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**Orbital inflammatory disease: Pictorial review and differential diagnosis**

Pakdaman MN *et al.* Orbital inflammatory disease: Pictorial review

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**Abstract**

Orbital inflammatory disease (OID) represents a collection of inflammatory conditions affecting the orbit. OID is a diagnosis of exclusion, with the differential diagnosis including infection, systemic inflammatory conditions, and neoplasms, among other conditions. Inflammatory conditions in OID include dacryoadenitis, myositis, cellulitis, optic perineuritis, periscleritis, orbital apicitis, and a focal mass. Sclerosing orbital inflammation is a rare condition with a chronic, indolent course involving dense fibrosis and lymphocytic infiltrate. Previously thought to be along the spectrum of OID, it is now considered a distinct pathologic entity. Imaging plays an important role in elucidating any underlying etiology behind orbital inflammation and is critical for ruling out other conditions prior to a definitive diagnosis of OID. In this review, we will explore the common sites of involvement by OID and discuss differential diagnosis by site and key imaging findings for each condition.

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**Key words:** Orbit; Inflammation; Pseudotumor; Orbital inflammatory disease; Nonspecific orbital inflammation; Dacryoadenitis; Myositis; Orbital cellulitis; Optic perineuritis; Orbital apicitis

**Core tip:** This review provides a pictorial summary of orbital inflammatory disease. It outlines many key aspects of OID on imaging that can be used to distinguish from other pathologic conditions. The review also provides an up-to-date overview of the best approaches to imaging workup when suspecting OID.

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**INTRODUCTION**

Orbital inflammatory disease (OID, aka orbital inflammatory pseudotumor, idiopathic orbital inflammatory syndrome, nonspecific orbital inflammation)[[1-3](#_ENREF_1)] was first described by Gleason in 1903[[4](#_ENREF_4)] and accounts for 6% of diseases involving the orbit. It is the third most common orbital disease after Grave’s orbitopathy and lymphoproliferative diseases[[5](#_ENREF_5)]. OID is most commonly unilateral with symptoms and clinical findings depending on the site involved as well as the degree of inflammation, fibrosis, and any mass effect. Generally, acute OID presents with proptosis, extraocular motility disturbance, pain, erythema, and chemosis[[2](#_ENREF_2)]. As OID is a diagnosis of exclusion, patients must be evaluated to rule out any malignancy, infection, systemic inflammatory process, or other concomitant medical conditions[[6](#_ENREF_6)]. The differential diagnosis includes local and systemic inflammatory conditions caused by neoplasm, infection, vascular malformation, and trauma[[5](#_ENREF_5)].

Inflammation occurs as a non-specific response to potentially harmful stimuli and is marked by increased blood ﬂow and vascular permeability, vasodilatation, release of soluble mediators, extravasation of ﬂuids, and cellular inﬂux[[7](#_ENREF_7)]. Imaging findings in inflammatory disease are most often related to increased blood-tissue permeability resulting in contrast enhancement, which is often best seen with the use of fat suppression. Other common imaging findings in inflammation include fibrosis and edema[[8](#_ENREF_8)].

The site of involvement by OID dictates the radiological differential diagnosis, which can be especially important given that the symptoms may be nonspecific. We will review the common sites of involvement by OID and discuss differential diagnosis by site, as outlined in Table 1. However, it is important to note that OID commonly involves multiple sites, and that this feature is often important in suggesting OID ahead of other lesions.

***Dacryoadenitis***

Inflammation of the lacrimal gland, termed “dacryoadenitis”, is commonly seen in OID. Clinically, dacryoadenitis presents as a painful, firm, erythematous mass with edema in the lateral upper lid, and possible ptosis[[9](#_ENREF_9),[10](#_ENREF_10)]. Because the abnormality diffusely involves the lymphoid structures of the lacrimal gland, the classic appearance is of diffuse enlargement of the gland, including the orbital and palpebral lobes (Figure 1)[[10](#_ENREF_10),[11](#_ENREF_11)]. This is an important feature in distinguishing inflammatory disease from an epithelial neoplasm, which will typically only involve a portion of the lacrimal gland, usually the orbital lobe (Figure 2). Additional features that suggest an inflammatory process are a compressed, “almond-shaped” appearance of the gland as well as a tapered posterior margin of the gland. In contrast, an epithelial neoplasm will typically be seen as well-circumscribed and round to oval in shape[[10](#_ENREF_10),[12](#_ENREF_12)]. The axial T2 MRI in Figure 1A shows diffuse enlargement of the left lacrimal gland. Note the tapered posterior margin, as well as the involvement of the orbital lobe. These findings suggest a lymphoid or inflammatory process rather than an epithelial neoplasm.

Although it is usually relatively straightforward to distinguish an epithelial lacrimal gland neoplasm from a process involving the glandular lymphoid tissue, it is not always easy to distinguish lymphoma of the lacrimal gland from inflammatory disease. There are a few features that can aid in this distinction. First, inflammatory disease is more commonly bilateral (30% of chronic and 20% of acute inflammatory disease *vs* 12%-18% of lymphoma cases)[[13-15](#_ENREF_13)]. Second, inflammatory disease is more commonly associated with inflammation of the surrounding soft tissues. Figure 1B is an axial fat-suppressed contrast-enhanced T1 that shows infiltration of the preseptal and post septal fat. These features suggest OID rather than orbital lymphoma. There are exceptions to these rules, however. Sarcoid commonly produces diffuse lacrimal gland enlargement without infiltration of surrounding fat, a pattern that is more suggestive of lymphoma. Lymphoma may also have a surrounding inflammatory component in some cases[[12](#_ENREF_12)].

Diffusion-weighted imaging (DWI) is perhaps the most reliable technique to distinguish lymphoma from inflammatory disease. The densely packed cells in lymphoma inhibit the non-random motion of water, causing lymphoma to appear bright on DWI, with associated reduction in ADC (Figure 3). An ADC of less than 0.92 × 10-3 mm2/s was shown to be 100% sensitive and specific in distinguishing lymphoma from inflammatory disease[[3](#_ENREF_3)], though we have seen a handful of exceptions to this rule. Politi *et al*[[13](#_ENREF_13)] found an ADC threshold of 0.775 × 10-3 mm2/s was 96% sensitive and 93% specific for diagnosing ocular adnexal lymphoma.

***Myositis***

Orbital myositis is a non-infectious inflammatory condition primarily affecting the extraocular muscles (EOM)[[16](#_ENREF_16)]. Clinically, it presents with unilateral orbital or periorbital pain (17%-69%), painful and restricted eye movement (46%-54%), proptosis (32%-82%), periorbital edema (42%-75%), and hyperemia of the conjunctiva (33%-48%)[[17](#_ENREF_17)]. The classic appearance of EOM myositis includes a unilateral thickening of one or two EOMs, often also involving the surrounding fat, tendon, and myotendinous junction (Figure 4). These are important features in distinguishing myositis from thyroid orbitopathy, which typically produces bilateral inflammation of EOM and spares the myotendinous junction. Of note, sparing of the myotendinous junction alone does not exclude OID. The lateral rectus and superior oblique muscles are also relatively spared early in the disease course in thyroid orbitopathy, and the condition often presents clinically with proptosis, chemosis, and diplopia. These findings may also suggest IgG4-related disease (IgG4-RD), which may present with similar clinical symptoms. The lymphocytic infiltration characteristic of IgG4-RD is often seen as inflammation of bilateral lacrimal glands and EOM’s[[18](#_ENREF_18)]. The most frequently affected muscle is the inferior rectus. In patients with normal TSH and thyroid, these findings may suggest IgG4-RD and a serum IgG4 level may be considered.

The differential diagnosis for myositis also includes orbital cellulitis, which is commonly accompanied by fever, leukocytosis, and a clinical history of head and neck infection. Contrast-enhanced CT imaging may identify the source of spread to the orbit and may also help identify any abscess that requires surgical intervention[[17](#_ENREF_17)]. Figure 5 demonstrates a case of infectious orbital cellulitis where corresponding sinus disease can be appreciated. Metastases and lymphoma may also mimic myositis and are often seen as a focal mass with increased signal intensity in the EOM’s[[17](#_ENREF_17)]. Patients with low-flow carotid cavernous fistula (CCF) may also share features with myositis, as the venous congestion may appear on CT and MRI as inflamed EOM[[19](#_ENREF_19)] (Figure 6). Enlarged superior ophthalmic veins are typically seen in CCF. Transcranial doppler ultrasonography allows visualization of retrograde flow through the superior ophthalmic vein (SOV), suggestive of CCF[[20](#_ENREF_20)] and angiography can be used to best characterize the fistulous communication (Figure 6C).

Contrast-enhanced T1 MRI with fat suppression best visualizes inflammation of the muscles, tendons, and surrounding fat, which is seen as swelling of the tendon and belly of the EOM. While not diagnostic, involvement of the perimuscular tendon is a distinguishing finding of non-thyroid inflammatory disease[[17](#_ENREF_17)]. In Figure 4C, a parasagittal oblique fat-suppressed contrast-enhanced T1 shows an enlarged superior rectus muscle belly with uncharacteristic sparing of the tendinous insertion. Nevertheless, unilateral disease, infiltration of the surrounding fat, and early involvement of the superior oblique muscle indicate pseudotumor ahead of thyroid eye disease. In cases where it is difficult to distinguish inflammation versus lymphoma, DWI can be used, as described above.

***Cellulitis***

Inflammatory orbital cellulitis describes inflammation of preseptal (peri-orbital) or postsetpal (orbital) fat[[21](#_ENREF_21)]. Patients typically present with proptosis, chemosis, and painful diplopia[[21](#_ENREF_21)]. Cellulitis of preseptal and orbital soft tissue is best evaluated on contrast-enhanced T1 MRI with fat suppression, where the most common finding is poorly-defined periorbital enhancement enveloping the globe and extending into post-septal fat[[4](#_ENREF_4)]. Figure 7 is a T1-weighted MRI image showing diffuse infiltration of the intraconal fat. Infectious cellulitis shares similar imaging features, and it is important to obtain any clinical history of fever, sinusitis, or meningitis, as well as any evidence of leukocytosis[[2](#_ENREF_2),[11](#_ENREF_11)]. Presence of an abscess is a clear indicator of an infectious process. On T2 MRI, infectious cellulitis typically presents as a hyperintense lesion, whereas OID lesions range from to hypo- to hyperintense[[2](#_ENREF_2)]. Additional features suggesting inflammation of orbital and pre-septal fat include increased density and enhancement of periorbital soft tissues, eyelids, and orbital septum. Intraconal extension is a sign of advanced disease.

The differential diagnosis for inflammatory orbital cellulitis includes infection, CCF, cavernous sinus thrombosis, and Wegener’s granulomatosis. Careful evaluation for any evidence of sinus disease is critical as infectious orbital cellulitis is a potentially life-threatening disease. Clinically, patients with infectious orbital cellulitis may have a history of diabetes or immunocompromise and a clinical history of sinus disease, recent dental procedures, or trauma. Due to the serious nature of infectious orbital cellulitis, a definitive diagnosis of OID may not be made until after a lack of response to empirical broad-spectrum antibiotic therapy[[5](#_ENREF_5)]. A CCF may be distinguished from OID by presence of an enlarged SOV, abnormal fullness of the cavernous sinus, or, in larger fistulas, flow voids on T2 MR imaging. Similar to CCF, cavernous sinus thrombosis presents with an enlarged SOV. A non-enhancing filling defect in the cavernous sinus on CT venography or contrast-enhanced MRI differentiates cavernous sinus thrombosis from CCF or OID. Wegener’s granulomatosis (*i.e.*, granulomatosis with polyangiitis) may also mimic OID but is often accompanied by surrounding sinonasal wall destruction, which is best appreciated on CT.

***Optic perineuritis***

When intraorbital inflammation extends along the optic nerve and nerve sheath, it is termed “perineuritis”[[9](#_ENREF_9)]. Because inflammation affects the nerve sheath rather than the nerve itself, the primary presenting clinical feature is pain, while visual acuity, visual fields, and color vision are typically unaffected[[22](#_ENREF_22)]. Because the abnormality involves a loosely organized inflammatory infiltrate around the optic nerve, the classic appearance is of increased signal intensity surrounding the optic nerve, and extending into adjacent fat on post-gadolinium T1 MRI with fat-suppression (Figure 8A)[[9](#_ENREF_9),[22](#_ENREF_22)]. Enhancement of the optic nerve sheath is often poorly-defined[[23](#_ENREF_23)], which, in addition to a history of pain, may serve as an important feature in distinguishing perineuritis from meningioma (Figure 8B). This finding, along with clinical history of acute, painful presentation, help distinguish perineuritic pseudotumor from en plaque optic nerve sheath meningioma. Features supporting a diagnosis of meningioma include a localized mass and calcifications on CT imaging[[9](#_ENREF_9)].

The differential diagnosis also includes demyelinating optic neuritis, though demyelinating disease almost always spares the soft tissues around the nerve while involving the nerve substance diffusely[[23](#_ENREF_23)]. It is important to distinguish perineuritis from optic neuritis, as the differential diagnosis and clinical course are quite different. Patients with ON are at high risk of developing multiple sclerosis and should be evaluated to rule out this disease. Diagnosis of OPN is also critical, as prompt corticosteroid treatment may help prevent vision loss. Clinically, both OPN and ON typically present with eye pain and a swollen optic disc. While less commonly compared to ON, patients with OPN may also complain of vision impairment, though the vision impairment in OPN is often paracentral or arcuate[[23](#_ENREF_23)]. MR imaging of perineuritis often shows a “tram-track” pattern of enhancement around the nerve, rather than involving the nerve itself. Additionally, syphilitic infection, sarcoidosis, and viral encephalitides should be considered in patients with perineuritis[[24](#_ENREF_24)].

***Periscleritis***

Periscleritis may refer to inflammation of the sclera, uvea (iris, ciliary body, choroid), or tenon’s capsule[[9](#_ENREF_9)]. This condition may present as a uveitis or a scleritis/episcleritis. Clinically, features of this inflammatory condition may mimic infection or tumor and are characterized by orbital pain, exophthalmos, and eyelid edema. Periscleritis can be clearly seen on MR or CT as a heterogeneous thickening along the outer rim of the eye[[25](#_ENREF_25)] (Figure 9), representing thickening of the sclera and/or uvea. Features of periscleritis can be best appreciated on axial T1 post-contrast MRI with fat saturation, which allows visualization of the enhancing vascular choroid as well as any extension into retrobulbar fat. A subchoroidal fluid collection displacing the retina may also be seen. Figure 9A shows an axial contrast-enhanced CT in an 87-year-old immunocompromised man with left eye pain and and ordering indication of “cellulitis”. Note the mild infiltration of the left periorbital fat, periscleral edema, and subtle high density along the temporal surface of the globe suggestive of a subchoroidal fluid collection. An axial fat-suppressed contrast-enhanced T1 MRI in this patient shows these findings more conspicuously (Figure 9B). Tenon’s capsule (aka fascia bulbi or bulbar sheath) is a thin membrane that lies between the sclera and orbital fat[[26](#_ENREF_26)]. Thickening is often seen in this area and may be accompanied by a periscleral fluid collection.

The differential diagnosis includes any systemic inflammatory disease that causes posterior scleritis, such as lupus or rheumatoid arthritis. Endophthalmitis may also have a similar imaging appearance, but clinical vitritis should be readily apparent in these cases. Infectious periscleritis often arises secondary to sinus infection and it is important to evaluate the paranasal sinuses, particularly the ethmoid sinus, in patients with uveoscleral thickening[[4](#_ENREF_4)].

***Focal mass***

OID may also present as a focal inflammatory mass, which represents up to 9% of all orbital mass lesions and is the most common cause of painful orbital mass in adults[[6](#_ENREF_6),[9](#_ENREF_9)]. Clinical presentation is highly variable as an inflammatory mass can be present anywhere in the orbit, with resulting symptoms related to mass effect and inflammation. A mass lesion in OID is best seen on axial T2 MRI, where it appears as a well-defined, T2 hypointense mass, discrete from adjacent EOM and from the lacrimal gland (Figure 10). The hypointensity appreciated in this image is secondary to fibrosis. On T1 MRI they appear slightly brighter, isointense to muscle, and show prominent post-gadolinium enhancement[[27](#_ENREF_27)]. As lesions progress, fibrosis develops, resulting in retraction of adjacent structures. Infiltration of inflammation and fibrosis into the sclera and periorbital soft tissue may lead to globe deformity. In fact, the degree of fibrosis and traction on other tissues often suggests a greater chronicity of disease.

Inflammatory pseudotumors are often difficult to distinguish from a true neoplasm[[28](#_ENREF_28)]. Lymphoma accounts for 20% of orbital mass lesions and is particularly difficult to distinguish from OID[[27](#_ENREF_27),[28](#_ENREF_28)]. Clinically, lymphomatous lesions present more commonly with palpable mass, while OID may present with eyelid edema, optic nerve atrophy, and conjunctival congestion[[27](#_ENREF_27)]. Imaging features of inflammatory pseudotumor that help distinguish it from lymphoma include marked T2 hypointensity and evidence of fibrosis. Lymphoma typically appears more lobular and, as described earlier, has greater diffusion restriction than OID on DWI. Metastases are usually brighter on T2 imaging. One exception to this is scirrhous breast cancer metastasis, which commonly produces a T2-hypointense, fibrotic mass with variable amount of traction on adjacent structures. Certain benign tumors, such as solitary fibrous tumor, can also show marked T2 hypointensity and overlap with OID in appearance[[29](#_ENREF_29)].

***Diffuse OID***

Diffuse orbital inflammation is found in approximately 4%-11% of patients with OID[[30](#_ENREF_30)]. Similar to focal mass, clinical presentation is highly variable as many sites of the orbit can be affected. Patients must be evaluated for systemic disease, including vasculitis and autoimmune conditions such as Churg-Strauss disease or Wegener's granulomatosis[[31](#_ENREF_31),[32](#_ENREF_32)]. Common characteristics of orbital involvement in Wegener's include diffuse infiltration of orbital fat and sinonasal destructive changes (Figure 11). Chest imaging and an immunologic workup are suggested prior to biopsy of diffuse OID. Lymphoma may also mimic diffuse OID and, as described earlier, appears more lobular and may be best distinguished from OID using DWI MRI[[3](#_ENREF_3)]. Chronic inflammation often contains regions with varying degrees of fibrosis, resulting in a heterogeneous appearance on MRI.

***Orbital apicitis***

Involvement of the orbital apex, while less common, is associated with the poorest outcome[[4](#_ENREF_4),[9](#_ENREF_9),[33](#_ENREF_33)]. Inflammatory lesions of the orbital apex are at risk of invading the optic nerve or extending into the cavernous sinus. Tolosa-Hunt syndrome is a rare clinical condition caused by cavernous sinus inflammation presenting with relapsing/remitting acute orbital pain and paralysis of cranial nerves III, IV, V1, and VI[[34](#_ENREF_34)]. Extension of OID into the cavernous sinus is a common cause of this clinical condition and, similar to other OID lesions, intravenous steroid treatment is the mainstay of care[[11](#_ENREF_11),[34](#_ENREF_34)]. On T1 MRI, inflammation appears as an intermediate intensity lesion, as inflammatory tissue replaces the normal high-intensity fat at the orbital apex. Similar to other inflammatory pseudotumors, OID of the orbital apex appears hypointense on T2, with a darker signal indicating higher degrees of fibrosis[[9](#_ENREF_9),[33](#_ENREF_33)]. In addition to the cavernous sinus, lesions of the orbital apex may also extend into the middle cranial fossa through the superior orbital fissure or optic canal, as well as the infratemporal fossa and pterygopalatine fossa through the inferior orbital fissure. Figure 12 shows an axial, fat-suppressed, contrast-enhanced T1 MRI in a patient with Tolosa-Hunt syndrome. Note the ill-defined enhancement involving the right orbital apex and extending into the middle cranial fossa along the margin of the cavernous sinus (arrow). Figure 13 shows bilateral cavernous sinus infiltration in a different patient, which resolved completely after treatment.

The differential diagnosis of orbital apex lesions includes meningioma, granulomatous disease, and local spread of CNS pathology. Evidence of cystic foci likely represents necrotic lesions, which leads the diagnosis away from OID. Enhancement or fullness of the cavernous sinus can be appreciated on dynamic imaging and angiography may demonstrate narrowing of the cavernous sinus. Careful examination for disruption of the dural barrier and intracranial extension is critical. Common features of CNS involvement include abnormal soft tissue extending into the middle cranial fossa, expansion of the ipsilateral cavernous sinus walls, and post-gadolinium enhancement of the meninges or dura[[9](#_ENREF_9)].

***Sclerosing orbital inflammation***

Sclerosing orbital inflammation is a rare condition representing 6%-8% of all inflammatory lesions of the orbit[[35](#_ENREF_35)]. Previously thought to be along the spectrum of OID, it is now considered a distinct pathologic entity. Clinically, it is characterized by proptosis, mild external inflammatory signs, restricted motility, diplopia, and dull, chronic pain[[5](#_ENREF_5)]. The natural history of the condition often involves a chronic, indolent, progressive process involving dense fibrosis and lymphocytic infiltrate. On CT or MRI, it is most commonly described as a homogenous, diffuse, ill-defined mass most frequently in the anterior orbit and mid-orbit.

Definitive diagnosis is by biopsy, revealing dense scarring & fibrosis. While no definitive treatment has been identified, early and aggressive steroid therapy is recommended as vision loss may occur in up to 30% of affected patients[[5](#_ENREF_5)].

**CONCLUSION**

OID or orbital pseudotumor, represents a group of heterogeneous inflammatory diseases, the exact etiology of which is unknown. The condition may involve a number of structures in the orbit, the clinical presentations and imaging findings of which are variable and overlapping. As OID is a diagnosis of exclusion, other pathologic conditions affecting the orbit must be ruled out. Imaging plays an important role in evaluation of OID, with proper identification of involved structures being a critical first step toward diagnosis. CT, MRI with fat suppression, and DWI all play a role in distinguishing OID from other pathologies affecting the orbit. Treatment for OID consists of pulsed corticosteroid therapy and the degree of response may often provide clues as to the diagnosis.

**REFERENCES**

1 **Swamy BN**, McCluskey P, Nemet A, Crouch R, Martin P, Benger R, Ghabriel R, Wakefield D. Idiopathic orbital inflammatory syndrome: clinical features and treatment outcomes. *Br J Ophthalmol* 2007; **91**: 1667-1670 [PMID: 17620331 DOI: 10.1136/bjo.2007.124156]

2 **Kapur R**, Sepahdari AR, Mafee MF, Putterman AM, Aakalu V, Wendel LJ, Setabutr P. MR imaging of orbital inflammatory syndrome, orbital cellulitis, and orbital lymphoid lesions: the role of diffusion-weighted imaging. *AJNR Am J Neuroradiol* 2009; **30**: 64-70 [PMID: 18842758 DOI: 10.3174/ajnr.A1315]

3 **Sepahdari AR**, Aakalu VK, Setabutr P, Shiehmorteza M, Naheedy JH, Mafee MF. Indeterminate orbital masses: restricted diffusion at MR imaging with echo-planar diffusion-weighted imaging predicts malignancy. *Radiology* 2010; **256**: 554-564 [PMID: 20656840 DOI: 10.1148/radiol.10091956]

4 **Yuen SJ**, Rubin PA. Idiopathic orbital inflammation: distribution, clinical features, and treatment outcome. *Arch Ophthalmol* 2003; **121**: 491-499 [PMID: 12695246 DOI: 10.1001/archopht.121.4.491]

5 **Gordon LK**. Orbital inflammatory disease: a diagnostic and therapeutic challenge. *Eye (Lond)* 2006; **20**: 1196-1206 [PMID: 17019419 DOI: 10.1038/sj.eye.6702383]

6 **Lee EJ**, Jung SL, Kim BS, Ahn KJ, Kim YJ, Jung AK, Park CS, Song SY, Park NH, Kim MS. MR imaging of orbital inflammatory pseudotumors with extraorbital extension. *Korean J Radiol* 2005; **6**: 82-88 [PMID: 15968146]

7 **Ferrero-Miliani L**, Nielsen OH, Andersen PS, Girardin SE. Chronic inflammation: importance of NOD2 and NALP3 in interleukin-1beta generation. *Clin Exp Immunol* 2007; **147**: 227-235 [PMID: 17223962 DOI: 10.1111/j.1365-2249.2006.03261.x]

8 **Narla LD**, Newman B, Spottswood SS, Narla S, Kolli R. Inflammatory pseudotumor. *Radiographics* 2003; **23**: 719-729 [PMID: 12740472 DOI: 10.1148/rg.233025073]

9 **Ding ZX**, Lip G, Chong V. Idiopathic orbital pseudotumour. *Clin Radiol* 2011; **66**: 886-892 [PMID: 21546008 DOI: 10.1016/j.crad.2011.03.018]

10 **Mafee MF**, Edward DP, Koeller KK, Dorodi S. Lacrimal gland tumors and simulating lesions. Clinicopathologic and MR imaging features. *Radiol Clin North Am* 1999; **37**: 219-39, xii [PMID: 10026740]

11 **Lutt JR**, Lim LL, Phal PM, Rosenbaum JT. Orbital inflammatory disease. *Semin Arthritis Rheum* 2008; **37**: 207-222 [PMID: 17765951 DOI: 10.1016/j.semarthrit.2007.06.003]

12 **Gündüz K**, Shields CL, Günalp I, Shields JA. Magnetic resonance imaging of unilateral lacrimal gland lesions. *Graefes Arch Clin Exp Ophthalmol* 2003; **241**: 907-913 [PMID: 14579116 DOI: 10.1007/s00417-003-0748-z]

13 **Politi LS**, Forghani R, Godi C, Resti AG, Ponzoni M, Bianchi S, Iadanza A, Ambrosi A, Falini A, Ferreri AJ, Curtin HD, Scotti G. Ocular adnexal lymphoma: diffusion-weighted mr imaging for differential diagnosis and therapeutic monitoring. *Radiology* 2010; **256**: 565-574 [PMID: 20656841 DOI: 10.1148/radiol.10100086]

14 Lacrimal Gland Tumor Study Group. An epidemiological survey of lacrimal fossa lesions in Japan: number of patients and their sex ratio by pathological diagnosis. *Jpn J Ophthalmol* 2005; **49**: 343-348 [PMID: 16187032 DOI: 10.1007/s10384-005-0224-x]

15 **Derr C**, Shah A. Bilateral dacryoadenitis. *J Emerg Trauma Shock* 2012; **5**: 92-94 [PMID: 22416166 DOI: 10.4103/0974-2700.93096]

16 **Kralik SF**, Kersten R, Glastonbury CM. Evaluation of orbital disorders and cranial nerve innervation of the extraocular muscles. *Magn Reson Imaging Clin N Am* 2012; **20**: 413-434 [PMID: 22877949 DOI: 10.1016/j.mric.2012.05.005]

17 **Costa RM**, Dumitrascu OM, Gordon LK. Orbital myositis: diagnosis and management. *Curr Allergy Asthma Rep* 2009; **9**: 316-323 [PMID: 19656480]

18 **Inaba H**, Hayakawa T, Miyamoto W, Takeshima K, Yamaoka H, Furukawa Y, Kawashima H, Ariyasu H, Wakasaki H, Furuta H, Nishi M, Nakao T, Sasaki H, Okada Y, Matsunaga K, Nakamura Y, Akamizu T. IgG4-related ocular adnexal disease mimicking thyroid-associated orbitopathy. *Intern Med* 2013; **52**: 2545-2551 [PMID: 24240795]

19 **Chapman PR**, Gaddamanugu S, Bag AK, Roth NT, Vattoth S. Vascular lesions of the central skull base region. *Semin Ultrasound CT MR* 2013; **34**: 459-475 [PMID: 24216454 DOI: 10.1053/j.sult.2013.09.003]

20 **Kiliç T**, Elmaci I, Bayri Y, Pamir MN, Erzen C. Value of transcranial Doppler ultrasonography in the diagnosis and follow-up of carotid-cavernous fistulae. *Acta Neurochir (Wien)* 2001; **143**: 1257-164, discussion 1257-164, [PMID: 11810390 DOI: 10.1007/s007010100022]

21 **Danesh-Meyer HV**, Rosser PM. Orbital inflammatory disease. *Int Ophthalmol Clin* 2007; **47**: 79-92, ix [PMID: 18049282 DOI: 10.1097/IIO.0b013e3181571eee]

22 **Szatmáry G**. Imaging of the orbit. *Neurol Clin* 2009; **27**: 251-84, x [PMID: 19055983 DOI: 10.1016/j.ncl.2008.09.008]

23 **Purvin V**, Kawasaki A, Jacobson DM. Optic perineuritis: clinical and radiographic features. *Arch Ophthalmol* 2001; **119**: 1299-1306 [PMID: 11545635]

24 **Nakamura M**, Hara R, Kimura R, Ohgiya N, Yamamoto N, Morino I, Yamamoto M. Optic perineuritis not associated with syphilitic infection. *Neuro-Ophthalmology* 1999; 21(3): 135-145 [DOI: 10.1076/noph.21.3.135.3900]

25 **Atlas SW**, Grossman RI, Savino PJ, Sergott RC, Schatz NJ, Bosley TM, Hackney DB, Goldberg HI, Bilaniuk LT, Zimmerman RA. Surface-coil MR of orbital pseudotumor. *AJR Am J Roentgenol* 1987; **148**: 803-808 [PMID: 3493667 DOI: 10.2214/ajr.148.4.803]

26 **Tenon JR**, Naus J, Blanken R. Anatomical observations on some parts of the eye and eyelids. 1805. *Strabismus* 2003; **11**: 63-68 [PMID: 12789585]

27 **Yan J**, Wu Z, Li Y. The differentiation of idiopathic inflammatory pseudotumor from lymphoid tumors of orbit: analysis of 319 cases. *Orbit* 2004; **23**: 245-254 [PMID: 15590527 DOI: 10.1080/01676830490487980]

28 **Kawakami K**, Ito R, Tono Y, Yazaki A, Murata T, Baba Y, Uchiyama T, Ito M. Orbital inflammatory lesion as an initial manifestation of systemic nasal type NK/T-cell lymphoma. *J Clin Exp Hematop* 2012; **52**: 137-139 [PMID: 23037631]

29 **Yang BT**, Wang YZ, Dong JY, Wang XY, Wang ZC. MRI study of solitary fibrous tumor in the orbit. *AJR Am J Roentgenol* 2012; **199**: W506-W511 [PMID: 22997401 DOI: 10.2214/AJR.11.8477]

30 **Yan J**, Qiu H, Wu Z, Li Y. Idiopathic orbital inflammatory pseudotumor in Chinese children. *Orbit* 2006; **25**: 1-4 [PMID: 16527767 DOI: 10.1080/01676830500505608]

31 **Takanashi T**, Uchida S, Arita M, Okada M, Kashii S. Orbital inflammatory pseudotumor and ischemic vasculitis in Churg-Strauss syndrome: report of two cases and review of the literature. *Ophthalmology* 2001; **108**: 1129-1133 [PMID: 11382641]

32 **Jordan N**, Verma H, Ekbote A, Sangle S, D'Cruz D. Dacryoadenitis and diffuse orbital inflammation: unusual first presentations of Churg-Strauss syndrome. *Orbit* 2011; **30**: 160-161 [PMID: 21574807 DOI: 10.3109/01676830.2011.569628]

33 **Kline LB**, Hoyt WF. The Tolosa-Hunt syndrome. *J Neurol Neurosurg Psychiatry* 2001; **71**: 577-582 [PMID: 11606665]

34 **Zurawski J**, Akhondi H. Tolosa-Hunt syndrome--a rare cause of headache and ophthalmoplegia. *Lancet* 2013; **382**: 912 [PMID: 24012271 DOI: 10.1016/S0140-6736(13)61442-7]

35 **Pemberton JD**, Fay A. Idiopathic sclerosing orbital inflammation: a review of demographics, clinical presentation, imaging, pathology, treatment, and outcome. *Ophthal Plast Reconstr Surg* ; **28**: 79-83 [PMID: 22262301 DOI: 10.1097/IOP.0b013e318238ecf7]

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**Table 1 Differential diagnosis of orbital inflammatory disease by site**

|  |  |  |  |
| --- | --- | --- | --- |
| **Structure involved** | **Clinical condition** | **Common imaging findings** | **DDx** |
| Lacrimal gland | Dacryoadenitis | Diffuse lacrimal gland enlargement | Epithelial neoplasm, lymphoma |
| Extraocular muscles | Myositis | Unilateral EOM inflammation, usually involving surrounding fat & myotendinous junction | Dysthyroid orbitopathy |
| Optic nerve sheath | Perineuritis | Peripheral enhancement about the optic nerve, with varying infiltration of surrounding fat. Variable enhancement of the nerve substance. | Optic nerve sheath meningioma, demyelinating optic neuritis |
| Orbital/periorbital fat | Cellulitis | Enhancing periorbital soft tissue with possible intraconal extension | Infectious orbital cellulitis, carotid cavernous fistula, cavernous sinus thrombosis |
| Orbital apex | Orbital apicitis, Tolosa-Hunt syndome | Ill-defined, T2 hypointense enhancing tissue at orbital apex, variably involving middle cranial fossa and cavernous sinus | Meningioma, other dural infiltrative process |
| Periscleral | Periscleritis | Scleral thickening with periscleral edema and fluid in Tenon’s capsule | Endophthalmitis |

EOM: Extraocular muscles.

**Figure 1 Dacryoadenitis.** A: Axial T2 shows diffuse enlargement of the left lacrimal gland. Note the tapered posterior margin (long arrow), as well as the involvement of the orbital lobe (short arrow). These findings suggest a lymphoid or inflammatory process rather than an epithelial neoplasm; B: Axial fat-suppressed contrast-enhanced T1 shows infiltration of the preseptal (long arrow) and post septal (short arrow) fat. These features suggest orbital inflammatory disease rather than orbital lymphoma.

**Figure 2 Adenoid cystic carcinoma of the lacrimal gland.** A: Axial T1 non-enhanced MRI showing an enlarged, heterogeneous left lacrimal gland (black arrow). Compare this to the contralateral normal gland (white arrow); B: Axial T1 non-enhanced MRI showing sparing of the palpebral lobe (arrows).

**Figure 3 Lacrimal gland lymphoma (A, B) compared to inflammatory dacryoadenitis (C, D).** A: DWI image in a patient with lacrimal gland lymphoma. Note the bright signal intensity (arrow) secondary to inhibition of water movement by the densely packed lymphoma cells; B: The corresponding ADC map of this patient shows an associated reduction in ADC, represented by the dark signal just lateral to the orbit (arrow); C: DWI image in a patient with inflammatory dacryocystadenitis. Note the dark signal compared to the patient with lymphoma (arrow); D: ADC map shows bright signal in the involved lacrimal gland (arrow) as compared to normal brain parenchyma. DWI: Diffusion-weighted imaging.

**Figure 4 Myositic pseudotumor.** A: Coronal fat-suppressed contrast-enhanced T1 shows enlarged left superior oblique (white arrow) and superior rectus (black arrow) muscles, and mild infiltration of the surrounding fat; B: Coronal fat-suppressed T2 shows low signal in the superior oblique muscle (white arrow), suggesting a more chronic, burned out process, whereas the superior rectus muscle (black arrow) shows brighter signal, indicative of a more acute process; C: Parasagittal oblique fat-suppressed contrast-enhanced T1 shows an enlarged superior rectus muscle belly (long arrow). The tendinous insertion (short arrow) is uncharacteristically spared by this process. Nevertheless, unilateral disease, infiltration of the surrounding fat, and early involvement of the superior oblique muscle indicate pseudotumor ahead of thyroid eye disease.

**Figure 5 Infectious orbital cellulitis.** A: Axial CT showing layering fluid in the ethmoid sinus and frontal recess on the left (black arrows), and infiltration of the orbital fat (white arrow); B: Coronal T1 fat saturated post-gadolinium MRI demonstrates orbitalfat infiltration (long white arrow). Fluid in the adjacent ethmoid sinus (black arrow) and intracranial extension of the process (short white arrow) are also features that indicate infection rather than OIS.

**Figure 6 Indirect carotid-cavernous fistula.** A: Coronal T2 MRI with fat saturation demonstrating mild infiltration of orbital fat (1) and thickening with high signal intensity in the EOMs. In this image, the lateral rectus muscle appears brightest (short arrow). Note the enlarged SOV (long arrow), suggesting CCF over myositis; B: Axial post-gadolinium T1 MRI with fat saturation. The SOV (long arrow) is engorged secondary to retrograde flow from the cavernous sinus. The superior oblique muscle (short arrow) is also enlarged; C: Angiogram with lateral projection common carotid artery injection (patient facing to the right) showing abnormal early filling in the cavernous sinus and SOV (short arrows), as well as an abnormal tangle of vessels along dorsal surface of cavernous sinus (long arrow), representing abnormally dilated intracavernous ICA branches.

**Figure 7 Diffuse cellulitic orbital inflammatory disease.** A: Coronal T1-weighted image shows diffuse infiltration of the intraconal fat on the left (arrow); B: Axial fat-suppressed contrast-enhanced T1 shows diffuse enhancement throughout the intraconal fat. No well-defined focal mass or focal fluid collection is seen.

**Figure 8 Perineuritic orbital inflammatory disease.** A: Coronal fat-suppressed contrast-enhanced T1 shows circumferential enhancement about the left optic nerve (long arrow), with sparing of the nerve substance. There is also mild infiltration of the surrounding soft tissues (short arrow); B: Axial fat-suppressed T2 shows a small amount of edema about Tenon’s capsule (arrow). This finding, along with clinical history of acute, painful presentation, help distinguish perineuritic pseudotumor from en plaque optic nerve sheath meningioma.

**Figure 9 Periscleritic orbital inflammatory disease.** 87-year-old immunocompromised man with left eye pain and ordering indication of “cellulitis” A: Axial contrast-enhanced CT shows mild infiltration of the left periorbital fat (short white arrow). There is also periscleral edema (long white arrow), and subtle high density along the temporal surface of the globe that is suggestive of a subchoroidal fluid collection (black arrow); B: Axial fat-suppressed contrast-enhanced T1 shows these findings more conspicuously. Note that the elevated choroid layer (black arrow) extends anteriorly to the region of the ciliary body. Periscleral edema (long white arrow) extending to Tenon’s capsule is better seen.

**Figure 10 Orbital inflammatory disease producing a focal mass.** Axial T2 shows a well-defined, T2 hypointense mass in the right orbit, discrete from adjacent extraocular muscles and from the lacrimal gland.

**Figure 11 Wegener's granulomatosis.** A: Non-enhanced axial CT through orbit demonstrating diffuse infiltration of orbital fat (1); B: Axial CT in through sinuses in bone window shows destruction of medial maxillary sinus walls, perforation of nasal septum (1), and chronic neoosteogenesis along sinus walls (arrows).

**Figure 12 Orbital apicitis (Tolosa-Hunt).** Axial fat-suppressed contrast-enhanced T1 shows ill-defined enhancement involving the right orbital apex, and extending into the middle cranial fossa along the margin of the cavernous sinus (arrow).

**Figure 13 Tolosa-Hunt syndrome, before and after treatment.** A: Axial fat-suppressed contrast-enhanced T1 showing bilateral cavernous sinus infiltration and enhancing tissue along the lateral margins of the cavernous sinus; B: Complete resolution after treatment.