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Pediatric Orbital Tumours – Saving Young Eyes and Young Lives

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Although rare, pediatric orbital tumours may be associated with significant morbidity and risk of mortality, thus identifying and properly managing these patients are of utmost priority. This issue of *Ophthalmology Rounds* reviews the most common orbital tumours of childhood. Familiarity with the common benign and malignant pediatric orbital tumours will facilitate the rapid diagnosis and proper management of these potentially life-threatening lesions.

The diagnosis and management of pediatric orbital tumours follow the adage learned in pediatrics that "children are not just small adults." Tumours in children represent a different spectrum of lesions than in adults, as particular tumours have the propensity to manifest during certain ages of childhood. The most common benign orbital lesions in children are dermoid cysts, followed by the vasculogenic lesions: capillary hemangiomas and lymphangiomas (Table 1). The most common orbital malignancy that may arise in or invade the orbit of young children is rhabdomyosarcoma, followed by metastatic disease, lymphomas, and leukemia.

Anatomy

Unlike that of the adult, the pediatric orbit grows substantially with time. During the first few months of life, the average orbital volume is 14 cm^3, reaches 77% of its final volume by 5 years, and increases by a factor of 1.7 to approximately 26 cm^3 by the time the child is 15 years old.[8] The pyramidal or cone-shaped space orbit is comprised of 7 bones: frontal, greater and lesser wings of the sphenoid, zygoma, maxilla, lacrimal, palatine, and ethmoid. The hard bony walls that surround and protect the globe simultaneously trap the orbital contents within; thus, orbital infection, inflammation, or growth of a mass may cause the globe's anterograde movement clinically seen as proptosis and measured by exophthalmometry. Several interconnecting fascia compartmentalize the orbit and may play a role in the pathogenesis of optic nerve compression in the presence of mild orbital signs.

Evaluation

The evaluation of a child with a presumed orbital mass begins with a careful history from the patient (if possible) and family members. Particular attention should be given to the duration and rate of progression of the patient's signs and symptoms, in addition to findings such as proptosis, ophthalmoplegia, pain, diplopia, pulsation, change in size with position or Valsalva manoeuvre, and decreased visual acuity. History of periocular trauma and pertinent family history should also be explored. Other symptoms such as fever or a history of sinusitis may raise suspicion for orbital cellulitis, the most common cause of childhood proptosis.[9] A thorough ophthalmic examination should be performed. Severe proptosis and chemosis may hinder the ocular examination because of the tightness of the eyelids against the globe. If possible, the use of Desmarres retractors should be avoided in children since the patient's forceful movements may cause an inadvertent eyelid laceration.

If the patient is able to open his/her eyelids, visual acuity should be documented, in addition to any changes of refraction or pupillary abnormalities. Ophthalmoplegia and diplopia should be measured and, if present, forced duction testing may distinguish between a restrictive or neurogenic process. Signs of an orbital mass in the slit-lamp examination may come in the form of chemosis, engorged conjunctival vessels, or sentinel vessels, while the dilated

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Table 1: Incidence of Pediatric Orbital Lesions

Tumour	Incidence
Benign	
Orbital dermoid cyst	46% (115 of 250)[1] 19% (65 of 340)[2] 30% (52 of 174)[3] 2% (6 of 572)[4] 29% (71 of 243)[5]
Lymphangioma	4% (54 of 1264)[6]
Capillary hemangioma	3% (36 of 1264)[6]
Malignant	
Rhabdomyosarcoma	0.2% (33 of 21 000)[7] 4% (10 of 250)[1] 3% (35 of 1264)[6]
Metastases	7% (91 of 1264)[6]

fundus examination may reveal optic disc edema or pallor, retinal detachment, choroidal folds, shunt vessels, or indentation of the posterior pole.

Examination of the orbit should include quantification of proptosis by Hertel exophthalmometry in patients with intact lateral orbital rims. Orbital masses may often be felt within the anterior orbit. Pain to palpation may suggest an inflammatory process, while a pulsatile lesion may denote arteriovenous communications or intracranial pressure changes transmitted through a bony defect within the orbit. A bruit on auscultation may be heard in the presence of an arteriovenous fistula. Other periorbital changes such as hypertelorism, lagophthalmos, eyelid lesions or edema, and engorged conjunctival vessels may also be noted on gross examination.

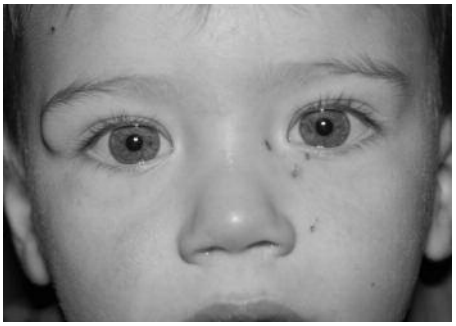
Benign Orbital Tumours

Cystic lesions

Dermoid cysts are common orbital lesions usually found in the anterior orbit of children.[1] They are epithelial-lined structures with dermal elements in their walls along with hair and keratin in the lumen.[6] In contrast, cystic lesions consisting of squamous epithelium without adnexal structures are called epidermoids. Orbital dermoids often develop adjacent to suture lines, most commonly the anterolateral frontozygomatic sutures.[1,10] They arise congenitally from abnormal ectodermal sequestration adjacent to suture lines.[6] Dermoid cysts are divided into superficial and deep types. The superficial dermoid cysts become apparent during the first decade of life, but deeper dermoid cysts commonly present later during the teenage years or adulthood.[6,11]

Clinically, superficial dermoid cysts often present near the lateral aspect of the eyebrow anterior to the frontozygomatic sutures as a slow-growing and painless subcutaneous mass that typically has been noted since birth (Figure 1).[6] They are firm, smooth, and mobile upon palpation.[11] Most patients have no visual symptoms. Large superficial dermoid cysts may cause inferior and medial displacement of the globe.[6] Deep dermoid cysts present with proptosis.[11] Dermoid cysts can present shaped in a dumbbell configuration with halves in the orbit and temporal fossa, connected through a defect in the sutures. These cysts would typically present upon mastication with pulsating proptosis.[12] Occasionally, small ruptures of the cyst wall may lead to a pronounced inflammatory response of the surrounding tissue.[6,11]

Figure 1: A 2-year-old boy with a right superotemporal quadrant dermoid cyst.



Ultrasonography has been demonstrated to be a cost-effective screening tool for localizing anterior orbit and mid-orbit lesions.[13] However, for better characterization of these as well as posterior lesions, computed tomography (CT) is indicated.[11,13] On CT, lesions are generally well-defined with an enhancing wall and nonenhancing lumen. Magnetic resonance imaging (MRI) of dermoid cysts is optimally appreciated with fat suppression techniques, with the cysts appearing as well defined and circular to ovoid structures.[6] Lumen signal intensity varies with substance present, often appearing hypointense (T1-weighted images) or hyperintense (T2-weighted images) as compared to orbital fat with minimal enhancement due to the absence of blood vessels in the cyst.[6]

Management is surgical with complete excision of the cyst lining, taking care to avoid rupture (Figure 2). All attempts should be made to remove the remnants of the cyst to avoid potential severe inflammatory reaction. After removal of the deflated cyst wall, some surgeons suggest irrigation of the operative site with antibiotic solution. Surgery is delayed until the risk of accidental rupture from trauma outweighs the general anesthesia risks, usually around 1 year of age. Smaller cysts can be followed for signs of growth, visual disturbances, or cosmetic deformity.

Other less common cystic lesions include mucoceles, colobomatous cysts, and hematic pseudocysts. The most important of the rarer cystic lesion is an orbital teratoma, a rare congenital germ-cell tumour that arises from primordial germ cells. These tumours are characterized by the presence of ectodermal, mesodermal, and endodermal components. They typically present at birth, and although benign with no bone invasion, often cause orbital enlargement with significant morbidity. With large intraconal masses, massive proptosis accompanied by conjunctival keratinization, exposure keratopathy, and corneal ulceration may be seen.[14] Massive teratomas traditionally are treated by orbital exenteration; however, salvage of the globe is possible with smaller lesions (typically without subsequent normal visual acuity).

Figure 2: Intraoperative photo of the patient in Figure 1. Note the surgical dissection plane has preserved the dermoid within its capsule.

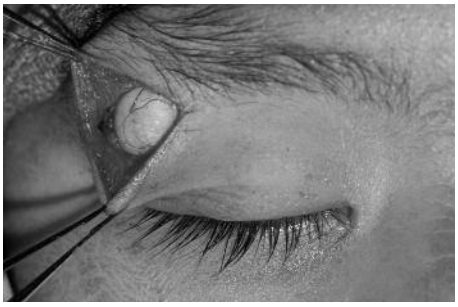
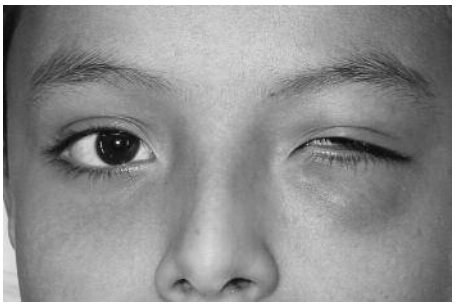


Figure 3: A child with acute left orbital hemorrhage secondary to a lymphangioma. Note the inferior orbital swelling and discolouration with associated hyperglobus.



Lymphangiomas

Comprising of a mixture of venous and lymphatic vessels, lymphangiomas are otherwise known as combined venous-lymphatic malformations or lymphaticovenous malformations.[15] These malformations are divided into superficial, deep, or combined lesions and may affect the conjunctiva, eyelids, or deep orbit. Pathologically, superficial lesions and superficial components of combined lesions contain lymphatic components, while deep lesions and deep components of combined lesions are venous in nature.[16-18] Lymphangiomas represent only 4% of pediatric orbital masses.[6]

Typically, lymphangiomas are identified within the first 2 decades of life. The course may present as slow enlargement with increasing proptosis over many years, or one of sudden proptosis from intralesional hemorrhage (chocolate cyst). Superficial lesions are more common and have a better prognosis for vision than deeper lesions. There is typically no enlargement of the tumour with a Valsalva manoeuvre. There is frequent extension of anterior lesions to the forehead, temporal region, and cheek.[16,19] Deep lesions usually present with acute proptosis that develops into an intralesional hemorrhage, or, less commonly, an acute enlargement from an upper respiratory infection (Figure 3). Upon further questioning, parents often report fullness or purple discoloration of the eyelid since birth, usually in the superomedial orbit. These lesions may also be associated with vesicles that appear in the conjunctiva, facial skin, or oral mucosa.[16,20,21] In fact, the visualization of hard/soft palate dilated vessels can provide clues to the diagnosis. Venous-lymphatic malformations usually grow in step with the patient, but hormonal changes associated with puberty or pregnancy may accelerate growth.[16,22] In up to 50% of patients, there may be complaints of restricted ocular motility. Vision is rarely affected, even with large lesions, unless they repeatedly hemorrhage deep within the orbit.[16,23]

In an older lesion with prior hemorrhage, fibrosis and hemosiderin are commonly observed. Imaging studies include CT and MRI, which both show the multicompartmental nature of the venous-lymphatic malformations. MRI is preferred over CT because it delineates the internal structure of the various cysts of the lesion. The management of orbital lymphangiomas is difficult due to the infiltrative nature of the tumour. Surgical debulking and cyst drainage is the treatment of choice for significant proptosis, corneal exposure or optic nerve compression. Complete surgical excision is often impossible. Recurrence may require further surgical debulking and possible sclerotherapy.

Capillary hemangioma (CAPH)

CAPHs – also referred to as infantile hemangiomas - are the most common orbital vascular tumour in the pediatric population. One-third are diagnosed at birth, and over 90% are visible by 6 months of age. Hemangiomas represent 3% of all orbital lesions and 17% of vasculogenic lesions of the orbit.[6] The most common presentation is superficial involvement appearing as tumour and telangiectatic vessels in the skin that with time develop the typical strawberry-like appearance (Figure 4). Deeper lesions may appear as raised, soft, purplish nodules. Deep orbital involvement may present solely with proptosis and no skin changes. Upon palpation, these lesions are warm and sometimes pulsatile. Extensive hemangiomas may produce proptosis and globe displacement. These tumours appear in newborns shortly postpartum and undergo a proliferative phase of growth for approximately 1–2 years. This is followed by a period of stabilization and then spontaneous involution by 4–8 years of age.[24]

Figure 4: Right lower lid margin capillary hemangioma.

Orbital involvement is best evaluated with CT or MRI, which show a diffusely infiltrating nonencapsulated mass, conforming to the surrounding orbital structures. Contrast material effectively enhances the tumour in a marked and uniform fashion, especially the lobulated contour. Ultrasound by an experienced practitioner can be useful for diagnostic evaluation of suspected anterior vascular lesions. Invasion of the bone is rare, with the mass commonly extraconal, although expansion of the orbital walls is possible. As the lesion ages, it becomes more heterogeneous with less enhancement.[24,25] MRI is well suited to imaging of this soft-tissue lesion, with dark fibrous septa demonstrated between hyperintense T2-weighted images. Gadolinium-based contrast material enhances the tumour intensely and uniformly during the proliferation phase. MR angiography may reveal enlarged feeding arteries.[22,26,27]

Additional lesions are found in the skin or viscera in close to one-third of the patients with orbital hemangiomas.[24] Aggressive histological variants of hemangioma can cause Kasabach-Merritt syndrome, which is a severe comsumptive thrombocytopenic coagulopathy. PHACES syndrome – an acronym for posterior fossa anomalies, hemangiomas of the face, arterial abnormalities (including coarctation of the aorta), cerebral vascular anomalies, eye abnormalities, and sterna or ventral developmental anomalies – is associated with some orbital hemangiomas. Pathologically, these lesions are vascular and multilobar. Histologically, the tumour growth appears infiltrative. Involution proceeds at the centre and then proceeds peripherally, with fibrosis and fat completely replacing the cellular components and atrophied vasculature.[28]

Long-term cosmetic sequelae are minimal following involution, though visual complications such as amblyopia and astigmatism from distortion of the globe are common. Major complications include superinfection, ulceration, and necrosis with possible hemorrhage. Rare but serious complications include Kasabach-Merritt syndrome and high-output cardiac failure (large lesions). Indications of treatment include any of the complications discussed previously. Lesions that do not affect visual or orbital development can be observed. In the past, medical therapy involved the use of intralesional steroid injection, systemic steroids, or interferon, all of which may cause serious side effects. A recent therapeutic option with impressive efficacy and generally good tolerance is oral propranolol.[29] Based on case reports and uncontrolled studies, propranolol given at 2 mg/kg a day until the end of the proliferative stage leads to significant regression of these tumours.[30] Timolol maleate gel may confer some benefit in children with superficial hemangiomas. Surgical resection is reserved for well-circumscribed lesions or those causing severe sequelae unresponsive to medical therapy.

Optic nerve glioma (ONG)

ONG is the most common optic nerve tumour, the third most common orbital tumour in children, and the fifth most common primary intraorbital tumour (1.5%–3.5% of all orbital tumours).[31] These tumours may occur randomly, but are often associated with neurofibromatosis type I (18%–50% of cases), and are often bilateral when occurring with this disease. The mean age of presentation is about 8 years. The typical presentation is proptosis and visual loss or visual field changes. Intracranial extension may produce headaches and pain. Upon eye examination, optic disk swelling or atrophy and decreased motility may be noted. Diagnosis can usually be made based on clinical examination and the characteristic appearance on CT. Radiographically, these lesions appear as a fusiform enlargement of the optic nerve, which is isodense with brain tissue. Intracranial extension into the optic canal and chiasm is best evaluated with MRI.

Despite their apparently benign and slow growth pattern, ONGs are associated with significant morbidity and mortality, especially when the tumour spreads to the optic chiasm, hypothalamus, and brain. Because of this, these tumours must be excised while still confined to the optic nerve. Once the tumour has extended to the chiasm, surgery is contraindicated. Radiotherapy at this point does not seem to improve prognosis and chemotherapy is unproven. Gliomas are indolent enough to warrant conservative management with serial radiographic studies when vision is intact. However, once the tumour extends to the optic canal or the eye becomes blind and/or proptotic, surgical excision is necessary.

Malignant Orbital Tumours

Rhabdomyosarcoma

Rhabdomyosarcoma, accounting for about 5% of all childhood cancers, is the most common mesenchymal tumour in children.[32] It is also the most prevalent extraocular malignancy in children. Rhabdomyosarcoma is a malignant neoplasm that can occur in several sites of the body, with 10% of the neoplasms occurring in the orbital region.[33,34] This neoplasm comprises mesenchymal cells with histopathological features of striated muscle in varying stages of embryogenic maturity. Rhabdomyosarcoma histologically can be divided into 4 main types: embryonal, alveolar, pleomorphic, and botryoid. The embryonal type was identified as the most common, comprising 221 patients (84%) of a series of 264 subjects.[35] The alveolar type was less common (11%), but is most malignant with a high frequency of metastases. The pleomorphic and botryoid types rarely occur in the orbit.[36] The pleomorphic type is the most differentiated type with the best prognosis.

Histologically, the embryonal type is characterized by elongated or spindle-shaped cells of varying degrees of differentiation. An eosinophilic cytoplasm and central hyperchromatic nuclei arranged in a herringbone pattern of interlacing fascicles are often seen. Frequently, bipolar cells with tapered cytoplasmic processes are observed. The alveolar type is characterized by thin fibrovascular septa. The tumour cells are large, abundant with eosinophilic cytoplasm, vary in shape from round to polygonal, and contain large and vesicular nuclei. These cells adhere loosely to the surrounding thin connective tissue with empty spaces in a pattern similar to alveoli in the lung.

Although rhabdomyosarcoma usually occurs in the orbit, it may also arise in the conjunctiva, eyelid, or in the anterior uveal tract.[7] Tumours are soft and fleshy, and range from light grey to pink or yellow in colour when sectioned. Smaller masses may be circumscribed, and larger masses may have irregular borders further to invasion into the pseudocapsule. Areas of hemorrhage or cyst formation may be present.[7] Rhabdomyosarcoma presents early in the first decade with rapid unilateral proptosis and displacement of the globe (Figure 5). The eyelid may be erythematous with conjunctival chemosis. Ptosis, tearing, headache, and epistaxis are less common complaints. A palpable mass is present in about 25% and with large intraconal lesions papilledema and retinal vascular congestion may be seen. Sinusitis and epistaxis may occur with extension of the mass into the paranasal sinuses.

Rhabdomyosarcoma grows rapidly, with bone erosion seen in 30%-40% of patients upon presentation.[26] Invasion of the paranasal sinuses occurs in around 20% of the patients; however, intracranial invasion is less common (3%).[26] Metastases are hematogenous, commonly spreading to the lungs and bones.[6]

CT scan shows an irregular tumour with moderately well-defined margins, soft tissue attenuation, and often evidence of bony destruction (50%; Figure 6). MRI demonstrates a signal similar to muscle on T1 and higher than muscle on T2-weighted images. A biopsy of a suspected rhabdomyosarcoma should be performed as soon as possible for a definitive diagnosis.

Figure 5: A child with a gradually enlarging, painless, left-orbital mass. The globe was not visualized due to its displacement from the rhabdomyosarcoma.

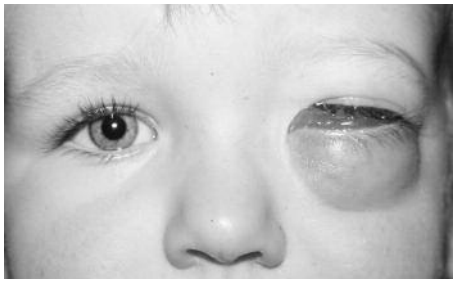
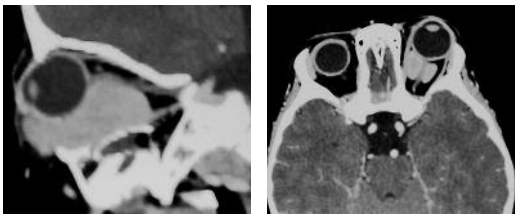


Figure 6a, 6b: Sagittal and axial CT scans showing the large inferior based orbital rhabdomyosarcoma encasing the optic nerve.



With the recent advances in treatment using chemotherapy and radiation, this once-fatal disease now carries a much better prognosis. Localized disease (Group I and II) carries a 90% 5-year survival. However, disseminated or gross residual disease (Group III and IV) has a 35% 5-year survival rate. Specific recommendations for management are based on staging and consist of various regimens of chemotherapy, external-beam radiation therapy, and surgery. The therapeutic role of surgery ranges from excisional biopsy to extensive surgery for the purpose of removing or debulking the tumour. Tumour excision should be performed if it can be done without damaging the vital structures of the orbit. Primary exenteration, although common before the advent of advanced chemotherapy protocols, is rarely if ever indicated for this condition.

Metastases

Metastatic cancer to the orbit accounted for 7% of Shield et al's[6] series of 1264 pediatric patients with orbital lesions. The most common pediatric orbital metastases are neuroblastoma, Ewing sarcoma, and leukemia. Acute lymphoblastic leukemia is the most common type of leukemia to metastasize to the orbit.

Neuroblastoma

Neuroblastoma is the most frequent metastatic orbital disease in children. The primary tumour site may be found in the retroperitoneum or posterior mediastinum. Neuroblastoma is common in children and accounts for about 10% of all malignancies.[31] The majority of cases occur before age 5 years (median 22 months). Bilateral disease is common; associated eyelid ecchymoses may initially prompt suspicion of non-accidental trauma. Patients with neuroblastoma and cervical involvement may develop Horner syndrome. Proptosis is the most common presenting signs, and additional symptoms may include abdominal fullness/pain, edema, and hypertension owing to the primary lesion, most commonly in the adrenal

gland. Urinalysis is positive for catecholamines in 90%–95% of patients. Incisional biopsy is necessary to confirm the diagnosis. Children presenting with orbital disease are stage IV, and have a survival rate of less than 15%. Therapy includes surgery, chemotherapy, radiation therapy, and bone marrow transplantation.

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