Orbital swelling: a simplified guide

Introduction

Swelling in and around the orbit is common but many doctors may have difficulty forming a differential diagnosis for an orbital swelling. It is important to be able to differentiate the causes of orbital swelling either because they are common (e.g. thyroid eye disease) or because they are rare (e.g. mucormycosis) but may result in loss of vision or even death (Gamba et al, 1986; Rootman, 2001; Tanaka et al, 2004; Kanski, 2007; Lutt et al, 2008). This article outlines the assessment of orbital swelling.

Anatomy

The orbit is a pyramidal structure formed by seven bones (frontal, sphenoid, zygomatic, maxilla, palatine, lacrimal, ethmoid). At the apex of the pyramid is the optic foramen (optic canal) (Drake et al, 2004), which carries the optic nerve and ophthalmic artery (a branch of the internal carotid artery and the orbit's arterial supply). Lateral to the optic foramen is the superior orbital fissure, which gives passage to three large nerves (oculomotor, trochlear and abducent), three branches of the ophthalmic nerve (lacrimal, frontal and nasociliary) and the superior ophthalmic vein. The orbit also contains the eyeball (globe), extraocular muscles, lacrimal system, vasculature, adipose tissue and fascia. Diagrams showing the orbital anatomy can be found in all good anatomy textbooks. *Table 1* shows a simple guide to examination of the orbit.

Orbital swellings

Some important causes of orbital swelling are discussed below; the list is comprehensive, but not exhaustive. Conditions such as angioedema cause facial swelling, but are beyond the scope of this review. The conditions are divided by the urgency of referral for an ophthalmology opinion.

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Emergencies

These conditions generally require immediate inpatient ophthalmology referral followed by, ideally, a same-day ophthalmology assessment. This should not delay initial treatment. Mucormycosis and orbital cellulitis are important causes of acute orbital swelling that may be fatal. Owing to the rapidly accumulating oedema, both may affect neuromuscular and vascular structures in the orbit, resulting in swelling, ophthalmoplegia, diplopia, cranial nerve palsies and loss of vision.

Acute orbital and preseptal cellulitis

Orbital cellulitis is an acute condition involving painful unilateral lid swelling, proptosis and erythema (*Figure 1*); systemic features include pyrexia and headache. It is commonly caused by spread of staphylococcal or streptococcal bacteria from the sinuses (particularly ethmoid), or alternatively through spreading infection from the oropharynx or face, fungal infections, foreign bodies, and pyemic cellulitis (Rootman, 2001; Lutt et al, 2008).

Infection anterior to the orbit is termed preseptal cellulitis, while posterior infection is termed orbital cellulitis (Hasanee and Sharma, 2004). Orbital cellulitis is likely when there is ocular pain, proptosis (resulting from oedema and pus within the bony orbit), chemosis and ophthalmoplegia (most often apparent on downward and lateral gaze). There may also be reduced visual acuity, poor colour vision and a relative afferent papillary defect, as a result of optic nerve compression and ischaemia or direct inflammation of the dura. Preseptal cellulitis is more likely when the eye is simply red with limitation of the infection to the eyelid (Tole et al, 1995). Preseptal cellulitis does not cause optic nerve compression or proptosis and eye movements are usually normal (Lutt et al, 2008).

Clinical differentiation between orbital and preseptal cellulitis may be difficult and, as delay in treatment may result in blindness or even progression to meningitis, cavernous sinus thrombosis or brain abscess, use of computed tomography is recommended to show the extent of inflammation in the orbits and concurrent sinus pathology and brain abscess (Tole et al, 1995).

If the diagnosis is clearly preseptal cellulitis no investigation is required and treatment with oral antibiotics can be initiated. If there is any diagnostic uncertainty then the patient should be treated for orbital cellulitis (with intravenous antibiotics) until blood cultures and a computed tomography scan of the orbit and sinuses have ruled out severe infection (Lutt et al, 2008). Orbital cellulitis is a medical emergency, requiring urgent ear, nose and throat and ophthalmology referral.

Orbital infection is more common in children and ease of clinical diagnosis varies according to the age and cooperation of the child. The same pathogens are com-

Figure 1. Orbital cellulitis showing unilateral lid swelling and erythema.

Table 1. Very simple orbit examination

Inspect	From in front for lid retraction from the side, behind and above for proptosis
Palpate	For a mass; retropulsion (pushing back of the globe with the eyelid closed; there may be increased resistance to this in orbital tumours)
Auscultate	Over the globe for bruit (lid closed)
Test the cranial nerves	Including range of ocular movement and optic nerve function (e.g. visual acuity, colour vision (using Ishihara charts) and testing for a relative afferent papillary defect)
General examination	For example, for thyroid status and signs of Wegener's granulomatosis

mon as in other age groups, except *Haemophilus influenzae* which is seen in reduced numbers since the widespread use of *H. influenzae* type b vaccination (Ho et al, 2007). Paediatric cases will require paediatric referral as well as input from ophthalmology and ear, nose and throat.

Mucormycosis

Mucormycosis is a rare but rapidly progressing *Phycomycetes* fungal infection often occurring in immunocompromised patients. Always consider this when there is orbital swelling in those with malignancy or poorly controlled diabetes. Acquisition is through inhalation of spores and spread is via the paranasal sinuses or nasal cavity to the orbit and possibly the brain. Affected tissue becomes necrotic and can result in severe facial disfiguration including loss of the eye and orbit. Diagnosis is by biopsy and fungal stain, and computed tomography may be helpful. Management includes intravenous antifungals such as amphotericin B, surgical debridement, and correction and control of any underlying immunocompromise (Gamba et al, 1986; Kanski, 2007).

Arteriovenous fistula

An arteriovenous fistula is an anastomosis between an artery and a vein which most often occurs secondary to trauma (75%) but may also be spontaneous or congenital. Blood flows preferentially through the fistula rather than the capillary bed, exposing the veins to high-pressure flow (Hamada et al, 2006; Kanski, 2007).

The fistula may present with ipsilateral pulsatile proptosis, chemosis and bruit. Other features include diplopia, decreased visual acuity, orbital oedema, raised intraocular pressure and an afferent pupillary defect. Imaging (with computed tomography or magnetic resonance imaging) may show enlarged extraocular muscles and a dilated superior ophthalmic vein. The fistula should be closed by catheter embolization (Hamada et al, 2006; Kanski, 2007).

There are also low flow, indirect or dural shunts which produce different symptoms (Hamada et al, 2006; Kanski, 2007).

Urgent conditions

These conditions require prompt ophthalmological assessment, preferably within 24 hours.

Idiopathic orbital inflammation

Idiopathic orbital inflammation is an inflammatory process of unknown cause (previously called pseudotumour) that can result in visual loss. It accounts for up to 6% of orbital disorders and is common in those aged 40–50 years. There are multiple presentations, which can result in misdiagnosis (Yuen and Rubin, 2003; Lutt et al, 2008).

Common features include unilateral (usually) pain, rubor and oedema. There may be restricted eye movement and proptosis. Magnetic resonance imaging or computed tomography should be requested and treatment is with systemic steroids and possibly cytotoxics or radiotherapy, although some recommend non-steroidal anti-inflammatory drugs initially (Yuen and Rubin, 2003; Kanski, 2007). An orbital biopsy should be performed to exclude other causes.

Focal orbital inflammation

Myositis and dacryoadenitis are inflammation of localized orbital structures affecting the extraocular muscles and lacrimal apparatus respectively. Myositis most often affects the lateral or superior rectus, causing pain and restricted eye movements and diplopia. Myositis is associated with female gender and upper respiratory tract infection, and may be diagnosed on magnetic resonance imaging (which shows complete involvement of the muscle, in comparison to thyroid eye disease where the tendinous insertion is spared). Treatment of myositis is with oral steroids (Yuen and Rubin, 2003; Isobe et al, 2004; Lutt et al, 2008).

Dacryoadenitis is uncommon, resulting in distortion of the lid into an S-shaped ptosis (*Figures 2a* and *b*), and a reduction in tear production; it often resolves spontaneously (Tomita et al, 2006; Kanski, 2007).

Inflammation in the superior orbital fissure and cavernous sinus results in an acutely painful eye with restricted movement and cranial nerve palsies (particularly 3rd, 4th, 5th and 6th nerves; the Tolosa–Hunt syndrome). Magnetic resonance imaging is the investigation of choice and treatment is with steroids (Lutt et al, 2008). This requires neurology or neuro-ophthalmology referral (depending on services available locally) for exclusion of other causes of cranial nerve palsies.

Urgent outpatient conditions

Whenever a tumour is suspected this should be referred via the 2-week wait pathway so that malignant conditions can be excluded and treatment can be initiated.

Orbital tumours

Benign and malignant tumours affecting the orbit are rare, presenting with gradually increasing proptosis. There is often an associated neurological deficit, such as cranial nerve palsies (including ophthalmoplegia and visual loss). Computed tomography or magnetic resonance imaging is recommended and most tumours require excision.

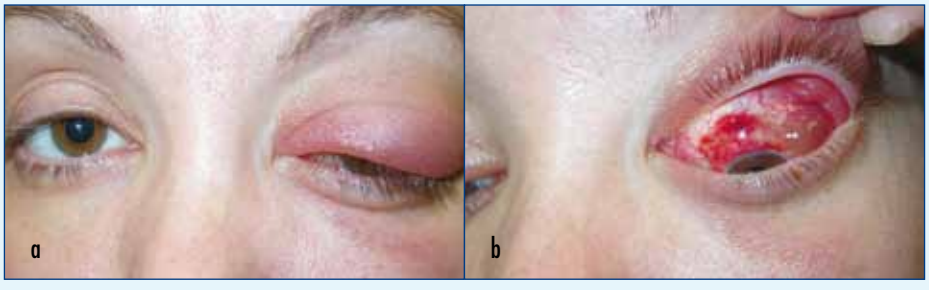
Meningiomas may arise from the optic nerve sheath or be secondary to an intracranial tumour. Prognosis is often good in adults (who may not require treatment) but poor in children (Kanski, 2007).

Schwannomas are encapsulated, slow-growing tumours that have a characteristic magnetic resonance imaging appearance (Tanaka et al, 2004).

Neurofibromatosis type one is associated with both optic nerve glioma (a slow-growing tumour usually present in childhood) and neurofibromas, which cause painful proptosis typically in patients in their mid-30s (Kanski, 2007).

Rhabdomyosarcoma is a rare musculoskeletal tumour accounting for 1–3% of all biopsied orbital malignancies (4–6% of orbital malignancies biopsied in children). Clinical features may include proptosis,

Figure 2. Lacrimal adenitis: demonstrating (a) classical S-shaped ptosis and erythema and (b) and resultant chemosis and conjunctival injection.



globe displacement and pain (around 10% of cases). Ophthalmoscopy may reveal choroidal folds, optic disk oedema and tortuous retinal veins. Onset of clinical signs may be rapid. If treated, rhabdomyosarcoma generally has a good long-term prognosis, even if metastasis has occurred (Shields and Shields, 2003).

Lacrimal gland tumours

The commonest lacrimal gland tumour is a pleomorphic adenoma. Associated ophthalmoplegia suggests posterior extension. Lacrimal gland carcinomas are rare and often painful; they may arise following incomplete excision of a pleomorphic adenoma. Surgical excision is best combined with radiotherapy (Kanski, 2007).

Lymphoproliferative tumours

Orbital lymphoma is usually derived from lacrimal gland mucosa-associated lymphoid tissue. Presentation is often as a rubbery (occasionally bilateral) lesion in an elderly person. Staging computed tomography scan is required to exclude the need for chemotherapy as local lesions are treated with radiotherapy (Kanski, 2007).

Capillary and cavernous haemangioma

Capillary haemangiomas are the commonest paediatric orbital tumours, often presenting at birth. Ultrasound scans and Doppler are required to ascertain the size and relations of the tumour, many of which will resolve spontaneously by the age of 7 years. If required, treatments include laser, steroids and cautery. Capillary haemangiomas are often associated with other systemic conditions (Kanski, 2007).

Cavernous haemangiomas are the commonest adult benign orbital tumours. They are more common in females in their mid-40s and are often located laterally on the muscle cone, posterior to the globe. Presentation is with painless unilateral, axial proptosis and sometimes optic nerve compression. Effective treatment requires surgical removal of the tumour, which is often uncomplicated (Tanaka et al, 2004; Kanski, 2007).

General medical problems

These require a general medical referral with outpatient ophthalmology input.

Thyroid eye disease

Thyroid eye disease is the commonest cause of orbital inflammation in adults in the UK, occurring most often in the context of hyperthyroidism. Up to 50% of people with Grave's disease have associated eye symptoms. Importantly 10% of individuals with thyroid eye disease are euthyroid at presentation. Thyroid eye disease is strongly associated with tobacco smoking, particularly in females. Other contributing aetiological factors include radioiodine treatment and genetic predisposition. Patients usually complain of gritty eyes, photophobia and an abnormal protruding appearance (proptosis) which, if present, reduces pressure in the orbit by increasing the space available (*Figure 3*). Both eyes are normally affected, but often not symmetrically (Cawood et al, 2004; Lutt et al, 2008). Thyroid eye disease is graded by the 'NO SPECS' classification (Cawood et al, 2004).

Inferior and medial recti are most commonly involved. Symptoms are caused by infiltration of inflammatory cells and accumulation of glycosaminoglycans resulting in hypertrophy of adipose tissue, which decreases venous drainage, causing periorbital oedema (Cawood et al, 2004; Lutt et al, 2008).

Diagnosis is by thyroid function tests including thyroid autoantibodies and a radioisotope scan. Computed tomography or magnetic resonance imaging may be performed and a biopsy may be taken to exclude other pathology (Lutt et al, 2008).

As thyroid eye disease is often self-limiting initial treatment is symptomatic such as administration of artificial tears (e.g. hypromellose drops), sleeping propped up on pillows, and cessation of smoking. Up to one third of patients will require medical treatment, possibly including immunosuppressants such as glucocorticosteroids to reduce the acute inflammation and radiotherapy (Cawood et al, 2004).

Thyroid eye disease becomes an emergency when optic nerve compression occurs. This can be detected using magnetic resonance imaging (Kirsch et al, 2009) (*Figure 4*) and clinically by detecting impaired colour vision and optic disc swelling on ophthalmoscopy. There may not be obvious proptosis or inflammation (McKeag et al, 2007). Optic nerve compression may be treated with sight-saving orbital decompression surgery.

Fibrosis and scarring often maintain a degree of the abnormal appearance, even once the condition has resolved, much to the distress of many patients (Yuen and Rubin, 2003; Cawood et al, 2004; Lutt et al, 2008).

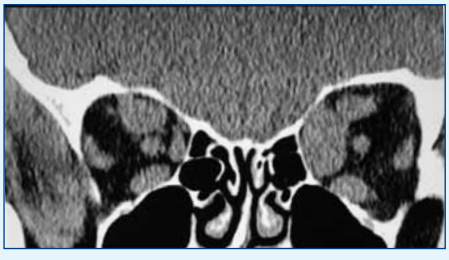
Wegener's granulomatosis

Wegener's is a form of necrotizing granulomatous inflammation and vasculitis affecting small and medium-sized vessels. The respiratory tract, kidneys (necrotizing glomerulonephritis) and sinuses are often affected. The eyes are affected in up to 58% of patients and are the presenting problem in up to 16%, either through small vessel vasculitis (causing episcleritis, scleritis, ulcerative keratitis or uveitis), or through granuloma production (Provenzale et al, 1996; Rootman, 2001; Yuen and Rubin, 2003; Kanski, 2007; Lutt et al, 2008).

Signs and symptoms include bilateral (occasionally unilateral) swollen, painful

Figure 3. Thyroid eye disease: asymmetrical changes and upper lid retraction.

Figure 4. Magnetic resonance imaging showing extraocular muscle enlargement in thyroid eye disease.



orbits, erythema, proptosis, restricted eye movements and signs of optic nerve ischaemia. Diagnosis can usually be confirmed by the presence of serum c-ANCA (circulating anti-neutrophil cytoplasmic antibody) – further tests include computed tomography imaging of the orbit, mastoid and paranasal sinuses, and biopsy. Treatment is with corticosteroids and cyclophosphamide, or occasionally rituximab. If untreated, the renal complications of Wegener's disease may result in death within 2 years (Rootman, 2001; Lutt et al, 2008).

Conditions requiring routine ophthalmological referral

Varices (exophthalmos on Valsalva manoeuvre)

Varices are a type of congenital vascular hamartoma often unilateral and located medially in the upper nasal quadrant (Yuen and Rubin, 2003; Islam et al, 2004). They have thin walls, with low pressure and flow, and are interspersed among normal vessels. Presenting features are caused by engorgement of the varices as a result of increased venous pressure and include intermittent proptosis, haemorrhage and pain. Varices can be differentiated from other causes of orbital swelling by performing Valsava's manoeuvre, which causes exophthalmos.

Surgery is often unsuccessful and so is performed only in severe cases (e.g. with recurrent thrombosis or optic nerve compression) (Islam et al, 2004).

Cysts: dermoid, sebaceous or mucocele

Sebaceous cysts result when the oil-producing sebaceous cysts on the skin and are often small and related to skin. Very rarely they can present as a large lesion producing significant periorbital swelling when inflamed. Sebaceous cysts do not normally require referral if the diagnosis has been made and vision is not affected.

A dacryops is a common, often bilateral, cyst of the lacrimal duct. It should be removed by aspiration.

Dermoid cysts result from displacement of ectoderm subcutaneously to produce a cyst lined by keratinized stratified squamous epithelium that contains sweat and sebaceous glands and possibly hair follicles or intracranial connections. They are painless, located supero-temporal to the orbit and often first occur in childhood. Dermoid cysts are clinically difficult to differentiate from other cysts until excision (Kanski, 2007).

Cephaloceles normally present in young children, often with other abnormalities such as neurofibromatosis type one or cleft palate. Congenital skull base defects allow herniation of intracranial contents, which may enlarge on crying or straining and there may be globe displacement or pulsatile proptosis (without bruit) (Kanski, 2007).

Mucoceles result from obstruction of a paranasal sinus as a result of trauma, allergy or infection. Symptoms are usually caused by pressure and may include diplopia and proptosis. The cyst should be completely removed surgically and sinus drainage should be restored (Kanski, 2007).

Conclusions

There are many causes of orbital swelling with varied degrees of urgency and importance. The commonest cause of orbital swelling is thyroid eye disease. Acute orbital inflammation and mucormycosis are ophthalmic emergencies and may even be life threatening. The on-call ophthalmology team should be informed of these conditions immediately.

Any condition resulting in visual loss, whichever category of urgency it appears to fall in, should result in emergency referral to an ophthalmologist.

Gradually progressive orbital swelling (especially if painful) may require imaging with computed tomography or magnetic resonance imaging to exclude neoplastic disease. Cysts require only routine outpatient ophthalmological referral.

The following mnemonic should to help remember the different causes of orbital swelling:

L Localized or idiopathic inflammation
O Orbital cellulitis
N Neoplastic
G Granulomatosis (Wegener's)

F Fungal infection (mucormycosis)
A Arteriovenous malformations (and other vascular)
C Cysts
E Endocrine (thyroid). BJHM

Conflict of interest: none.

Cawood T, Moriarty P, O'Shea D (2004) Recent developments in thyroid eye disease. *BMJ* **329:** 385–90

Drake E, Vogl W, Mitchel A (2004) *Gray's Anatomy for Students.* 1st edn. Churchill Livingstone, London

Gamba JL, Woodruff WW, Djang WT, Yeates AE (1986) Craniofacial mucormycosis: assessment with CT. *Radiology* **160**(1): 207–12

Hamada J, Morioka M, Kai Y, Sakurama T, Kuratsu J (2006) Spontaneous arteriovenous fistula of the orbit: case report. *Surg Neurol* **65:** 55–7

Hasanee K, Sharma S (2004) Ophthaproblem. Orbital cellulitis. *Can Fam Physician* **50:** 365–7

Ho CF, Huang YC, Wang CJ, Chiu CH, Lin TY (2007) Clinical analysis of computed tomography-staged orbital cellulitis in children. *J Microbiol Immunol Infect* **40**(6): 518–24

Islam N, Mireskandari K, Rose G (2004) Orbital varices and orbital wall defects. *Br J Ophthalmol* **88:** 1092–3

Isobe K, Uno T, Kawakami H et al (2004) Radiation therapy for idiopathic orbital myositis: two case reports and literature review. *Radiat Med* **22:** 429–31

Kanski JJ (2007) *Clinical Ophthalmology: a Systematic Approach.* 6th edn. Elsevier Butterworth-Heinemann, London

Kirsch E, Hammer B, von Arx G (2009) Graves' orbitopathy: current imaging procedures. *Swiss Med Wkly* **139**(43-44): 618–23

Lutt J, Lim L, Phal P, Rosenbaum J (2008) Orbital Inflammatory Disease. *Semin Arthritis Rheum* **37**: 207–22

McKeag D, Lane C, Lazarus JH et al; European Group on Graves' Orbitopathy (2007) Clinical features of dysthyroid optic neuropathy: a European Group on Graves' Orbitopathy (EUGOGO) survey. *Br J Ophthalmol* **91**(4): 455–8

Provenzale J, Mukherji S, Allen N, Castillo M, Weber A (1996) Orbital involvement by Wegener's granulomatosis: imaging findings. *Am J Roentgenol* **166**(4): 929–34

Rootman J (2001) Inflammatory diseases of the orbit. *J Fr Ophtalmol* **24**(2): 155–61

Shields JA, Shields CL (2003) Rhabdomyosarcoma: Review for the ophthalmologist. *Surv Ophthalmol* **48**(1): 39–57

Tanaka A, Mihara F, Yoshiura T et al (2004) Differentiation of cavernous hemangioma from schwannoma of the orbit: a dynamic MRI study. *Am J Roentgenol* **183:** 1799–804

Tole DM, Anderton LC, Hayward JM (1995) Orbital cellulitis demands urgent recognition, urgent admission and aggressive management. *J Accid Emerg Med* **12**(2): 151–3

Tomita M, Shimmura S, Tsubota K, Shimazaki J (2006) Dacryoadenitis associated with Acanthamoeba keratitis. *Arch Ophthalmol* **124:** 1239–42

Yuen SJA, Rubin PAD (2003) Idiopathic orbital inflammation: distribution, clinical features, and treatment outcome. *Arch Ophthalmol* **121**(4): 491–9

KEY POINTS

- Orbital swelling may require routine, urgent or emergency management.
- Acute orbital inflammation and mucormycosis are emergencies.
- The commonest cause of orbital swelling is thyroid eye disease.
- Any condition resulting in visual loss should be referred to an ophthalmologist.
- The mnemonic 'LONG FACE' helps recall some causes of orbital swelling.