

## REVIEW ARTICLE

## Pediatric orbital tumors - An overview

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**Abstract**

The spectrum of pediatric orbital tumors differs from that of adults and further varies according to the age. Tumors seen in teenage are similar to those seen in adults, while congenital space-occupying lesions such as colobomatous cyst and teratoma form an entity unique to infancy and early childhood.

**Introduction**

The spectrum of pediatric orbital tumors differs from that of adults and further varies according to the age. Tumors seen in teenage are similar to those seen in adults, while congenital space-occupying lesions such as colobomatous cyst and teratoma form an entity unique to infancy and early childhood.

The incidence of various space-occupying lesions of pediatric orbit, as reported in literature, is extremely variable. The reporting facility (pathology or ophthalmology), location of the facility, and interest of the treating specialist affect the outcome of such studies.<sup>[1,2]</sup> However, most studies show that benign lesions are more common; the most common is being cystic lesions comprising mainly of dermoids and/or vascular lesions [Table 1].<sup>[3-5]</sup> Studies from the developing world report a greater percentage of malignant lesions in pediatric orbit as compared to North America and Europe.<sup>[6,7]</sup> This could perhaps be explained because most inflammatory causes of proptosis such as orbital cellulitis are not biopsied and/or there is in fact a greater incidence of pediatric orbital malignancies; for example, orbital retinoblastoma constitutes nearly 50% of all cases of retinoblastoma in India, while in the western world, it constitutes <10%.<sup>[8]</sup> Therefore, orbital retinoblastoma constitutes a large percentage of childhood orbital lesions in our country. A report from a tertiary care center of our country shows that rhabdomyosarcoma and orbital retinoblastoma are

the most common malignant lesions in the pediatric orbit, while lymphangioma constitutes the most common benign lesions.<sup>[6]</sup>

**Diagnosis**

Although benign lesions are more common in the pediatric orbit if not managed on time, they may cause severe morbidity from amblyopia, corneal exposure, or optic nerve damage.<sup>[1,3,8,9]</sup> Malignant lesions, on the other hand, if not diagnosed and treated in time will affect survival.

**Difficulties peculiar to pediatric orbital lesions**

The examining ophthalmologist faces difficulties that are typical to pediatric age; for example, the child may not be able to report all the symptoms, and investigations like imaging (magnetic resonance imaging [MRI] and computed tomography [CT] scan) and biopsy may require general anesthesia. Apart from these problems, the risk of amblyopia is typical to children <9 years of age and is a major cause of morbidity in cases of benign lesions of pediatric orbit.

When a child presents with proptosis, the following may indicate malignancy:

1. Acute onset/rapidly progressing proptosis
2. History of leukocoria

**Table 1:** Incidence of pediatric orbital space occupying lesions

Shields <i>et al.</i> <sup>[3]</sup> n=250	Kodsi <i>et al.</i> <sup>[4]</sup> n=340	Bullock <i>et al.</i> <sup>[5]</sup> n=141
Dermoid cysts: 46%	Cystic lesions: 23%	Cystic orbital and vasculogenic tumors - 58%
Inflammatory lesions: 16%		
Vascular tumors (hemangioma or lymphangioma): 7%	Vascular processes (hemangioma and lymphangioma): 18%	
Adipose tissue (either orbital fat or dermolipomas): 7%		
Rhabdomyosarcomas or secondary orbital malignancies: 4%	Rhabdomyosarcoma 7%	
Lymphoid tumors and optic nerve tumours: 2.4%	Optic nerve and central nervous system: 16%	
	Bone lesions 9%	

- History of recurrent fever, bone pains, bleeding, or any other extraorbital masses like in the abdomen
- Family history of childhood malignancy.

However, one should remember that acute onset proptosis may also result from benign lesions such as orbital cellulitis, orbital cysticercosis, or hemorrhage in a pre-existing orbital lymphangioma.<sup>[11]</sup>

## Imaging

Ultrasonography (USG): Orbital USG is a very useful tool in making a differential diagnosis. Ultrasound reveals the nature and location of the lesion. The lesion may be cystic, solid, or mixed, infiltrative, or well defined. In case of solid space-occupying lesions, USG reveals the internal architecture of the tumor (regular or irregular, high or low internal reflectivity), presence of calcifications, and its relation to and effect on other orbital structures (whether the space-occupying lesion conforms to the shape of the globe or causes globe indentation, if the mass is arising from the globe or is confined to one of the orbital structures such as extraocular muscle, lacrimal gland, or optic nerve).

On USG, cystic lesions such as cysticercus cyst and hydatid cyst have characteristic features and dermoid cysts are seen as cystic lesions with irregular, high internal reflectivity. An infiltrative lesion with multiple, variable sized cysts on USG and a typical history of recurrent proptosis associated with upper respiratory tract infection is diagnostic of lymphangioma.

## CT scan

CT scan of orbit must be done in all cases of orbital tumors. It provides useful information about the bony orbit. It demonstrates whether the lesion is arising from bone or is causing secondary bone changes like erosion (sign of malignancy) or remodelling (seen in long-standing masses). The exact location, internal architecture, and calcification may be better appreciated on CT scan. Any extension from or into adjacent intracranial space, paranasal sinuses, or nose

may be detected. The effect of contrast on the lesion provides information regarding vascularity of the tumor; for example, lymphangioma usually enhances minimally with contrast while capillary hemangioma will show feeder vessels with good contrast enhancement.

## MRI

MRI is an extremely useful tool for orbital imaging, especially in cases of orbital tumors. Due to better soft tissue contrast and no risk of radiation, it has become an indispensable modality for characterization of orbital lesions. It is ideal for visualization of the entire course of the optic nerve and the pituitary gland. Thus, it has a central role to play in the diagnosis and prognostication of retinoblastoma. It is also the modality of choice in imaging of non-vascular tumors such as pseudotumor, orbital cellulitis, and orbital cysticercosis. MRI also helps to diagnose any extension of the lesion to the orbital apex, optic canal, or brain. However, it is expensive and cannot be performed in patients with any metallic implants/foreign bodies.

## The Common Benign and Malignant Orbital Lesions of Pediatric Age Group

The list of pediatric orbital space-occupying lesions is long, but here is a brief clinical, imaging, and treatment outline for the most commonly encountered lesions of pediatric orbit.

### Cystic lesions

#### *Dermoid cyst*

These are the most common cystic lesions of the pediatric orbit.<sup>[3]</sup> They present as long-standing, slowly growing hard masses that are located at the external angle of eye (lacrimal fossa) [Figure 1a]. Occasionally, they may rupture secondary to trauma and present with acute inflammation. On USG, they are characteristically seen as cystic lesions with variable internal reflectivity that is high to moderate and often harbors the areas of calcification. CT scan is performed to look for bone remodeling

and rule out intracranial involvement. Fat shadows are usually seen as dark areas within the cyst. Simple excision of the intact cyst is the treatment of choice.<sup>[12]</sup>

#### *Parasitic cysts*

##### A. Cysticercosis

Parasitic cysts of ocular adnexa and orbit are commonly seen in the developing world.<sup>[13]</sup> Cysticercosis of orbit typically affects young individuals and has a wide spectrum of clinical manifestations. It most commonly involves anterior orbit (extraocular muscles), followed by subconjunctival space, eyelid, and posterior orbit.<sup>[13]</sup> The affected child presents with acute onset, painful diplopia, squint, or proptosis. Visual acuity may be affected when the cyst involves the orbital apex or the globe. There may be single or multiple cysts. On USG, they appear as cystic lesions with a single spec of high (100%) reflectivity [Figure 1b]. A CT scan of the brain and indirect ophthalmoscopy should be done in all cases to rule out neurocysticercosis and intraocular cysticercosis, respectively. A stool test may be done to rule out autoinfection. The choice of treatment is medical therapy with the antihelminthic drug albendazole (15 mg/kg body weight in two divided doses for 6–8 weeks) given under the cover of oral steroids. The changes in the USG characteristics of the cysticercus cyst in response to medical therapy have been described in literature.<sup>[15]</sup> In case of subconjunctival cysticercus cysts or residual cysts after medical therapy, one may excise the cyst. The inflammation associated with cysticercus cysts may be clinically confusing and a misdiagnosis of orbital cellulitis is often made.<sup>[16]</sup> Therefore, in all cases of orbital cellulitis, imaging should be carefully evaluated to rule out any cysticercus cyst, in which case, there will be no/poor response to systemic antibiotics and anti-inflammatory medications alone. In cases associated with neurocysticercosis, the treatment is guided by neural involvement. Despite resolution of cysticercosis with medical management, a significant proportion of patients will have residual functional deficits.<sup>[13]</sup>

##### B. Hydatid cyst

Hydatid cyst of orbit may be seen in pediatric orbit, especially in countries endemic for this disease. Around 1% of all cases involve orbit. The affected child presents with a long-standing, slowly increasing, painless proptosis [Figure 1c]. Ultrasound features are characteristic and reveal an anechoic cyst with two highly reflective linings (double wall sign).<sup>[17]</sup> A history of contact with dogs is usually present. CT scan shows a cystic lesion with orbital expansion and bone remodeling due to long-standing nature of the lesion [Figure 1d]. Globe indentation leads to refractive changes, which if not taken care of may lead to anisometropic amblyopia. Unlike in cysticercosis, where the management of choice is medical therapy, the treatment of choice for a single orbital hydatid cyst is surgical excision. Hydatid cyst is lined by three layers: The endocyst, ectocyst, and pericyst. The aim of surgical excision is to remove the endocyst (that harbors the daughter cysts) intact after incising the pericyst and the ectocyst. Cryoprobe is helpful in holding

and delivering the endocyst which has very thin and delicate walls.<sup>[17]</sup> A leak from the endocyst during the surgery will invariably lead to daughter cyst implantation and result into multiple recurrences in the orbit. In cases of recurrence or multiple cysts, oral treatment with albendazole may be tried as complete surgical excision is difficult.<sup>[18,19]</sup>

#### *Vasculogenic tumors*

These include lymphangioma, capillary hemangioma, varicose veins, and cavernous hemangioma. Of these, lymphangioma and capillary hemangioma occur very commonly in pediatric orbit and are discussed here.

#### *Lymphangioma/combined venous-lymphatic vascular malformation*

Apart from cystic lesions, lymphangioma is the most common vasculogenic benign orbital space-occupying lesion of the pediatric orbit, reported from our country.<sup>[6]</sup> According to the ISSVA classification for vascular tumors, the preferred terminology for this lesion is no flow vascular malformation.<sup>[20]</sup> The patient usually presents with a long-standing proptosis or eyelid swelling that has suddenly increased in size. The swelling characteristically increases in size following an episode of cough and cold and responds dramatically to oral steroids [Figure 1e]. Sometimes, massive hemorrhage may occur within the lymphangioma that may require urgent surgical intervention to decompress the orbit.<sup>[21]</sup> Indications for such an urgent surgical drainage include optic nerve compromise (suggested by appearance of relative afferent pupillary defect and/or deterioration of vision) or corneal exposure due to lagophthalmos. The acute presentation in such cases may often confuse the treating clinician who may misdiagnose it as a malignancy. However, a careful history taking and clinical examination will usually lead to correct diagnosis.

Clinical examination on slit lamp may reveal clear lymphatic fluid-filled cysts in the subconjunctival space. USG shows diffuse infiltrative lesion with multiple variable sized cysts. CT scan orbit, similarly, shows an infiltrative, ill-defined orbital lesion with minimal/no contrast enhancement, as it is isolated with respect to the vascularity. Many times, large cysts may be seen with fluid-fluid levels [Figure 1f].

Being an infiltrative lesion, complete surgical excision is usually not possible. Surgical intervention may cause more hemorrhage in the lymphangiomatous tissue. Hence, of late, sclerosing agents are at the forefront of therapy for lymphangiomas. Intralesional bleomycin has been successfully used in a dose of 0.5 IU/kg body weight (with a maximum of 15 IU/mL).<sup>[22,23]</sup> Oral steroids are also used to manage any increase in the size of lesion. Surgical excision is restricted for large orbital lymphangiomas that are cosmetically disfiguring. As patients reach the second decade of life, some lymphangiomas may show regression or may stabilize.

#### *Capillary hemangioma*

It is the most common congenital vascular tumor in the periorbital region.<sup>[24]</sup> They are benign vasoproliferative tumors

of vascular endothelial cells that are defined by their unique histology and evolution. Most of them are located in the head and neck region [Figure 1g]. When located around the orbit, they can cause significant cosmetic deformity and amblyopia, the latter due to strabismus or mechanical ptosis causing visual deprivation.<sup>[25,26]</sup> Orbital involvement may lead to proptosis, exposure keratopathy, or compressive optic neuropathy. Although the natural course of disease in capillary hemangioma is spontaneous regression, many children still require treatment. Many therapeutic options have been used, including intralesional or systemic steroids, surgery, embolization, radiation, interferon therapy, and laser therapy.<sup>[26-29]</sup> Systemic therapy with propranolol was serendipitously found to induce involution in capillary hemangiomas and is now popularly being used as a first-line treatment, especially for deep orbital lesions. The most common dose used is 2 mg/kg/day.<sup>[30]</sup>

### Orbital malignancies

#### *Rhabdomyosarcoma*

It is the most common orbital malignancy of childhood. Around 5% of cases occur in orbit. It usually presents at a mean age of 7.5 years.<sup>[31]</sup> The patient presents with a rapidly increasing proptosis or an upper eyelid mass. Clinical examination reveals a firm orbital mass with variable consistency, usually involving superior orbit. Clinically, it may mimic orbital cellulitis. On imaging, a well-defined heterogeneous mass can be seen which involves the extraocular muscle, may have calcification, and is usually associated with erosion of adjacent bony orbit. There are variable contrast enhancement and globe indentation but intraocular structures are normal.

An incision biopsy confirms the diagnosis in most cases. Sometimes histopathology may only reveal features of a round cell tumor; in such cases, further immunohistochemical staining is required to reach a diagnosis. Other round cell tumors that are differentiated on immunohistochemical staining include retinoblastoma, medulloepithelioma, Ewing's sarcoma, granulocytic sarcoma, and neuroectodermal tumor. Of these, retinoblastoma is a common cause of orbital tumor in pediatric orbit in developing countries.

The current standard of treatment for rhabdomyosarcoma is chemoradiotherapy. The majority of patients are cured with the use of both chemotherapy and radiation therapy, but a considerable number experiences late sequelae of treatment. A 10-year event-free and overall survival reported are 77% and 87%, respectively, for primary orbital RMS.<sup>[32]</sup> The challenge with current therapy is to reduce undesirable effects of radiotherapy.

#### *Retinoblastoma*

Retinoblastoma is the most common intraocular malignancy of childhood worldwide; furthermore, it is an important cause of orbital malignancy of pediatric orbit in developing world.<sup>[8]</sup>

Along with rhabdomyosarcoma, it constitutes the most common cause of orbital malignancy in a pediatric age group in India.<sup>[6]</sup> The clinical presentation is similar to rhabdomyosarcoma that is a rapidly increasing proptosis. However, parents will usually give a history of leukocoria preceding the orbital symptoms. Such a history should always be elicited in all the cases of rapidly progressing childhood proptosis.

USG reveals an intraocular mass filling the globe with intralesional calcification. CT scan orbit and brain should be done in all cases and reveal a heterogeneous mass lesion within the globe with areas of calcification and extending into the orbit either as an extraocular mass or as thickened optic nerve [Figure 1h]. It may also reveal any intracranial extension. Locally invasive and malignant retinoblastoma constitutes nearly half of all cases of retinoblastoma in our country.<sup>[8]</sup> The survival prognosis is only 50% at 5 years for locally invasive retinoblastoma.<sup>[33,34]</sup> Diagnosis is evident on imaging and is confirmed by histopathological examination in cases of doubt.

Currently, the standard line of treatment of locally invasive retinoblastoma comprises of neoadjuvant chemotherapy (3 cycles) with standard VEC regimen followed by limited surgery (enucleation) and adjuvant chemotherapy (9 cycles) and radiotherapy. Malignant retinoblastoma is treated using high-dose chemotherapy and stem cell transplant.

#### *Granulocytic sarcoma*

Leukemia is the most common malignancy of childhood. Around 15–20% of cases of leukemia are myelogenous and 8% of these develop extramedullary solid tumors of primitive granulocyte precursor cells known as granulocytic sarcoma/myeloid sarcoma/chloroma. These occur more commonly in children, are typically multifocal, and have a predilection for occurrence in orbit and orbital bones. They present as a rapidly expanding orbital mass at a mean age of around 7–8 years [Figure 1i].<sup>[35]</sup> The temporal association with systemic disease may be variable, but they usually present 2 months to 3 years before systemic disease becomes advanced. Symptoms of systemic disease such as paleness, lethargy, or epistaxis may suggest the diagnosis. Orbital granulocytic sarcoma may occur bilaterally in 10% of cases. They usually arise in the subperiosteal region of the osseous wall of the orbit. CT scan shows a homogeneous mass usually in the lateral orbit which is iso/hypodense to extraocular muscle and hypodense to sclera and enhances uniformly with contrast [Figure 1j]. They usually do not cause bone destruction and mold to one or more orbital walls.<sup>[36,37]</sup> Incision biopsy is diagnostic and may show features of small round cell tumor. Staining for Auer rods in the cytoplasm is diagnostic.

In cases of acute onset bilateral proptosis/orbital masses in children, granulocytic sarcoma should be suspected. In such cases, a peripheral blood film and/or bone marrow biopsy should always be done to rule out leukemia. This may preclude the need for a biopsy. Although granulocytic sarcoma is highly responsive to chemotherapy and local radiotherapy, survival prognosis is

universally poor. Sometimes, orbital granulocytic sarcoma may occur in isolation.<sup>[38]</sup>

Other causes of acute proptosis in setting of acute leukemia include hemorrhage and orbital abscess. However, these can be differentiated on imaging. Less commonly acute lymphocytic leukemia may also infiltrate orbit or eyeball.

To conclude, pediatric orbital tumors constitute a clinically distinct entity from that of adult orbital tumors and pose some unique challenges to the treating ophthalmologist. The treating ophthalmologist/oculoplastic surgeon should be aware of conditions that may require early medical/surgical intervention.

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