Orbital Alveolar Rhabdomyosarcoma –Unusual Presentation and Dreadful Experience

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Abstract

Introduction: Orbital Rhabdomyosarcoma (RMS) is one of the few life-threatening diseases seen by ophthalmologists and prompt diagnosis and treatment can save the life of the affected patient. Survival after treatment of RMS has improved from 25% in 1970 to 70% in 1991.

Case Report: A 15 year girl presented with 5.5cmx5cmx4.8cm multi-lobulated mass lesion with necrosis in right medial orbital fossa and pre-auricular and submandibular lymphadenopathy. MRI suggested possibility of malignant soft tissue tumor with extensive spread into sinuses and necessitated tissue diagnosis. Incisional biopsy revealed alveolar rhabdmyosarcoma. Due to extensive involvement of sinuses patient was advised primary chemoradiation therapy. Despite full regimen of primary chemo-radiation, within 4 months it spread to involve whole of the face and other eye pursuing a devastating course.

Conclusion: This is a rare case of orbital alveolar Rhabdomyosarcoma in a 15 year female with poor response to chemo-radiation.

Keywords: Chemo-radiation, Orbital alveolar Rhabdomyosarcoma (RMS), lymphadenopathy

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Introduction

Rhabdomyosarcoma (RMS), malignant neoplasm composed of cells with histopathologic features of striated muscle in various stages of embryogenesis, account for approximately 5% of all childhood cancers and for about 20% of all malignant soft tissue tumors .The primary sites of Rhabdomyosarcoma include head and neck area (45%), trunk (40%), and extremities (15%) and about 25%–35% of head and neck Rhabdomyosarcomas arise in the orbit .[1,2,18,19] Mean age at diagnosis is 8 years .[20] There is a slight predilection for males, with roughly 5:3 male to female ratio .[21] There appears to be no racial predisposition. The

tumor is invariably unilateral .Orbital RMS is one of the few life-threatening diseases seen by ophthalmologists and prompt diagnosis and treatment can save the life of the affected patient. The Intergroup Rhabdomyosarcoma Study Committee (formed in 1972) has organized large collaborative randomized trials (I,II,III,IV) for treatment of Rhabdomyosarcoma.[3,4,5,6,7,8,9,10,11,12,13,14,15,16]

As a result of these trials, survival after treatment of Rhabdomyosarcoma at all sites has improved from 25% in 1970 to 70% in 1991.[17]

Case Report

A 15 year girl presented with progressively increasing swelling over right upper eyelid and sac area with bleeding and decreased appetite since 1 month. On examination, mass was multi-lobulated (5.5cmx5cmx4.8cm) firm, warm, tender with bleeding and necrosis in right upper lid extending to sac area (Figure-1a, 1b). Examination of the affected eye revealed Best Corrected Visual Acuity (BCVA) 6/6, eyeball deviated down and out, lid swollen, and conjunctiva congested with decreased palpebral fissure width whereas posterior segment was normal. Examination of other eye was within normal limits. The pre-auricular and submandibular lymph nodes were palpable and had hard consistency. Complete Blood Count with Peripheral Smear (to rule out abnormal and immature cells) was normal.USG abdomen, X-RAY chest, Renal Function Tests and Liver Function Test came out to be normal.

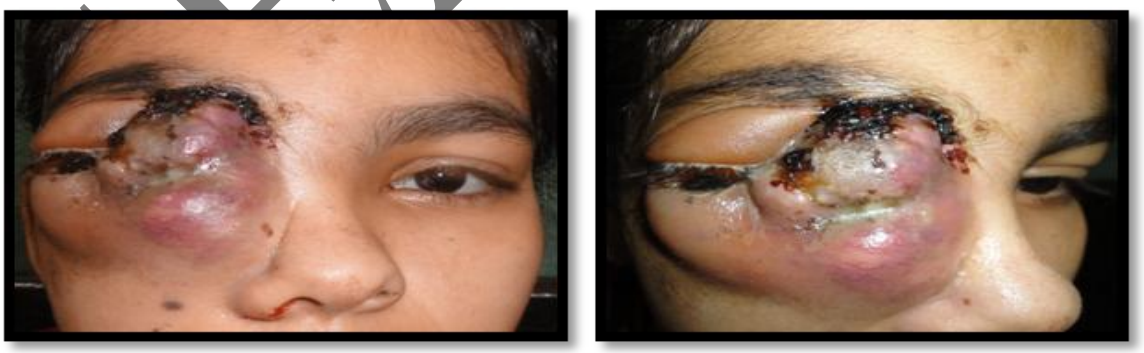


Figure 1a, 1b: Firm, multi-lobulated mass in medial orbit with areas of necrosis

MRI of orbit and brain (Figure 2a,2b,2c) revealed 5.5cmx5cmx4.8cm multilobulated extraconal mass lesion in right medial orbital fossa extending into right half of ethmoid sinus, nasal cavity, right maxillary sinus , right frontal recess, right pre-maxillary subcutaneous soft tissue with minimal involvement of sphenoid and right posterior ethmoid sinus with normal optic nerve.

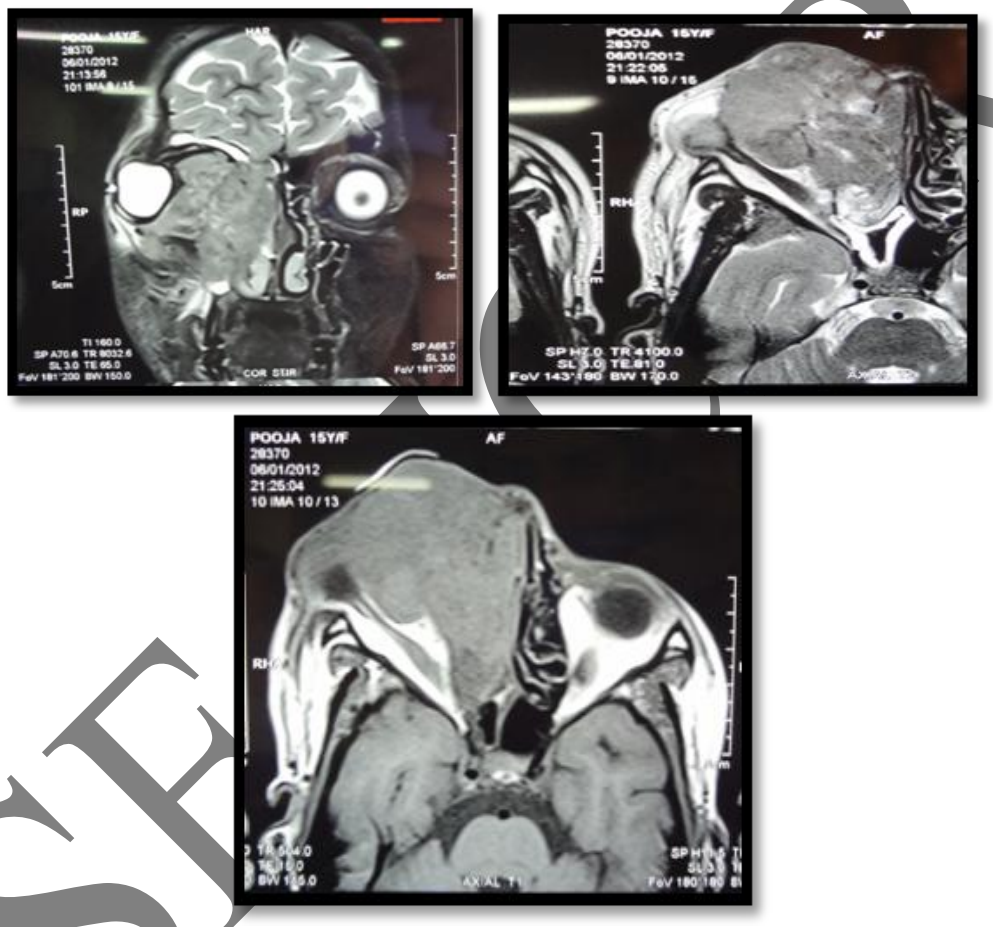


Figure 2 a) Coronal STIR b) Axial T2, c) Axial T1

Histopathology of tissue sample revealed small round to oval cells with minimal pleomorphism having scanty cytoplasm and hyper chromatic nuclei with inconspicuous nucleoli arranged in alveolar pattern, lobules & solid nests having central fibrovascular

core suggestive of suggestive of alveolar Rhabdmyosarcoma. (Figure 3)

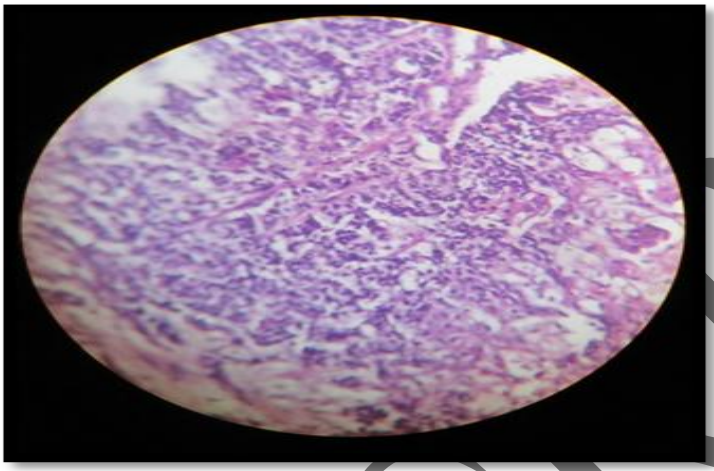
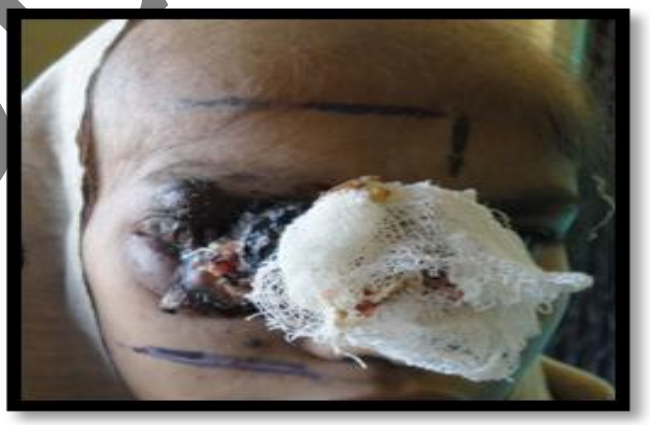


Figure 3: Histopathological appearance of tissue

Due to extensive involvement of sinuses , patient was advised primary chemo radiation with 4 courses of VAC-Adr (Vincristine 2mg, Actinomycin-D 0.5 mg, Cyclophosphamide 600mg, Adriamycin 50mg) and 5 cycles of radiation therapy (610 cGy). Despite full regimen within 4 months, it spread to involve whole of the face and other eye pursuing a devastating course. (Figure 4, 5). She was on morphine for pain till the end of her life .From time of presentation she survived only for 6 months.



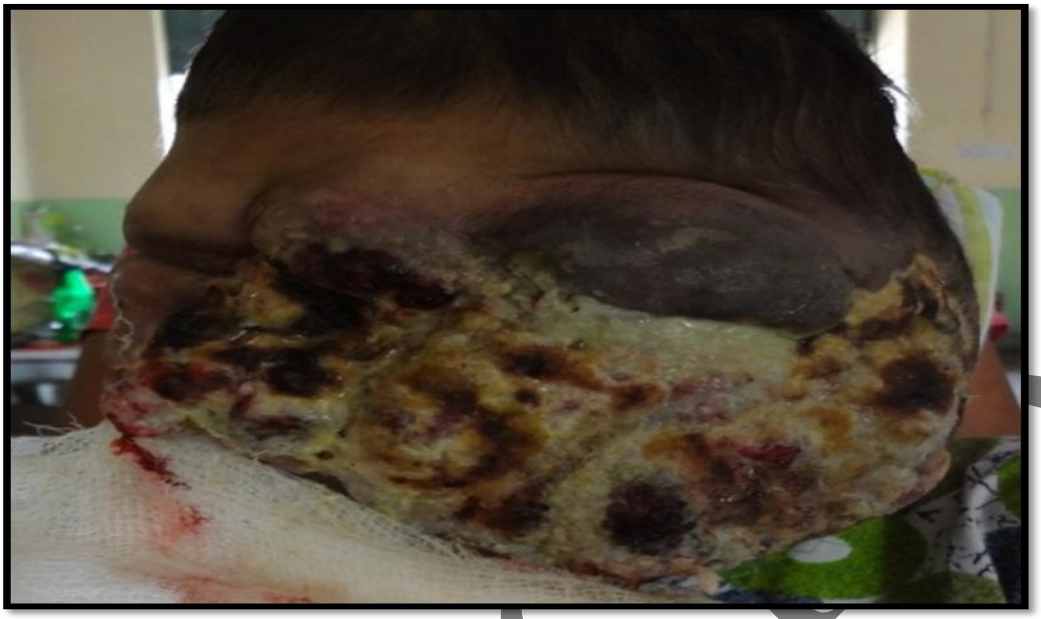


Figure 4, 5: Course of disease

Discussion: Weber is generally credited with providing the first acceptable description of RMS, which occurred in tongue of a 21-year-old man.[22] The report of Bayer, in 1882, is probably the first published description of an orbital RMS.[22,23] The first comprehensive histopathologic study of RMS was published in 1946.[24] Subsequently, several authors expanded on the clinical and histopathologic features of orbital RMS. In recent years, the clinical diagnosis of RMS has been facilitated by imaging studies like computed tomography (CT) and magnetic resonance imaging (MRI). More recently, emphasis has been placed on improved methods of management, particularly adjunctive chemotherapy and irradiation.

Orbital RMS is primarily a disease of young children with a mean age at diagnosis of 8 years[20]. There is a slight predilection for males, with roughly 5:3 male to female ratio .[21] our patient was 15 year old female. Orbital RMS generally presents with proptosis (80–100%), globe displacement (80%), blepharoptosis (30–50%), conjunctival and eyelid swelling (60%), palpable mass (25%), and pain (10%).[25, 26]

Visual impairment in usually minimal until the tumor becomes advanced. The blepharoptosis is often the first sign in patients with a superior orbital tumor. Slightly more advanced cases show downward and lateral displacement of the globe due to the usual superior or superonasal location of the mass in 70%.Our patient presented with globe displacement, conjunctival and lid swelling, pain, palpable mass and normal visual acuity.

As orbital RMS progresses, it can invade orbital bone and even extend into the cranial cavity. Metastatic disease from orbital RMS has become relatively uncommon in recent years. When it does occur, it has a tendency to metastasize most often to lung and bone[27]. Metastasis generally occurs via hematogenous dissemination. Regional lymph node metastasis from orbital Rhabdomyosarcoma is rare, perhaps because the orbit is largely void of lymphatics.[28] However, tumors that extend from the orbit anteriorly into the conjunctiva or eyelid can gain access to lymphatic channels and can metastasize to regional lymph nodes. Distant metastasis from RMS is usually fatal; in spite of intensive chemotherapy and symptomatic treatment[29]. Our patient had submandibular and preauricular lymphadenpathy with extensive involvement of sinuses. There was no distant metastasis.

Grossly, orbital Rhabdomyosarcoma is a well circumscribed tumor in the early stages. Larger, more aggressive tumors have an irregular border as a result of tumor invasion though the pseudocapsule. In fresh sections, the tumor has a light gray to pink color and may show areas of hemorrhage and cyst formation. Histopathologically , there are four types of RMS pleomorphic, embryonal, alveolar, and botryoid.[18] There may be overlap of these types and pure classification can occasionally be difficult. Embryonal Rhabdomyosarcoma is by far the most common variant found in the head and neck region, including the orbit. The alveolar and botryoid types are less common, and the pleomorphic type is extremely rare in the orbit. Embryonal Rhabdomyosarcoma is characterized histopathologically by spindle to round cells that show features characteristic of skeletal muscle in various stages of embryogenesis. The predominant cell is an elongated spindle

cell that can assume a variety of arrangements and degrees of differentiation of cytoplasm is generally highly eosinophilic and cross striations can sometimes be identified on routine histopathologic sections. The alveolar type appears as loosely arranged, malignant cells with septae that are reminiscent of the alveoli of the lung .The botryoid type may be a variant of the embryonal type that assumes a papillary configuration. On histopathology our patient had alveolar type of RMS.

Until the late 1960s, orbital exenteration was generally considered to be the treatment of choice for orbital Rhabdomyosarcoma.[25] It was believed by most authorities that complete surgical removal of the tumor would offer the patient the best chance of survival. However, the mortality rate for patients with orbital Rhabdomyosarcoma continued to be greater than 70% in the early 1970s.[22] It was gradually recognized that orbital exenteration did not provide affected patients with a better prognosis and there was a gradual trend toward treatment with limited biopsy, followed by various regimens of irradiation and chemotherapy. Hence, orbital exenteration is rarely performed as a primary treatment today; It may be justified for extremely advanced disease that has destroyed the eye, as frequently seen in third-world countries. In medically advanced countries, it is still employed for some aggressive tumors that have been resistant to irradiation and chemotherapy.

In 1972, the Intergroup Rhabdomyosarcoma Study (now called IRSG) was established to increase knowledge and to improve therapeutic results for Rhabdomyosarcoma from all locations. Four consecutive clinical trials have been conducted since then. A staging classification of Rhabdomyosarcoma, employed by the IRSG, is summarized in Table 1,2 . In brief, group I is defined as localized disease, completely resected. Group II is microscopic disease remaining after biopsy. Group III is gross residual disease remaining after biopsy. Group IV is distant metastasis present at onset. This classification can assist in selecting treatment and in predicting prognosis.

Table 1 Staging of Rhabdomyosarcoma by the Intergroup Rhabdomyosarcoma Study Group Staging Classification

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[a]
IIc	Grossly resected regional disease with microscopic residual tumor[a]
III	Incomplete resection with biopsy or gross residual disease
IV	Distant metastatic disease present at onset
[a] - *Regional disease implies involvement of the regional lymph nodes.*	

Table 2: Primary Orbital Rhabdomyosarcoma in 30 Consecutive Patients: Staging by the Intergroup Rhabdomyosarcoma Study Classification

Group	Description	Number (%)
I	Completely resected	2 (7)
II	Residual microscopic disease	11 (37)
III	Residual gross disease	16 (53)
IV	Distant metastasis present at onset	1 (3)
Modified from Shields et al.[30]		

The management of orbital Rhabdomyosarcoma should include any combination of surgery, irradiation, and chemotherapy Table 3, 4.

Table 3: Intergroup Rhabdomyosarcoma Study Group IV: Current Recommendations for Treatment of Orbital Rhabdomyosarcoma (Groups I, II, and III)

Group	Radiation Therapy[a]	Chemotherapy
I	None	VA × 32 weeks (regimen 44, VA)
II	4,140 cGy CFI	VA
III	5,040 cGy CFI or 5,940 cGy HFI	VA + C × 52 weeks (regimen 41, VAC) or VA + I × 52 weeks (regimen 42, VAI) or VI + E × 52 weeks (regimen 43, VIE)

Radiotherapy should begin at week 9.

CFI = conventional fractionated irradiation; HFI = hyperfractionated irradiation; V = Vincristine; A = Actinomycin D; C = Cyclophosphamide; I = Ifosfamide; E = Etoposide.

From Wexler and Helman[31] and Lanzkowsky.[32]

There was local tumor recurrence in 6 patients (20%), and orbital exenteration was necessary in 2 patients (6%). Regional lymph node metastasis occurred in 2 patients (6%) and distant metastasis occurred in 2 patients (6%). With a mean follow-up of 8.3 years, tumor-related death occurred in 1 patient (3%). This seems to support the fact that the overall prognosis is better when the Rhabdomyosarcoma is confined to the orbit. Long-term visual outcome in the 28 patients who maintained the globe was 20/20 to 20/40 in 11 (39%), 20/50–20/100 in 5 (18%), and 20/200 to no light perception in 12 (43%).

Due to extensive involvement of sinuses, primary resection or de-bulking was not done in our patient. Incisional biopsy was done to confirm diagnosis. Chemoradiation with 4 courses of VAC-Adr (Vincristine 2mg , Actinomycin-D 0.5 mg ,Cyclophosphamide 600mg ,Adriamycin 50mg) and 5 cycles of radiation therapy (610 cGy) was given by oncologist .Unfortunately our patient received survived only for 6 months with spread to contra lateral orbit and face.

Conclusion

Ophthalmologists should be cognizant of the clinical features of Rhabdomyosarcoma and

order prompt imaging studies to determine the extent of the disease. A carefully planned biopsy should be performed and it the diagnosis is confirmed, the child should be referred to pediatric oncologists for appropriate management. Patients are staged and managed according to the IRSG protocol. The ophthalmologist has an important role in the initial diagnosis and subsequent follow-up of affected patients.

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