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 extracranal 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 sequelae 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).
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).

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).

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).
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.

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

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


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