Kuala Terengganu, Terengganu, Malaysia

SUMMARY

Orbital rhabdomyosarcoma is the most common primary malignant orbital tumour in children. It typically presents with rapidly progressing unilateral proptosis and may resemble other orbital conditions, making timely and accurate diagnosis essential. We present a case of a 5-year-old girl with progressive left eye proptosis over two weeks. Visual acuity and optic nerve function were initially preserved. Magnetic resonance imaging (MRI) revealed a lobulated mass encasing the left optic nerve, initially diagnosed as optic nerve glioma. Chemotherapy was initiated to address the optic nerve glioma, and the patient responded well after four cycles. However, one month later, the proptosis recurred with rapid progression, and her vision declined from 6/15 to finger counting. Fine needle aspiration biopsy (FNA) was inconclusive. An incisional biopsy performed three months later confirmed rhabdomyosarcoma. Due to the aggressive course, the patient underwent left orbital exenteration and completed chemotherapy. Eight months later, she presented with systemic symptoms. Imaging revealed a residual orbital mass, suggesting recurrence. As the family declined radiotherapy, second-line chemotherapy was initiated. Unfortunately, the patient passed away before completing treatment.

INTRODUCTION

Rhabdomyosarcoma is a soft-tissue sarcoma originating from mesenchymal cells that differentiate to form skeletal muscle.[1] Consequently, it can present in various parts of the body, resulting in complex and diverse needs for its clinical management. Approximately 40% of rhabdomyosarcoma cases occur in the head and neck region,[2] underscoring the importance of this area, concerning the disease's impact on patients and the challenges faced in treatment. The prevalence of rhabdomyosarcoma, along with the associated treatment difficulties, significantly influences paediatric oncology.

In this case report, we present a rare case of orbital rhabdomyosarcoma that was initially interpreted as an optic nerve glioma, making diagnosis and treatment particularly challenging. Empirical chemotherapy, started based on the initial impression, led to significant tumour shrinkage at first but was followed by an aggressive rebound. This ultimately required left orbital exenteration due to the rapid progression of the disease.

CASE PRESENTATION

A 5-year-old female with no known comorbidities presented with painless, progressive left eye proptosis that developed over a two-week period. She had no complaints of reduced vision, no history of ocular trauma, and exhibited no systemic symptoms. On ocular examination, there was left eye nonaxial proptosis with inferonasal displacement of the globe and almost complete ptosis of the upper eyelid. Hertel's exophthalmometry measurements revealed an anterior projection of the left eye at 13 mm compared to 9 mm for the right eye, exceeding the normal difference of 2 mm between both eyes. There was mild decreased ocular motility in the left eye during abduction and elevation. Visual acuity was 6/15 bilaterally, with intact other optic nerve function. Both anterior segment findings were unremarkable. Fundoscopic examination of the right eye was normal. However, the left eye showed a hyperaemic optic disc with blurred margins.

Magnetic resonance imaging (MRI) revealed a large lobulated mass occupying the left intraconal space and encasing the optic nerve. The mass was hyperintense on T2-weighted and FLAIR sequences, measuring 2.9cm x 2.5cm x 2.6cm (AP x W x CC) (Figure 2).

Given the patient's preserved vision but cosmetically disfiguring proptosis, treatment was initiated with four cycles of intravenous (IV) chemotherapy. The regimen included IV carboplatin (400 mg/m²), etoposide (100 mg/m²), daunorubicin (300 mg/m²), vincristine (1.5 mg/m²), actinomycin D (1.5 mg/m²), and cyclophosphamide (60–120 mg/m²/day), based on an initial working diagnosis of presumed optic nerve glioma. The patient demonstrated a favourable early response to the treatment (Figure 1).

Unfortunately, five months after completing the fourth cycle of chemotherapy, her left eye proptosis worsened rapidly. This led to a decline in vision from 6/15 to finger counting, along with a positive relative afferent pupillary defect (Figure 3A) in the left eye. She developed total ophthalmoplegia of her left eye, resulting in an almost "frozen" eye. Fine needle aspiration biopsy (FNA) was performed but yielded only adipose tissue. Due to the aggressive nature of the disease, a decision was made to perform a left orbital eye exenteration.

Histopathological analysis of the incisional biopsy revealed features consistent with spindle-cell rhabdomyosarcoma. The specimen showed sheets of malignant cells arranged in long sweeping fascicles and herringbone patterns, with areas of

This article was accepted: 24 July 2024
Corresponding Author: Julieana Muhammed
Email: drjulieana@usm.my

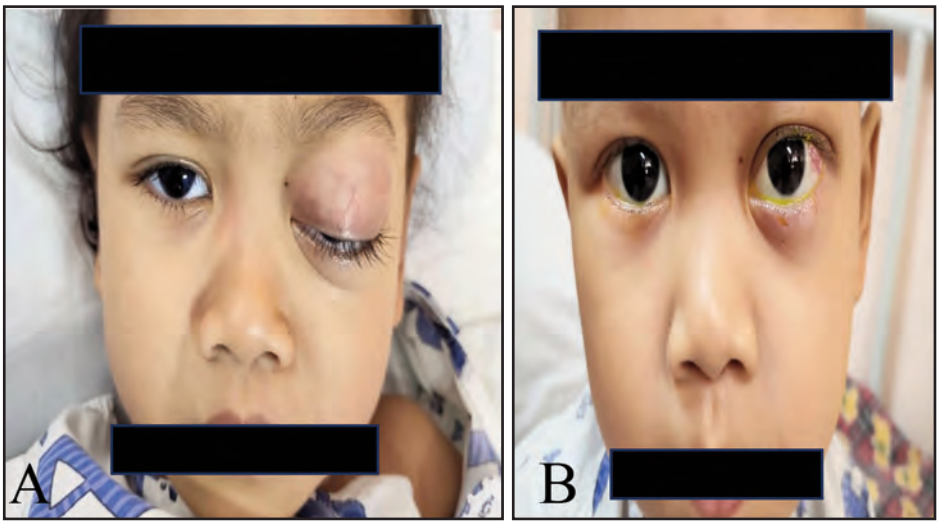

Fig. 1: Pictures before and after empirical chemotherapy (A) Left eye nonaxial proptosis with inferonasal displacement of the globe and almost complete ptosis of the upper eyelid. (B) Restored left eye position following completion of chemotherapy

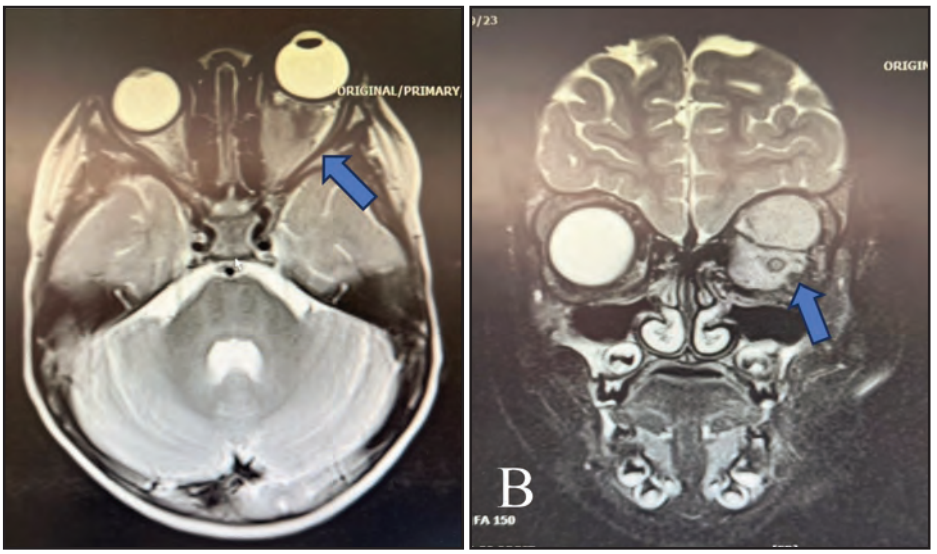

Fig. 2: MRI of the patient's brain and orbit. (A) T2-weighted axial MRI showing a lobulated mass encasing the optic nerve in left retrobulbar region. (B) T2-weighted coronal MRI showed the mass occupying the whole orbit space.

Fig. 3: (A) Left proptosis worsening 5 months after completed four cycles of chemotherapy. (B) Left orbital exenteration. (C) Post left orbital exenteration.

geographic necrosis. The tumor cells were oval to spindle-shaped, with elongated, vesicular nuclei, supporting the diagnosis.

The patient's condition initially improved within three months following left orbital exenteration, although a postoperative infection at the surgical site required one week of treatment. However, eight months later, the patient represented with constitutional symptoms. A repeat MRI revealed a residual orbital mass, suggestive of tumour recurrence. Due to parental refusal of radiation therapy, she was started on second-line chemotherapy. Unfortunately, she passed away three years after the initial diagnosis, before completing the second-line treatment.

DISCUSSION

Orbital rhabdomyosarcoma (RMS) is the most common primary orbital malignancy in children, typically affecting those between 5 and 10 years of age,[3] which aligns with our patient's presentation. Despite its well-established clinical and radiological features, RMS can occasionally present atypically, making diagnostic and therapeutic challenges. In our case, a 5-year-old girl presented with intraconal rhabdomyosarcoma that was initially diagnosed as an optic nerve glioma, illustrating the diagnostic difficulty of such atypical presentations.

Rhabdomyosarcoma most frequently originates in the extraconal space, typically within the superonasal quadrant of the orbit.[1,4] In contrast, our patient had an intraconal mass encasing the optic nerve which is a much rarer anatomical location. This intraconal origin altered the clinical impression and likely contributed to the initial radiologic diagnosis of optic nerve glioma. Anatomically, intraconal RMS may remain clinically silent longer due to deeper positioning, which could delay the onset of visible signs like eyelid swelling or significant globe displacement. Therefore, this case emphasizes the importance of considering RMS in atypical orbital locations, especially in children presenting with rapidly progressive proptosis.

As with most orbital tumours, histopathological confirmation is essential for an accurate diagnosis. In our case, the initial FNA was inconclusive and only yielded adipose tissue. This is a known limitation of FNA in rhabdomyosarcoma, as the sample is often too small to evaluate the tumour's structure properly. An incisional biopsy performed three months later confirmed the diagnosis of spindle-cell rhabdomyosarcoma, a subtype generally associated with a more favourable prognosis.[5] The delay in getting the right diagnosis probably gave the tumour time to grow, which shows how important it is to get a proper tissue sample early, especially when the diagnosis is uncertain.

Standard treatment for orbital RMS includes multi-agent chemotherapy, radiotherapy, and, when necessary, surgical excision.[6] According to the Intergroup Rhabdomyosarcoma Study (IRSG) protocols, orbital RMS is typically classified as Group III (gross residual disease after biopsy only) and falls into an intermediate-risk category when not resected fully. For intermediate-risk patients, the standard chemotherapy regimen is VAC (vincristine, actinomycin D, cyclophosphamide).

The patient was initially treated with a combination of carboplatin, etoposide, daunorubicin, vincristine, actinomycin D, and cyclophosphamide. Although this regimen may appear more intensive than standard first line treatment, it can be justified by the advanced local disease, the initial diagnostic uncertainty, and the tumor's location encasing the optic nerve.

The tumour initially responded well, however, it recurred aggressively five months later. Given the rapid progression and vision loss, orbital exenteration was required. Exenteration is generally reserved for recurrent or refractory cases and is associated with increased morbidity, both physically and psychologically.[6] Radiotherapy is usually considered when surgery cannot completely remove the tumour or in recurrence cases.[7] However, the patient's parents declined this modality despite evidence of tumour recurrence in repeated MRI.

The International Classification of Rhabdomyosarcoma categorizes tumours into botryoid, embryonal, alveolar, and spindle/sclerosing subtypes. Spindle-cell RMS typically has a favourable prognosis, particularly in children, with reported overall survival as high as 87.5%.[8]

However, our patient experienced rapid progression and recurrence, suggesting a more aggressive clinical course despite the histologic subtype. Certain molecular variants particularly those involving TFCP2 gene fusions are now known to be highly aggressive, with poor response to standard chemotherapy and early metastasis.[10] Zhao et al. (2015) described a series of spindle-cell/sclerosing RMS cases that exhibited high rates of recurrence and poor outcomes.[10] Similarly, Kumar et al. (2014) observed a disease-free survival rate of just 62.5%, despite an overall survival rate of 87.5% in their paediatric cohort.[11]

According to the Intergroup Rhabdomyosarcoma Study (IRS-IV), patients who began treatment promptly had a 10-year overall survival rate of up to 87%, and event-free survival of 77%, particularly when chemotherapy was combined with timely local therapy such as radiotherapy.[7]

Our case reflects this trend. The patient initially responded well to treatment, however, she experienced early relapse and, unfortunately, passed away within three years of diagnosis. She was unable to complete second-line chemotherapy and did not receive radiotherapy, as it was declined by her parents. This highlights the variability in clinical behaviour of spindle-cell RMS and suggests that early molecular profiling may help identify high risk cases and guide more personalized treatment strategies

CONCLUSIONS

This case highlights the challenges in diagnosing and managing orbital rhabdomyosarcoma, especially when it presents in an unusual location and mimics other conditions like optic nerve glioma. Although spindle-cell

rhabdomyosarcoma usually has a good prognosis in children, our patient experienced rapid progression and poor outcome. This shows that even favourable subtypes can behave aggressively. It also highlights the importance of performing an early incisional biopsy to ensure accurate diagnosis through adequate tissue sampling. Prompt treatment and considering molecular testing early may help guide better, more personalised care in similar cases.

ACKNOWLEDGEMENT

The authors express their sincere gratitude to the multidisciplinary team involved in the management of this patient, including the Departments of Ophthalmology, Paediatric Oncologist, Radiologist, Pathologist and Oculoplastic Surgeon. We sincerely thank the patient's guardian for their invaluable cooperation and consent in sharing this case report. Additionally, we extend our appreciation to the reviewers for their valuable contributions to the publication of this case report.

DECLARATION

The authors declare no actual or potential conflict of interest in relation to this article.

REFERENCES

1. Jurdy L, Merks JH, Pieters BR, Mourits MP, Kloos RJ, Strackee SD, et al. Orbital rhabdomyosarcomas: a review. Saudi J Ophthalmol 2013; 27(3): 167-75.
2. Korkmaz I, Yaman B, Ceylan N, Kantar M, Kamer S, Palamar M. Orbital rhabdomyosarcoma. Eur Eye Res 2023; 3(1): 26-31.
3. Nithyanandam S, Bharadwaj V, Karat S, Janardhanan A, Punnoliparambil LA. Orbital rhabdomyosarcoma: an atypical presentation. Kerala J Ophthalmol 2021; 33(1): 71-4.
4. Piaser Guerrato G, Raimondo FM, Bianchi F, Frassanito P, Tamburrini G, Massimi L. Orbital embryonal rhabdomyosarcoma: a case based update. Childs Nerv Syst 2024; 40(12): 3907-14.
5. Chen J, Liu X, Lan J, Li T, She C, Zhang Q, et al. Rhabdomyosarcoma in adults: case series and literature review. Int J Womens Health 2022; 14: 405-14.
6. Bastola P, Bastola S, Khadka M, Koirala S. Orbital rhabdomyosarcoma in the pediatric population: a prospective, observational study from Mid-West Nepal. Acad J Health Sci 2022; 37(3): 108-12.
7. Raney RB, Maurer HM, Anderson JR, Andrassy RJ, Donaldson SS, Qualman SJ, et al. The Intergroup Rhabdomyosarcoma Study Group (IRSG): major lessons from the IRS-I through IRS-IV studies as background for the current IRS-V treatment protocols. Sarcoma 2001; 5(1): 9-15.
8. Whittle S, Venkatramani R, Schönstein A, Pack SD, Alaggio R, Vokuhl C, et al. Congenital spindle cell rhabdomyosarcoma: an international cooperative analysis. Eur J Cancer 2022; 168: 56-64.
9. Fang Z, Duan C, Wang S, Fu L, Yang P, Yu T, et al. Pediatric spindle cell/sclerosing rhabdomyosarcoma with FUS–TFCP2 fusion: a case report and literature review. Diagn Pathol 2024; 13(1): 178-91.
10. Zhao Z, Yin Y, Zhang J, Qi J, Zhang D, Ma Y, et al. Spindle cell/sclerosing rhabdomyosarcoma: case series from a single institution emphasizing morphology, immunohistochemistry and follow-up. Int J Clin Exp Pathol 2015; 8(11): 13814-20.
11. Kumar A, Singh M, Sharma MC, Bakshi S, Sharma BS. Pediatric sclerosing rhabdomyosarcomas: a review. ISRN Oncol 2014; 2014: 640195.