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Case Report

Pediatric Orbital Rhabdomyosarcoma: A Case Report

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Abstract

Rhabdomyosarcoma (RMS) stands as the predominant malignant mesenchymal tumor among children, constituting 5% of all pediatric malignancies. Its clinical presentation typically includes unilateral proptosis, ptosis, and eyelid swelling, often progressing rapidly. Imaging assumes a pivotal role in guiding diagnosis and ruling out alternative conditions. While MRI remains the cornerstone imaging modality, ultrasonography and CT complementarily contribute to the diagnostic process.

Differential diagnosis encompasses various etiologies of orbital swelling in pediatric patients, such as trauma, infection, and orbital masses. These masses are anatomically classified based on the involved compartment-Intraocular, intra-conal, extra-conal compartments, and the bony orbit. A compartmental approach aids in refining diagnostic orientation by limiting potential differentials.

Definitive diagnosis entails biopsy and histological examination. Staging, according to the Intergroup Rhabdomyosarcoma Study (IRMS) guidelines, entails a comprehensive review of imaging, clinical examination, and residual tumor assessment post-initial surgery, if applicable. Chemotherapy represents the cornerstone of treatment, with radiotherapy and/or surgical debulking serving as adjunct therapeutic options.

This article aims to elucidate the distinctive imaging features of orbital RMS, emphasizing differentiation from potential mimicking conditions. It delineates specific radiological criteria for each diagnosis, offering valuable insights for accurate clinical identification.

Keywords: *Rhabdomyosarcoma; Orbit; MRI; CT; Child*

Introduction

Rhabdomyosarcoma (RMS) stands as the most prevalent malignant mesenchymal tumor in children, constituting 5% of all pediatric malignant tumors [1]. Comprised of cells of striated muscle in various embryonic stages, RMS develops at the expense of supporting tissue [2]. This ubiquitous tumor can arise from any soft tissue in the body. Notably, orbital RMS accounts for 10 to 12% of all RMS cases [1,3]. Characterized by its extreme virulence, early diagnosis plays a pivotal role in significantly enhancing both survival rates and visual prognosis [4]. This article presents a case of left orbital rhabdomyosarcoma, manifested as an isolated left palpebral swelling in a 9-year-old child.

Case Report

We present a case of a 9-year-old child with no significant pathological history, who presented with a rapidly progressive diffuse swelling of the left palpebral area two months previously, evolving in a context of apyrexia and preservation of general condition. Upon clinical examination (Figure 1), the mass caused ptosis, without proptosis, local inflammatory signs or ophthalmologic abnormalities, the rest of the somatic examination was normal. The infectious work-up was negative. Given the unavailability of immediate MRI, an orbital ultrasound on B-mode and Doppler was performed (Figure 2), it revealed a tissue-like vascularised orbital mass extending deep into the orbit. CT brain (Figure 3) showed hyper enhancing heterogeneous mass in the left superior extraconal compartment. There was no mass effect on the adjacent structures, nor was there any invasion of the surrounding bone.

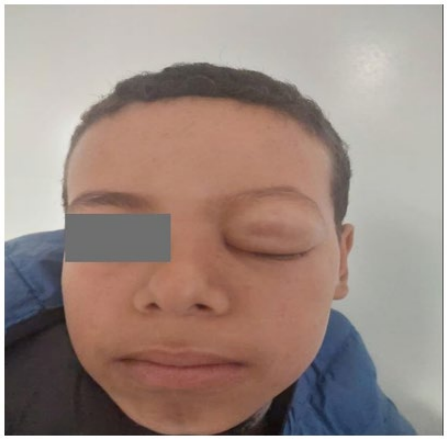

Figure 1: *Photograph of the patient displaying left palpebral swelling. The image illustrates the ptosis, with the absence of proptosis or local inflammatory signs.*

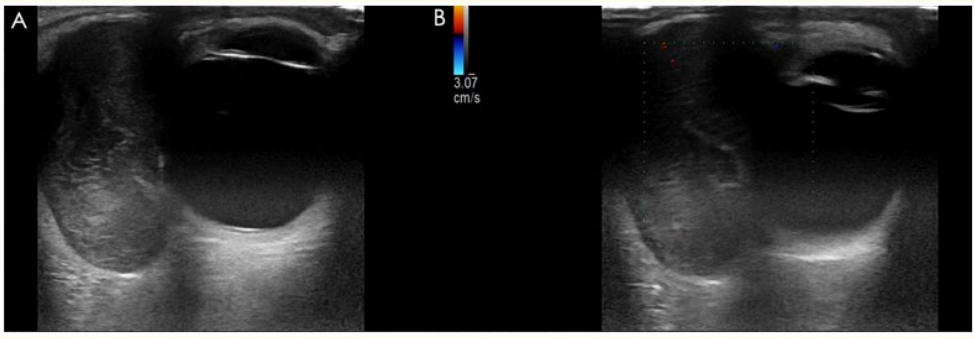

Figure 2: *B-mode and Doppler ultrasound scan of the left palpebral swelling, revealing a well-defined oval tissue-like mass extending deep into the orbit (A) Notably, the mass is vascularized, as demonstrated on color Doppler imaging (B).*

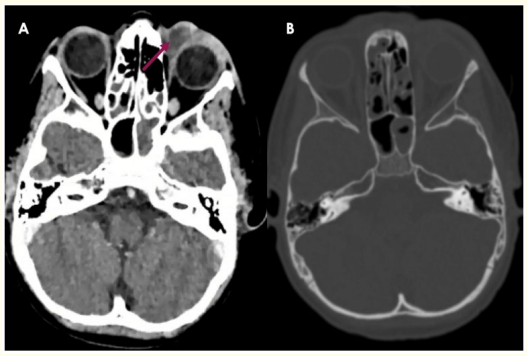

Figure 3: *Orbito-cerebral enhanced CT scan with axial sections on parenchymal (A) and bone (B) windows showing a hyper enhancing heterogeneous mass in the left extraconal compartment without mass effect on adjacent structures or invasion of the surrounding bony orbit.*

Brain MRI (Figure 4 and 5) showed left superior extraconal mass, originating from the superior rectus muscle. The mass exhibited a pronounced high T2-weighted signal, diffusion restriction, and a diminished apparent diffusion coefficient (ADC) value of 0.9×10^{-3} mm^2/sec. Additionally, heterogeneous enhancement was observed, and the mass demonstrated invasion into the superior oblique muscle, extraconal fat, and ipsilateral subcutaneous palpebral soft tissue. Importantly, there was no evidence of invasion or mass effect on the eyeball or the optic nerve, nor any indication of intracranial extension.

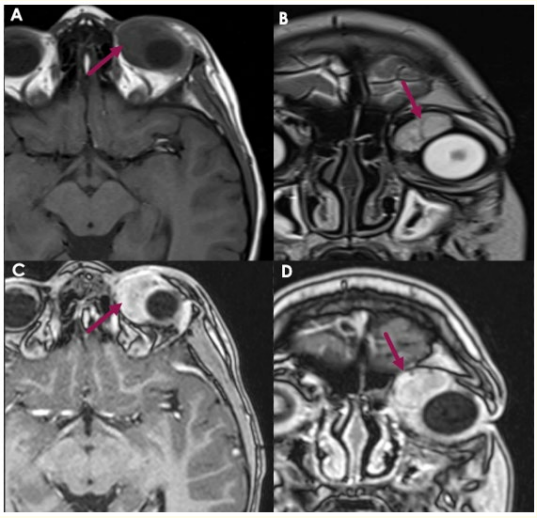

Figure 4: *Orbito-cerebral MRI comprising axial T1-weighted (A), coronal T2-weighted (B) images, axial (C) and coronal (D) images post-Gadolinium injection, reveals a left superior extraconal mass, originating from the superior rectus muscle. It appears isointense on T1-weighted images, exhibits a high T2-weighted signal, with heterogeneous Gadolinium enhancement. The invasion is notable into the superior oblique muscle, extraconal fat, and ipsilateral subcutaneous palpebral soft tissue. Note the absence of invasion or mass effect on the eyeball or the optic nerve, nor any indication of intracranial extension.*

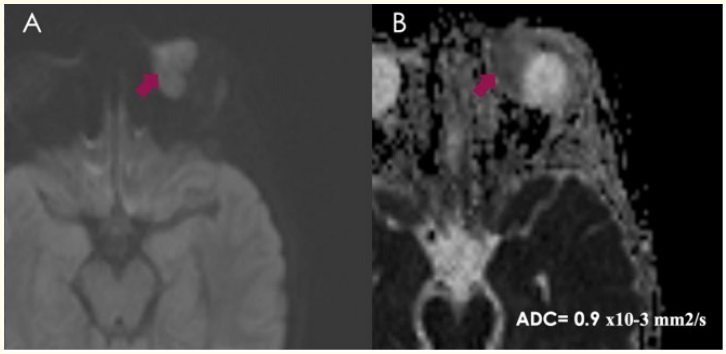

Figure 5: *Orbito-cerebral MRI on Diffusion sequence and ADC mapping reveals diffusion restriction, manifested by a diminished apparent diffusion coefficient (ADC) value of 0.9 × 10-3 mm2/sec, indicating malignancy.*

Patient underwent excisional biopsy. Histopathological examination (Figure 6) confirmed the diagnosis of embryonic rhabdomyosarcoma.

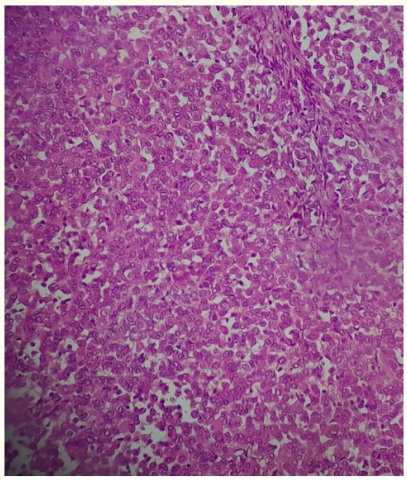

Figure 6: *Histological examination with Hematoxylin-Eosin staining HE x 20 showing Embryonal orbital RMS characterized by elongated to round spindle cells exhibiting features reminiscent of skeletal muscle in various stages of embryogenesis. These cells display a highly eosinophilic cytoplasm and hyperchromatic nuclei.*

Thoraco-abdomino-pelvic CT scan was performed for evaluation of extension, the patient was diagnosed of stage III orbital embryonal rhabdomyosarcoma without lymph node or distant metastases. He was treated with chemoradiotherapy according to standard protocol with orbital radiotherapy. The evolution was marked by complete remission on post-treatment evaluation (Figure 7).

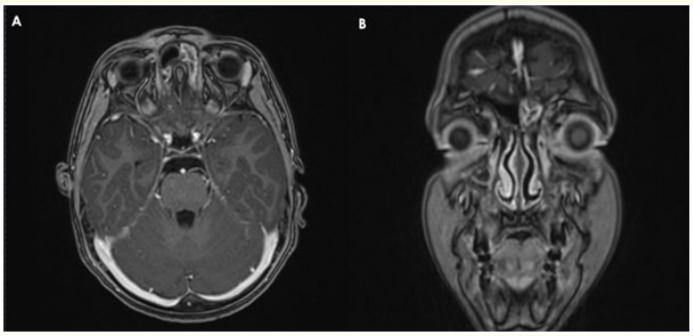

Figure 7: *Post-treatment MRI assessment reveals the absence of any persistent tumor lesions in the left orbit.*

Discussion

First described by Weber in 1854, RMS is a mesenchymal malignant tumor arising from striated muscle cells. It ranks as the third most common pediatric tumor following neuroblastoma and Wilms' tumor [5]. Orbital rhabdomyosarcomas can affect children of any age, with a peak frequency observed before the age of 10 and during adolescence [1]. There exists a slight male-to-female predilection, with a male-to-female ratio of 5:3 [6]. While most cases occur spontaneously, the disease has been associated with familial syndromes such as Neurofibromatosis and Li-Fraumeni syndrome, the p53 tumor suppressor gene, and congenital malformations such as Beckwith-Wiedemann syndrome. Instances of its occurrence as a secondary tumor alongside hereditary retinoblastoma have also been documented [7].

Rhabdomyosarcomas (RMS) predominantly occur in children, with the head and neck region being the primary site in 40 - 45% of cases [8]. Additionally, these tumors may manifest in the urogenital tract (23%), retroperitoneal region (17%), and extremities of the limbs [9]. Orbital RMS accounts for 10 - 12% of all RMS [6] and 25 - 35% of head and neck RMS cases [8]. RMS of the head and neck is typically classified as orbital, parameningeal (involving sites adjacent to meninges), or nonparameningeal and/or nonorbital [8]. Most ocular rhabdomyosarcomas arise in the soft tissues of the orbit, but they can rarely occur in other ocular adnexal structures and even within the eye [7]. These are usually categorized as extraconal lesions due to their tendency to arise from extraocular musculature or eyelid [8], although tumors may involve both intra- and extraconal compartments and invade surrounding orbital bones with intracranial extension [6].

If an orbital RMS invades the bony orbit or the optic nerve, it is classified as parameningeal [10]. Invasion of the conjunctiva and, rarely, the uveal tract can also occur [6]. In most cases, the disease develops exclusively in the orbit [3]. Additionally, RMS can access the orbit secondarily via direct extension from the paranasal sinuses or nasopharynx [7]. Very rarely, RMS can metastasize to the orbit from distant sites. Although the orbit contains few lymphatics, anterior tumors in the conjunctiva and eyelid can metastasize to regional lymph nodes [7] such as pretracheal or cervical lymph nodes [3].

Metastatic spread of orbital RMS is uncommon, occurring in less than 2% of cases. However, if left untreated, it has a propensity to metastasize to the lung, bone, and bone marrow, primarily through hematogenous spread. Orbital RMS typically presents in young patients with a rapid onset of unilateral proptosis, ptosis, and eyelid swelling [10,11]. Clinical symptoms include proptosis (80 - 100%), globe displacement (80%), blepharoptosis (30 - 50%), conjunctival and eyelid swelling (60%), palpable mass (25%), ptosis (25%), and pain (10%) [7].

Typically, clinical symptoms of orbital rhabdomyosarcomas exhibit a rapid onset. However, they may also present with a slower onset, with chronic eyelid and conjunctival edema preceding proptosis and globe displacement [7].

MRI serves as the primary imaging modality for evaluating orbital masses in children, while ultrasonography and CT play complementary roles [10]. MRI enables characterization of the lesion, determination of its topography, assessment of tumor volume, and accurate evaluation of locoregional extension [12,13]. Ultrasound confirms the tissue nature of the lesion, delineates its extension deep into the orbit, and specifies its vascularization using Doppler. CT scans are valuable for identifying bone invasion.

On MRI T1-weighted images, the tumor may exhibit hypointensity compared to orbital fat and isointensity with respect to extraocular muscles. Conversely, on T2-weighted images, the lesion typically appears hyperintense to orbital fat and extraocular muscles, although it may display variable T2 signal intensity [10]. Areas of chronic hemorrhage may present focal areas of increased signal on both T1- and T2-weighted images. Notably, they usually demonstrate moderate contrast enhancement with gadolinium injection, particularly with fat suppression [7]. RMS typically demonstrates restricted diffusivity, resulting in a decreased apparent diffusion coefficient (ADC) value [10]. An ADC value below 1.159 x 10^{-3} mm^2/sec is suggestive of malignancy. On ultrasound, the mass presents as an echogenic tissue mass, extending deeply into the orbit and showing vascularity on Doppler imaging. On CT scans, these tumors appear as homogenous, well-defined, round to ovoid masses, with density similar to muscle, primarily located within the orbital soft tissues. While earlier tumors do not invade bone, larger tumors may exhibit less defined margins, potentially eroding bone and extending into the nasopharynx or sinuses. Areas of focal hemorrhage or necrosis may appear heterogeneous on CT scans. Rhabdomyosarcomas typically demonstrate moderate to marked contrast enhancement.

The differential diagnosis encompasses causes of orbital swelling in childhood. As depicted in the decision tree (Figure 8), orbital swelling can stem from three main origins: trauma, infection, and orbital mass or mass like lesions [10]. Orbital masses and mass like lesions can be categorized based on the predominant compartment involved: intraocular, intra-conal, and extra-conal compartments, as well as the bony orbit [10].

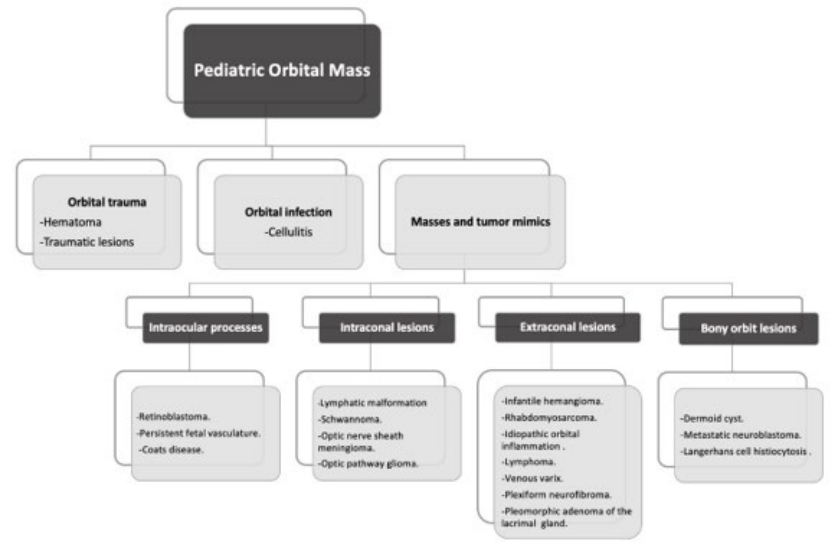

Figure 8: *Decision tree illustrating the three main origins of an orbital swelling.*

In our patient's case, the absence of a traumatic context and of clinical and biological signs of infection means that orbital cellulitis and traumatic lesions of the orbit can be ruled out. Ultrasound confirms the presence of a tissue-like orbital mass. Cross-sectional imaging, which delineates the extraconal muscular origin of the lesion and looks for any signs of malignancy (locoregional invasion, reduced ADC), aids in excluding the diagnosis of certain orbital masses, particularly benign masses and those that do not develop in the extraconal compartment. By applying a compartmental approach narrowing the range of differential diagnoses [7]. The main diagnoses that can simulate orbital RMS in our case are represented by: Infantile hemangioma, orbital lymphoma and idiopathic orbital inflammation. The table below highlights the distinguishing criteria between the different diagnoses of orbital rhabdomyosarcoma in the case of our patient (Table 1).

Discriminating Criteria	Rhabdomyosarcoma	Infantile hemangioma	Lymphoma	Idiopathic orbital inflammation
Age	9 years old (peak).	Weeks after the birth.	9 years old (peak).	11-12 years old.
Clinical symptoms	-Unilateral proptosis, ptosis, and eyelid swelling. +/-Local inflammatory aspect.	-Proptosis, ptosis, eyelid swelling. -Absence of inflammatory signs.	-Non-painful palpebral swelling Proptosis, ptosis. -Altered general condition.	-Periorbital oedema, palpable mass. -Limited ocular motility +/- Pain. -Autoimmune background.
Evolution	Rapidly progressive.	Three phases : Proliferation/Plateau/Regression	Insidious	Recurrences
MRI features	-Lobular orbital mass. -Isointense/ hyperintense on T1-weighted images. -Variable signal intensity on T2-weighted images. -Reduced diffusivity. -ADC value of <1.159 3 10−3 mm2/ sec. -Variable enhancement with Gadolinium. -Vascular RMS may have flow voids.	-Lobular orbital mass. -Proliferative phase: Heterogeneous T2 signal +/- signal voids (Rapid vascular flow). - High diffusivity. -ADC value of >1.159 3 10-3 mm2/ sec. -Early intense lobular enhancement in the arterial phase. -Regression phase: Decrease in enhancement.	-Well-defined infiltrative mass involving the preseptal space. -Mildly hyperintense on T1-weighted images. -Minimally hypointense on T2-weighted images. -Moderate to marked homogeneous enhancement. -Reduced diffusivity. -Decreased signal on ADC maps (<0.6 3 10−3 mm2/sec to <0.8 3 10−3 mm2/ sec) with increased perfusion.	-Ill-defined infiltrative masslike. - Hypointense on T1-weighted images -Variable signal onT2-weighted images. -Less reduced diffusivity. -Enhancement with Gadolinium. -Relatively hypoperfused.
Adjacent soft tissues	Can be invaded	Non invaded	Enhancing adjacent soft-tissue.	Enhancing adjacent soft-tissue.
Bony orbit	Possible bone invasion	No bone invasion	The mass molds the orbital contour without invading the bone.	The masslike molds the orbital contour without invading the bone.

Table 1: *Distinguishing criteria between the different diagnoses of orbital rhabdomyosarcoma.*

A positive diagnosis is confirmed histologically through direct excisional or incisional biopsy of the orbital mass [13]. Histopathological confirmation relies on the identification of rhabdomyoblasts using light microscopy, immunohistochemistry, and/or electron microscopy [7]. Rhabdomyosarcoma encompasses four major histopathologic subtypes: embryonal, alveolar, pleomorphic, and botryoid [7]. The embryonal subtype accounts for 80% of orbital rhabdomyosarcomas and primarily affects young children (mean age 7 - 8). It is characterized by spindle-shaped cells in various stages of differentiation with highly eosinophilic cytoplasm [7].

After the age of 10, the most common histological type shifts to the alveolar subtype, which typically carries a poorer prognosis. Immunohistochemistry plays a crucial role in identifying skeletal muscle proteins, such as alpha-actin, myosin, desmin, and myoglobin. Additionally, electron microscopy can support the diagnosis by revealing actin-myosin bundles or specific muscle proteins like A, I, or Z band proteins.

Upon confirmation of diagnosis, referral to pediatric oncologists is imperative for appropriate management, which often involves chemotherapy and possibly radiation [7].

The current staging system utilized by the Intergroup Rhabdomyosarcoma Study (IRMS) is outlined below (Table 2). Staging entails a comprehensive assessment involving imaging review, clinical examination, and evaluation of residual tumor post-initial surgery [7].

Staging of Rhabdomyosarcoma by the Intergroup Rhabdomyosarcoma Study	
Group	**Description**
I	Completely resected localized disease implying both gross impression resection and microscopic confirmation of complete resection and absence of regional lymph node involvement
Ia	Confirmed to muscle or organ of origin
Ib	Contiguous involvement outside the muscle or organ of origin
II	Residual disease and/or regional lymph node involvement
IIa	Grossly resected localized tumor with microscopic residual disease and no evidence of gross residual tumor or regional lymph node involvement
IIb	Completely resected regional disease with no microscopic residual tumor
IIc	Grossly resected regional disease with microscopic residual tumor
III	Incomplete resection with biopsy or gross residual disease
IV	Distant metastatic disease present at onset

Table 2: *Staging system of the Intergroup Rhabdomyosarcoma Study (IRMS) [7].*

Moreover, the patient should undergo a metastatic workup, which includes a chest X-ray, complete blood count, renal and liver function tests, bone marrow aspiration for cytology, and a bone scan. In cases where there is suspicion of meningeal spread, cerebrospinal fluid cytological examination should be performed. Metastases from orbital sites typically affect the lungs and bones, with lymphatic extension being exceptionally rare.

Treatment should be initiated promptly, as the prognosis is closely associated with the timing of diagnosis and treatment. It is imperative that the patient's treatment plan is overseen by a seasoned oncologist. Radiotherapy and/or surgical debulking continue to serve as complementary therapeutic options [1]. These updated therapeutic protocols provide enhanced management with a focus on conservative treatment for orbital RMS [14].

Patients with a completely resected localized tumor (group I) typically undergo chemotherapy alone. For patients in groups II, III, and IV, combination chemotherapy and radiation therapy are administered. The staging determines the duration and types of chemotherapeutic agents used in the treatment regimen. While vincristine and actinomycin are traditional agents associated with favorable outcomes, newer agents like ifosfamide and etoposide have also demonstrated efficacy. Some researchers have proposed reserving radiation therapy for patients who do not achieve a complete response to chemotherapy, considering the adverse side effects of radiation [7].

The frequency of metastases and/or recurrences necessitates prolonged clinical and radiological monitoring [15].

Follow-up after treatment of RMS typically involves regular clinical monitoring and systematic radiological examinations of the primary site [15,16]. The prognosis is generally excellent, with 5-year survival rates of approximately 95% [10], attributed to advances in chemotherapy. However, the prognosis of childhood RMS is influenced by factors such as clinical group, tumor stage, histology, and age [17,18]. Intracranial extension represents a significant negative prognostic factor [19].

In addition to close follow-up by the pediatric oncologist, the child should undergo a comprehensive ocular examination every 3 - 4 months initially after completion of treatment [7]. This assessment should include clinical and ophthalmological examination, supplemented by imaging such as orbital CT or MRI to evaluate for any residual or recurrent tumor [20].

Conclusion

Despite being the most prevalent malignant mesenchymal tumor in children, RMS remains a rare clinical entity that should not be underestimated in the presence of rapidly progressive unilateral palpebral swelling. Imaging plays a crucial role in guiding diagnosis and ruling out differential diagnoses. Early intervention and treatment utilizing modern chemotherapy protocols combined with radiotherapy have enhanced both the vital and functional prognosis. Prolonged clinical and radiological monitoring is essential for optimal management.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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