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Case Report

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Orbital Rhabdomyosarcoma; Case Report and Review of Literature

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Abstract

Background: The wide varieties of rare intraocular and orbital neoplasms differ in presentation in the pediatric population when compared to these same lesions in adults. While most pediatric ophthalmic tumors are benign, they may have a significant impact on vision and may result in significant morbidity and mortality.

Case description: 8-year-old girl presented with diffuse swelling of the right eye for one month followed by sudden dystopia, pain and proptosis in the same eye two days prior to ED visit. Examination revealed visual acuity severely impaired 20/100, IOP 25 with dystopic globe inferiorly and palpable mass, restricted supraduction, disc swelling in the right eye. CT brain showed Hyper-enhancing heterogeneous mass in the right superior extraconal compartment. MRI brain showed an extraconal mass with heterogeneous enhancement and faint diffusion restriction, invasive of right orbicularis oculi muscle and no intracranial extension. Patient underwent excisional biopsy through pterion-orbital craniotomy. The histopathology suggested Rhabdomyosarcoma, most probably alveolar type. The tumor cells were positive for desmin and myogenin immunostains. On the basis of the histopathological-confirmed diagnosis of RMO, the patient was assigned as stage I grade II rhabdomyosarcoma. Patient was started on chemotherapy protocol ARST0531 on week 1 and radiotherapy protocol ARST0531.

Conclusion: RMO is the most common pediatric orbital tumor. Treatment modalities includes: surgery, chemotherapy and radiation therapy. Radiation-related ophthalmic sequalae is devastating and it is important to have regular ophthalmic follow-up. With excellent survival in patients with RMO, the continued efforts are encouraged to reduce the post treatment morbidity by reducing the intensity of treatment or adopting newer treatment techniques.

Keywords: Orbital; ophthalmic; rhabdomyosarcoma; radiotherapy; North American Intergroup Rhabdomyosarcoma Study Group (IRSG).

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Introduction

Most pediatric ophthalmic tumors are benign. However, they may have a significant impact on vision and may result in significant morbidity and mortality [1,2]. The wide varieties of rare intraocular and orbital neoplasms differ in presentation in the pediatric population in comparison to same entities in adults [1,2].

Rhabdomyosarcoma is a rare childhood cancer but the most common primary orbital malignancy occurring in this age group with estimated incidence of 4.5 cases per million with 50% occurring in the first decade of life [1-3]. Generally, rhabdomyosarcoma is classified into four major subtypes; including embryonal, alveolar, botryoid and pleomorphic (57%, 19%, 6% and 1% respectively) [2]. The most common presenting clinical features were unilateral proptosis (30%), eyelid edema (21%), and blepharoptosis [2,3]. Other manifestations are Nasal congestion and epistaxis [2]. Orbital apex syndrome, manifested by complete ophthalmoplegia, ptosis, decreased corneal sensation, and vision loss, was reported by Machleder et al. as a result of RMO [4,5].

Rhabdomyosarcoma of the orbit (RMO) is managed through a multidisciplinary approach including surgery, chemotherapy and irradiation [6]. Little evidence is available regarding details of the management and the choice of intervention in RMO [7]. Current treatment guidelines use a staging system by the Intergroup Rhabdomyosarcoma Study Group dividing the patients into four stages and four groups to allocate each to a certain combination of treatment modalities [7].

Stages are categorized based on universal TNM staging [8]. In short, Groups are divided into: localized disease and completely resected is considered group I, microscopic remnants after biopsy as group II, gross residual disease detected after biopsy as group III while presence of distant metastasis onset as group IV [7].

In Saudi Arabia, only one large scale study was conducted targeting pediatric patient regarding orbital lesions [9]. Alkatan et al reported only 11 cases of RMO in the largest specialized tertiary ophthalmology center in Saudi Arabia over a period extending from 2000 to 2013 [9]. Here, we report a case of RMO, outlining the clinical presentation, histopathological features and treatment outcomes.

Case report

Clinical presentation: 8-year-old girl who is medically free, presented with diffuse swelling of the right eye for one month followed by sudden dystopia, pain and proptosis in the same eye two days prior to emergency department visit. There was no history of trauma and significant family history of similar condition. Upon initial assessment of the right eye, visual acuity was severely impaired 20/100, Intraocular pressure was 25 mmhg with dystopic globe inferiorly and palpable mass, restricted supraduction. Disc swelling was also noted. The left eye was normal on examination (Figure 1).

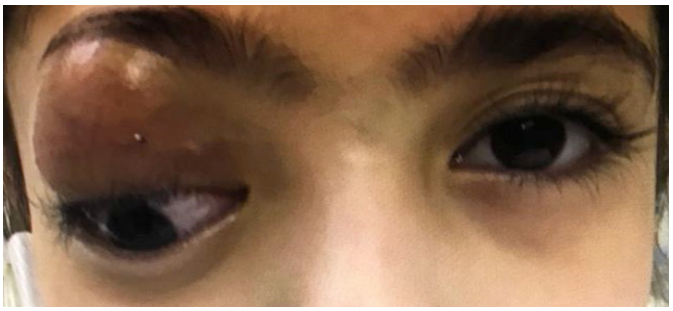

Figure 1: Eight-year-old girl with diffuse swelling of the right eye, dystopia, restricted supraduction, pain and proptosis. Visual acuity was 20/100 in the right eye, intraocular pressure was 25mmhg. Disc swelling was also noted. The left eye was normal on examination.

***Radiological imaging*:** Computed Tomography (CT) brain showed Hyper-enhancing heterogeneous mass in the right superior extraconal compartment, loss of interface with superior rectus and a small superior orbital wall erosion. Contrasted Magnetic resonance Image (MRI) brain showed an extraconal mass with heterogeneous enhancement and faint diffusion restriction, invasive of right orbicularis oculi muscle and no intracranial extension (Figure 2A-C).

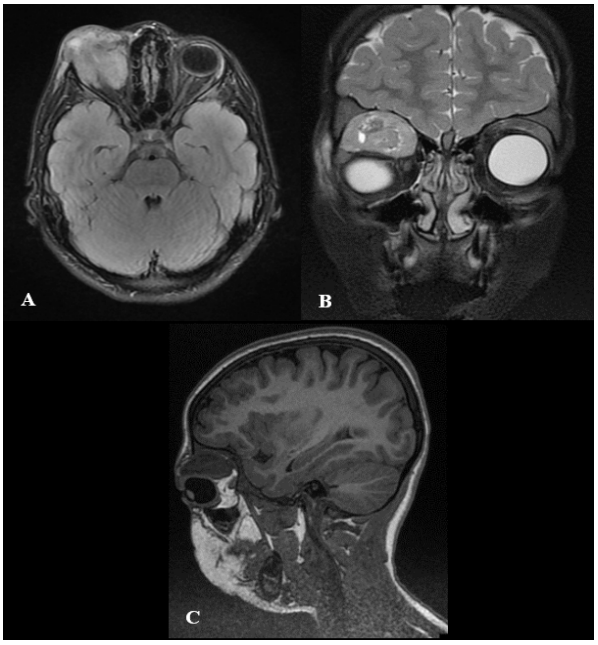

Figure 2: (A,B) Axial and coronal T2-weighted brain MRI with Gadolinium administration. **(C)** sagittal T1-weighted brain MRI. **(A-C)** The images demonstrate an enhancing lesion, invasive of right orbicularis oculi muscle abutting and adherent to right superior rectus and superior oblique muscles and there is rarefaction of anterior frontal bone with no intracranial extension . There is sever orbital proptosis.

Surgical intervention: The patient was planned for gross total resection but due to the high vascularity and loss of clear surgical plan, small biopsy was obtained and sent to histopathology. Unfortunately, pathology came inconclusive. The patient was planned for excisional biopsy through pterion-orbital craniotomy in which tumor was resected as one piece successfully (Figure 3).

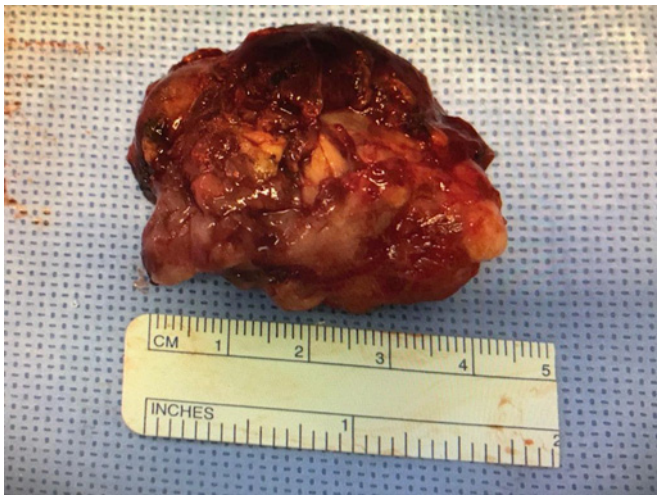

Figure 3: Gross appearance of the excisional biopsy through pterion-orbital craniotomy in which the tumor was resected as one piece successfully.

Histopathological features: The excisional biopsy suggested Rhabdomyosarcoma, most probably alveolar type (Figure 4A,B). The tumor cells were positive for desmin and myogenin immunostains (Figure 4C). The Myo-D1 stain is non-contributory. CD99, SMA, Chromogranin and Cytokeratin cocktail staining are negative.

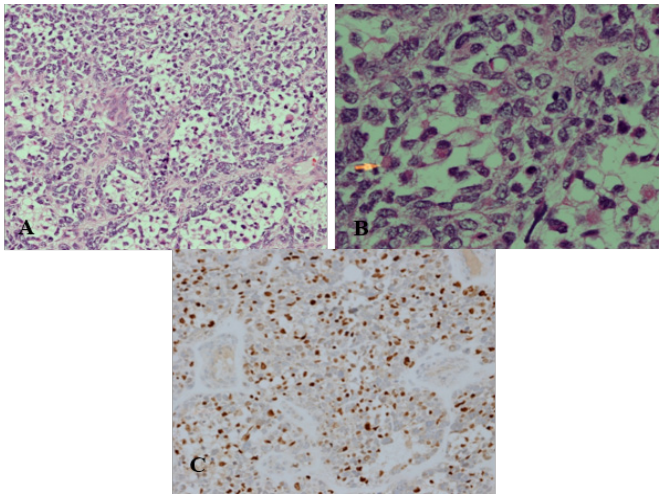

Figure 4: (A) Low power microscopic view of the right orbital tumor. Note the presence of distinctive alveolar pattern of the malignant cells in this alveolar rhabdomyosarcoma H/E stain X200. **(B)** High power microscopic view of the alveolar rhabdomyosarcoma of the right orbit. Note the presence of malignant pleomorphic cells showing evidence of eosinophilic rhabdomyoblastic differentiation H/E stain X600. **(C)** Microscopic view showing the strong positive immunohistochemical stain for myogenin. This finding, in addition to the alveolar morphologic pattern are confirmatory of alveolar rhabdomyosarcoma. IHC stain for myogeninX200.

Outcome and follow-up: contrasted CT brain post-operatively showed no enhancing tissue to suggest residual tumor (Figure 5A-C). On the basis of the histopathological-confirmed diagnosis of RMO, a complete workup was done by oncology team which all came negative. The patient was assigned as stage I grade II rhabdomyosarcoma. Patient was started on chemotherapy protocol ARST0531 on week 1 and radiotherapy protocol ARST0531 on week 4. During the 8th week of chemotherapy, ophthalmology examination showed: right eye eyelid ptosis, redness, tenderness, blepharitis, eyelid skin abrasion in the medial and lateral canthus, conjunctiva showed mild follicular reaction and the lens showed early post subcapsular cataract. The rest of the examination was normal. Initial management included antibiotics, antiviral and heavy lubrication. Later-on, patient developed more radiotherapy-related ophthalmic complications like blepharoconjunctivitis, pre-septal cellulitis, cataract and exposure keratopathy and had multiple ophthalmology surgeries and progressive rapid visual acuity deterioration over the course of five years. Four years post-surgery follow up brain MRI showed stable postsurgical changes in the right orbit with no signs of tumor recurrence (Figure 6A-C). In the last follow up, five years after the surgery, she was only able to count fingers 4ft in the right eye.

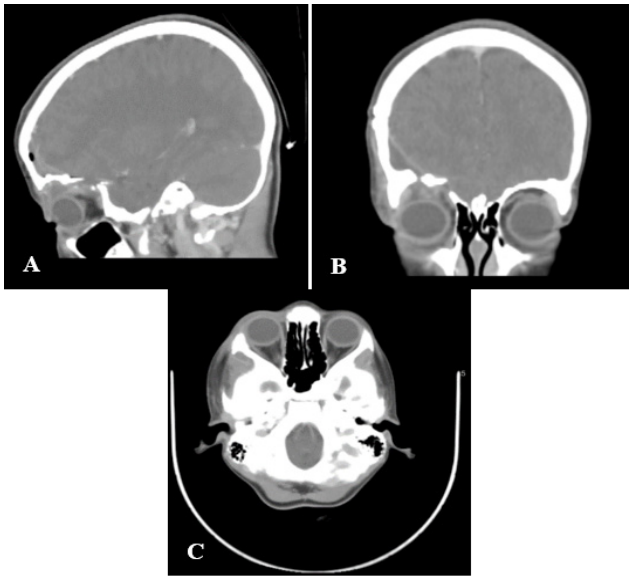

Figure 5: post operatively, **(A-C)** sagittal, coronal and axial enhanced CT scan of the brain. **(A-C)** The images demonstrate Postsurgical changes with complete excision of the right orbital mass. No residual enhancing soft tissue is seen. Small epidural fluid collection is noted along supraorbital aspect of the right anterior cranial fossa measuring about 7 mm in maximum thickness. Mild edematous swelling of superior oblique and superior rectus muscles is related to recent surgery.

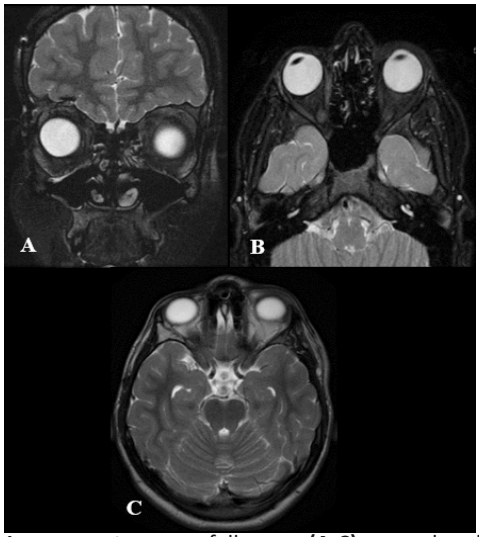

Figure 6: 4 years post-surgery follow up **(A-C)** coronal and axial T2-weighted brain MRI. **(A-C)** The images demonstrate stable postsurgical changes in the right orbit with no signs of tumor recurrence.

Table 1: Summary of the reported cases of orbital rhabdomyosarcoma in the literature.

Author	Study type	Year	Age	Gender	presentation	Histology	Grade	Intervention	Outcome
Machleder et al [4]	Case report	2004	12y	female	progressive visual loss + difficulty in eye movements + mild headache	alveolar	IV	radiation therapy + systemic chemotherapy	complete return of extraocular movement, visual acuity remained impaired with persistence of a left afferent defect.
Yazici et al [15]	Case report	2014	15y	Male	progressive painful proptosis+ loss of vision	embryonal	NA	radiotherapy + chemotherapy	orbital symptoms were improved and visual acuity increased to 20/20
Elomrani et al [16]	Case report	2014	20y	Male	NA	embryonal	NA	chemotherapy	local recurrence and cutaneous Metastasis
Sarkar et al [17]	Case report	2012	18y	male	pain in the right hip + inability to fully extend the joint, followed by proptosis of the right eye + blurred vision + photophobia	alveolar	IV	chemotherapy + radiation therapy	patient died 3 weeks after initiation of treatment
Amato et al [18]	Case report	2002	29y	Male	nasal obstruction + epistaxis + headache + subacute visual loss in the left eye	Inconclusive biopsy	NA	Chemotherapy + radiation therapy	The patient died 2 years after the initial diagnosis of disseminated disease.
Kaliaperumal et al [19]	Case series	2007	10y	Female	proptosis	embryonal	NA	Chemotherapy + radiotherapy	No recurrence in 3 years
Kaliaperumal et al [19]	Case series	2007	4y	Male	Proptosis	embryonal	NA	Chemotherapy + radiotherapy + surgery	No recurrence in 2 yeas
Kaliaperumal et al [19]	Case series	2007	29y	Female	proptosis	embryonal	NA	Chemotherapy + radiotherapy + surgery	Loss of follow up
Kaliaperumal et al [19]	Case series	2007	10y	female	proptosis	embryonal	NA	Chemotherapy	No recurrence in 1 year
Kaliaperumal et al [19]	Case series	2007	9y	Female	proptosis	alveolar	NA	Chemotherapy + radiotherapy + surgery	No recurrence in 2 years
Kaliaperumal et al [19]	Case series	2007	7y	Male	proptosis	embryonal	NA	Chemotherapy + radiotherapy	No recurrence in years
Wang et al [20]	Case report	2019	6 m	Female	congenital skin lesion involving the left glabella and orbit	embryonal	NA	proton therapy + chemotherapy	No recurrence in 1 year
Dziedzic et al [21]	Case report	2015	4y	Female	swelling + proptosis	embryonal	NA	Chemotherapy + radiotherapy + surgery after recurrence	local recurrence treated by Endonasal endoscopic surgery with gross-total resection
Rustemeyer et al [22]	Case report	2011	7y	Male	proptosis	embryonal	NA	Chemotherapy + radiotherapy + surgery after recurrence	local recurrence 3 times after the third time no recurrence
Li et al [23]	Case report	2018	6y	Female	proptosis	embryonal	III	Chemotherapy + radiotherapy + excisional biopsy	regression of the residual orbital mass
Kim et al [24]	Case report	2019	6y	Female	Mild injection + eyelid swelling	NA	NA	Chemotherapy + radiotherapy	NA
Chitsike et al [25]	Case report	2012	4m	Female	Swelling + proptosis	embryonal	NA	Chemotherapy	Didn't respond to chemotherapy and offered palliative care
Othmane et al [26]	Case report	1999	34y	Male	Painless mass of the eyelid	embryonal	NA	Chemotherapy + radiotherapy + excisional biopsy	No recurrence
Van den bogaert et al [27]	Case report	1992	6y	Male	Mass	embryonal	NA	Chemotherapy + radiotherapy	Multiple local recurrence then intracranial extension

Maurya et al [28]	Case report	1990	4y	Male	Painless proptosis	embryonal	NA	Surgery + radio-therapy	NA
Sanz-marco et al [29]	Case report	2014	25y	Female	headache and discom-fort in the right eye	alveolar	III	Chemotherapy + radiotherapy	remission and resolution of the proptosis and ophthal-moplegia

NA: Not Available. Chemotherapy: deferent regimens used. Radiotherapy: deferent regimens used. Y: years. M: months.

Discussion

Radiologically, rhabdomyosarcoma could show different features based on the type and location [10]. On CT, these lesions tend to show moderate to highly enhanced homogenously well circumscribed masses [11]. Calcification could be also seen in case of bony destruction which is another common feature of these lesions [11]. In the present case, CT showed hyper-enhancing heterogeneous mass in the right superior extraconal compartment having loss of interface with superior rectus and a small superior orbital wall erosion. Such lesions appear isointense to muscles on T1 and hyperintense to muscles on T2 on Magnetic Resonance Images (MRI) [11]. Post-contrast, these lesions usually exhibit moderate to substantial enhancement [11]. MRI findings in the present case were similar to the previous description.

Histopathological-confirmation of the diagnosis and staging of orbital RMS, which was done by evaluating imaging (MRI of primary tumor, chest-CT and bone scan), and subsequent workup for metastases, are used to make therapy decisions [6,7,12].

Management strategies include surgery, radiotherapy and chemotherapy [6,7,12]. Patients allocated to stage 1 group II, like in the presented case, can receive different choices of treatment based on which protocol is being followed [12]. North American Intergroup Rhabdomyosarcoma Study Group (IRSG) suggest treatment with a combination of chemotherapy (vincristine and actinomycin and cyclophosphamide; VAC) and radiotherapy (36 Gy) for group II patients [12]. The European pediatric Soft tissue sarcoma Study Group (EpSSG) protocol (EpSSG-RMS-2005) propose chemotherapy VA and in the first four courses Ifosfamide is added; if complete remission is achieved after three chemotherapy courses radiotherapy (36 Gy) is added which can be replaced with addition of more ifosfamide [12] if remission is not achieved following chemotherapy radiotherapy (45 Gy) is added without further ifosfamide [12].

Long term ophthalmic sequalae after chemotherapy and radiotherapy could be devastating [1,13]. The most common complication is cataract [1,13]. Other complications including keratopathy, ptosis, lacrimal duct stenosis, keratoconjunctivitis and retinopathy could also be seen [1,13]. In the present case, patient developed multiple complication secondary to radiotherapy including: blepharoconjunctivitis, conjunctival abrasion, cataract, severe dryness, inflammation, and decrease in the visual acuity.

In this type of lesions, the long-term visual acuity outcome is a crucial aspect to consider [1]. Eade et al, reported in their study which included 18 cases that 29% of the patients attained vison better than 6/12 and 43% had vision worse than 6/60 [1]. In the present case, the visual acuity declined over the course of four years as result of multiple complications after the radiotherapy until she is only able to count fingers 4ft. Patient survival is related to a number of factors but the most important of which is whether the main tumor is T3 or above according to the AJCC TNM staging system for Orbital Sarcoma [14].

Conclusion

RMO is the most common pediatric orbital tumor. Treatment modalities includes: surgery, chemotherapy and radiation therapy. Radiation-related ophthalmic sequalae is devastating and it is important to have regular ophthalmic follow-up. With excellent survival in patients with RMO, the continued efforts are encouraged to reduce the post treatment morbidity by reducing the intensity of treatment or adopting newer treatment techniques.

Declarations

Conflict of interest: The authors declare that the article content was composed in the absence of any commercial or financial relationship that could be constructed as a potential conflict of interest.

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