Acquired unilateral proptosis – an overview of aetiology and radiological considerations

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Introduction
Proptosis, a common sign with a broad differential diagnosis, is the anterior displacement and protrusion of one or both orbital globes. Patients present with varying degrees of chronicity, visual loss and associated symptoms, with some requiring urgent treatment. Proptosis can be axial, where the pathology lies within the extraocular muscle cone (intraconal) or non-axial, where the lesion is extracranial. In general medical parlance, proptosis and exophthalmos are often used interchangeably, but different authors have made distinctions in the terminology. Some clinicians utilise exophthalmos to signify anterior globe displacement related to underlying endocrine dysfunction, with proptosis referring to non-endocrine causes. Others distinguish according to severity, with proptosis implying protrusion of ≤18mm and exophthalmos protrusion of >18mm. For clarity, this article will use only the term proptosis.

In addition to clinical assessment, proptosis may be quantified with CT or MR imaging, assuming the patient looks straight ahead with both eyes open. Using the axial slice which best demonstrates the lenses, a line is drawn between the anterior zygomatic margins (interzygomatic line – IZL). The distance between this line and the anterior globe margin is measured. Values >21mm are diagnostic of proptosis. Alternatively, the distance from the posterior globe margin to the IZL is measured, which should be 5mm or >5mm in normal eyes.

Differential diagnoses for bilateral proptosis are considerably narrower than for unilateral disease. Absolute symmetry in nature is unusual, therefore every case of bilateral proptosis can initially present unilaterally. This article is solely concerned with the causes of acquired proptosis which may present unilaterally. We have divided these into a “surgical sieve” in Table 1, thereafter describing the more common entities with important radiological features (highlighted in red) in greater detail.

Table 1
Causes of acquired unilateral proptosis and pseudo-proptosis (conditions highlighted in red will be discussed in more detail).

<table>
<thead>
<tr>
<th>Vascular</th>
<th>Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid-cavernous fistula</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Cavernous sinus thrombosis</td>
<td>Schwannoma</td>
</tr>
<tr>
<td>Cavernous haemangioma</td>
<td>Sinonasal tumour</td>
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<tr>
<td>Orbital varix</td>
<td>Lacrimal gland tumour</td>
</tr>
<tr>
<td>Giant aneurysm of intracavernous internal carotid/ophthalmic artery</td>
<td>Meningioma</td>
</tr>
<tr>
<td>Pseudoproptosis: Contralateral globe rupture</td>
<td>Neurofibroma</td>
</tr>
<tr>
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<td>Optic nerve glioma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trauma</th>
<th>Endocrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial fracture, soft tissue swelling and retrobulbar haemorrhage</td>
<td>Thyroid associated ophthalmopathy</td>
</tr>
<tr>
<td>Post-traumatic mucocele</td>
<td>Pseudoproptosis: Ipsilateral lid retraction</td>
</tr>
<tr>
<td>Pseudoproptosis: Contralateral enophthalmos</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Inflammatory</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory orbital pseudotumour/IgG4-RSD</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>Dacryoadenitis</td>
<td>Fibrous dysplasia</td>
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<td>Orbital myositis</td>
<td>Langerhan cell histiocytosis</td>
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<td>Tolosa-Hunt syndrome</td>
<td>Erdheim-Chester disease</td>
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<tr>
<td>Wegener’s granulomatosis</td>
<td>Pseudoproptosis: Contralateral silent-sinus syndrome</td>
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<td>Sinus mucocele</td>
<td>Contralateral ptosis</td>
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<td>Sarcoïd</td>
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<td>Churg-Strauss syndrome</td>
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<tr>
<td>Orbital cellulitis</td>
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<td>Mucormycosis</td>
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Vascular
Carotid-cavernous fistula
Direct carotid-cavernous fistulas (CCF) are formed by abnormal communication between the carotid artery and cavernous sinus. It usually occurs secondary to trauma, but may be spontaneous in the presence of atherosclerosis. While rarely life-threatening, CCF carries a risk of permanent visual loss secondary to central retinal vein occlusion and ischaemic optic neuropathy. With slower blood flow from
the meningeal branches of the carotid arteries into the cavernous sinus, an indirect CCF often presents with more subtle signs.

CT and MR demonstrate proptosis secondary to muscle enlargement and venous engorgement, with prominence of the superior ophthalmic vein.\(^9\) Contrast enhanced CT angiogram or time-of-flight MRA studies are sensitive, less invasive methods than interventional angiography of investigating suspected fistulae. Prompt neuro-interventional treatment is important to reduce venous congestion and salvage residual vision.

**Cavernous sinus thrombosis**

Spreading infection from orbital cellulitis, mucormycosis or nasal and dental infections may result in cavernous sinus thrombosis. The condition starts unilaterally, but untreated will invariably become bilateral. Potentially fatal, urgent intravenous antibiotics and abscess drainage are sometimes required. Diagnosis is primarily clinical, although radiological studies are helpful to confirm the diagnosis. Non-contrast CT demonstrates superior ophthalmic vein distension and periorbital swelling, while contrast studies show non-enhancement of the affected cavernous sinus.

**Cavernous haemangioma**

This is the commonest benign orbital tumour in adults, resulting in painless, axial proptosis.\(^7\) The lateral aspect of the intracanal and retrobulbar space is the commonest anatomical site. Although rare, they can extend intracranially and compress the optic nerve and vessels at the orbital apex. Apical lesions may cause optic nerve compromise in the absence of significant proptosis.

With CT, cavernous haemangiomas appear as well-defined, homogenous, high-attenuation lesions, often oval in shape. Their characteristic delayed pattern of venous enhancement is best visualised on double or triple phase contrast enhanced CT. MR demonstrates hyperintensity to muscle on T1W and T2W sequences, with areas of signal void (microcalcification). Enhancement is most striking during the delayed phase.\(^8\)

**Trauma**

**Facial fracture, soft tissue swelling and retrobulbar haemorrhage**

Facial fractures may cause proptosis due to displacement of the intact globe and an apparently reduced globe volume.\(^9\) Unilateral proptosis may be secondary to soft tissue swelling and importantly, retrobulbar haemorrhage. Retrobulbar haemorrhage is an ophthalmic emergency and should be diagnosed clinically—a sight-saving lateral canthotomy and inferior cantholysis should not be delayed.

Non-contrast thin slice (0.625-1.25mm) CT with volumetric reconstructions is the modality of choice for acute orbital trauma.\(^7\) With CT, soft tissue windows help identify haematoma, organic foreign bodies (eg wood), air and extraocular muscle herniations (eg blow-out fracture) and enable assessment of globe integrity with visualisation of the superior ophthalmic vein. Surgical emphysema is readily apparent (figure 1). Bony windows permit detailed evaluation of fracture patterns and identification of inorganic foreign bodies.

**Endocrine**

**Thyroid associated ophthalmopathy (TAO)**

This is the commonest cause of acquired proptosis and may present bilaterally or, as in half of cases, an asymmetric unilateral process.\(^10\) Muscle enlargement can lead to optic nerve compression and risks permanent visual loss secondary to optic neuropathy.

Imaging is used to assess the degree of proptosis, the presence of optic nerve compression and the extent of muscular infiltration. STIR sequence MRI can be used to distinguish active from dormant disease, with muscle high signal seen in more active disease.\(^11\) Early TAO appearances on CT are non-specific, potentially only demonstrating bulky retro-orbital fatty stranding. The inferior rectus muscle is almost always affected first, followed by the medial, superior and then lateral recti consecutively. Oblique muscle infiltration is rare.\(^12\) On CT the striking, reliable difference between TAO and inflammatory orbital pseudotumour is sparing of the inserting ligaments occurring in TAO, without pain. While most clinical quandaries can be answered with thin slice CT and volumetric reconstruction, MRI better delineates soft tissue involvement.

**Inflammatory**

**Inflammatory orbital pseudotumour**

This is a diagnosis of exclusion, with a proportion of cases thought to be a manifestation of the increasingly recognised concept of IgG4-related systemic disease (IgG4-RSD).\(^14\) Although essentially a disease of the orbital adnexae, its clinical presentation is highly variable depending on the site of pathology. Onset may be acute, sub-acute or chronic, unilateral or bilateral. It may present focally involving conal muscles, lacrimal gland or optic nerve, or diffusely involving the entire orbit. Occasionally, it can result in posterior scleritis with secondary chorioidal detachments, both of which may be visible with contrast CT (figure 2). The radiographic appearance of chorioidal detachments may resemble a tennis ball (figure 2). The tennis-ball sign is a recognised feature in aortic dissection, but to our knowledge has not previously been described in relation to chorioidal detachments. Extraorbital extension into the cavernous sinus, infra-temporal fossa, naso-pharynx and maxillary sinuses have also been reported.\(^15\)

Diagnosis is predominantly based on serological and histological findings. High-resolution contrast enhanced CT or MRI are necessary to exclude other orbital pathologies. Retro-orbital fat and muscle bellies are often involved. In contrast to TAO, tendons are frequently affected, with the lateral rectus muscle usually being involved first. The lacrimal glands are invariably affected, appearing enlarged and ill-defined. This feature is similar to lymphomatous infiltration which is often painless. Where there are concerns regarding the possibility of lymphoma, or if a patient is unresponsive to treatment, fine needle aspiration or tissue biopsy may be needed.\(^16\)

MR with contrast and diffusion weighted imaging (DWI) may further characterise the soft tissue involvement and is increasingly utilised to differentiate tumour from infective or haemorrhagic tissue. Intracranial and extraorbital extension is best characterised with multi-planar MR. However, MR appearances are variable and sometimes non-specific. On T1W imaging, the infiltrated region is iso-intense to the adjacent muscle. With T2W, the appearances vary between hypo-, iso- or hyper-intense and there is invariably increased enhancement post-contrast administration.

**Infective**

**Orbital cellulitis**

Being most prevalent in children following sinusitis or in adults with odontogenic sepsis, the distinction between pre-septal and orbital cellulitis is important radiologically. Although the orbital septum separates these two compartments, cellulitis can cross this divide.\(^17\) CT and MR findings can appear similar to pseudotumour. The primary examination is a contrast-enhanced CT to define sinus bony anatomy, exclude abscess formation (figure 3) and rule out serious intracranial complications.\(^16\)

Table 2 summarises the key radiological considerations in orbital cellulitis.
<table>
<thead>
<tr>
<th>Non-contrast CT</th>
<th>Post-septal/pre-septal</th>
<th>Intra-conal inflammation?</th>
<th>Globe intact?</th>
<th>Drainable collection?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contrast CT brain</strong></td>
<td>Intracranial extension?</td>
<td>Sinus thrombosis?</td>
<td>Optic sheath / nerve involvement</td>
<td></td>
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<tr>
<td><strong>MR</strong></td>
<td>Hyperintense on T2W</td>
<td>Necrosis: hypo-intense</td>
<td>Variable contrast enhancement</td>
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</table>

**Table 2** Radiological considerations in orbital cellulitis.

**Tumour**

**Lymphoma**

Most orbital lymphomas are extracranial, usually beginning in lacrimal gland tissue and conjunctiva due to lymphoid tissue content. The superolateral position of a bulky involved lacrimal gland usually presents with downward proptosis. Less frequently, perineural infiltrates around the optic nerve can occur. Lymphoma typically insinuates and encases adjacent structures without bony erosion. In 75%, the orbital findings are part of systemic disease.

Orbital CT appearances are variable and may show a well or poorly defined, moderately enhancing lesion, sometimes seemingly identical to lacrimal involvement with pseudotumour. Clinical history and assessment of potential nodal and systemic involvement with a staging CT are pivotal in making the appropriate diagnosis.

**Schwannoma**

These arise from the peripheral cranial oculomotor, trochlear and trigeminal nerves. They are rare, non-tender, frequently benign, slowly enlarging tumours with eccentric proptosis. Radiographically, the lesion is well defined with minimal structural change to adjacent orbital structures. Hyper-density with enhancement is seen on CT. Enhancement is also seen on MRI, the lesions being hypointense on T1W imaging and hyperintense on T2W.

**Sinonasal tumour**

Sinonasal tumours can present with epistaxis, nasal obstruction, headache, cranial neuropathies and proptosis. Squamous cell carcinoma (SCC) accounts for 60-85% of sinonasal malignancies, with more than half occurring in the maxillary antrum. Radiologically, the lesion is well defined with minimal structural change to adjacent orbital structures. Hyper-density with enhancement is seen on CT. Enhancement is also seen on MRI, the lesions being hypointense on T1W imaging and hyperintense on T2W.

**Optic nerve glioma**

This pathology commonly occurs in children but can present as late as the third decade. A CT will demonstrate a well-defined uniform encasement of the optic nerve. Gliomas with concurrent NF-1 often appear irregular, heterogeneous and poorly defined. MR demonstrates an iso/hypointense lesion on T1W that is hyperintense on fluid sensitive sequences. Both MR and CT show contrast enhancement.

**Conclusion**

The aetiology of acquired unilateral proptosis is diverse, ranging from benign to life-threatening. Accordingly, a thorough analysis and inter-disciplinary discussion is required to agree a differential diagnosis (table 1). This differential can be significantly narrowed with targeted investigations including appropriate neuro imaging. This article provides a non-exhaustive summary of the more common entities, and those with characteristic radiological features.

**References**

Figure 1
Trauma with orbital emphysema.

Figure 2
Left: CT demonstrating right inflammatory orbital pseudotumour with posterior scleritis (note posterior scleral thickening) and choroidal detachments resembling tennis ball. Right: Same patient with contralateral involvement during previous episode of orbital pseudotumour, again demonstrating posterior scleral thickening and tennis ball sign.

Figure 3
Left: Left orbital cellulitis with proptosis, ethmoid opacification and slim subperiosteal abscess. Right: Coronal slice of same patient.