Orbital Infections and Infestations - A Narrative Review

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ABSTRACT

Introduction: Orbital infections and infestations present with varying clinical presentations and incidences ranging from benign ocular condition to disseminated systemic disease. The diagnosis is often difficult initially, due to similar ocular presentations.

Materials and methods: This review was compiled using articles available on PubMed using key words like orbital infections, orbital cellulitis, orbital infestations, orbital tuberculosis, orbital fungal infections. Clinical experience in presentation and management at our centre was also included.

Results: The varied presentations, management, complications and follow-ups have been summarised in this review.

Conclusion: As the management is cause-specific, thus lies the importance of early accurate diagnosis, both clinical and radiological. This article aims to review existing literature on orbital infections and infestations for aiding in early accurate diagnosis and management.

Key words: Orbital cellulitis; orbital fungal infections; orbital infections; orbital infestations; orbital tuberculosis.
INTRODUCTION

Orbital infections and infestations are rampant worldwide with different clinical profiles and incidences varying from mild disease to severe sight threatening complications. Various aspects of orbital infections and infestations are summarised to simplify the understanding of the disease.

ORBITAL INFECTIONS

Orbital infection, a type of orbital inflammation, is caused by infective agents and therefore, orbital infections need to be differentiated from non-infective inflammations (autoimmune). Infections of the orbit can be classified depending upon the infective organisms into pyogenic, fungal, and tubercular; pyogenic being the commonest.

ORBITAL PYOGENIC INFECTIONS

Epidemiology and incidence

Orbital pyogenic infections are commoner in children, than in adults. Orbital complications subsequent to ipsilateral paranasal sinus infection varies from 0.5% to 3.9%. Ethmoid sinusitis is common in children and frontal sinusitis in adults. Ipsilateral sinus disease is common. Indian data points towards an increase in incidence of orbital pyogenic infections during monsoon whereas western data show an increase in winter season (Sharma, 2010). The incidence of orbital or periorbital abscesses varies from 0% to 25% in different studies (Hornbluss et al., 1984).

Infection routes

Infection into the orbit may spread as a direct extension from the paranasal sinuses or inoculation of the orbit from trauma (accidental or iatrogenic), or through haematogenous spread (bacteraemia).

Infection can gain access into the orbit through thin bones of the orbital wall, venous channels, foramina and dehiscences (lamina papyracea, Zuckerkandl dehiscence). Orbital veins are valveless which allow passage of infection, both anterograde and retrograde.

Within the orbit, infection spreads rapidly in the posterior part where the intermuscular septum is thin and incomplete (Lee and Yen, 2011).

Dental infections reach the orbit via the maxillary sinus. Microorganisms inherent to mouth, (commonly Bacteroides species) are pathogenetic.

Pathophysiology

Oedema of the mucosa of paranasal sinus results in narrowing of the sinus ostia. There occurs cessation of normal sinus drainage and proliferation of microflora, invading the oedematous mucosa and resulting in suppuration. Hypoxia further aggravates the suppurrative process.

Classification

Orbital cellulitis has been divided into five groups according to Chandler’s classification (Healy, 1997).

Preseptal cellulitis

Preseptal cellulitis refers to infection of eyelid and periorbital tissues anterior to the orbital septum (Figure 1a). It is more common than orbital cellulitis and has good prognosis (Chandler et al., 1970; Jain et al., 2001).
Preseptal cellulitis presents with eyelid oedema and erythema, with normal vision, non-congested conjunctiva, full ocular movements without proptosis. On computerised tomography (CT) scan, diffuse thickening of soft-tissues with contrast enhancement is seen anterior to the orbital septum (Figure 1b).

**Orbital cellulitis**

Orbital cellulitis is an infection of tissues behind the orbital septum (Figure 2). In the paediatric population, the incidence is higher, with ethmoid sinusitis being the most common underlying cause (Ferguson and Franco, 1999).

Patients with diabetes mellitus, multiple blood transfusions or immunocompromised patients with severe neutropenia (absolute neutrophil count <1.5x10^3 cells/mm^3) are predisposed (Gupta and Dhingra, 2016). Purulent focus may be present at the nose, ear, or face.

Clinical characteristics include eyelid oedema and erythema, conjunctival chemosis, proptosis, painful ophthalmoplegia, decreased vision, dyschromatopsia, relative afferent pupillary defect, increased orbital tonometry and

Figure 1(a): Clinical presentation of preseptal cellulitis (left side)- eyelid oedema and erythema. (b): CT scan (axial section) - diffuse contrast enhancing soft tissue thickening anterior to the orbital septum (left side).

Figure 2: Clinical picture of orbital cellulitis: eyelid oedema and erythema with proptosis, chemosis, fixed laterally displaced eyeball (right side).
elevated intraocular pressure. Orbital cellulitis is associated with significant complications, both ocular (exposure keratopathy, vision loss) and extraocular (cavernous sinus thrombosis, orbital apex, intracranial abscess) and thus, prompt diagnosis and treatment are important (Yeh et al., 2010).

**Mechanism of vision loss**

Visual loss due to orbital cellulitis is multifactorial including exposure keratopathy, reactionary optic neuritis, optic nerve ischaemia due to thrombophlebitis and compressive central retinal artery occlusion (Duke-Elder et al. 1975; Patt et al., 1991).

Systemic signs include fever, headache, rhinorrhoea and increasing malaise. In the paediatric group, more than 91% cases have radiologically confirmed ipsilateral sinus disease. The involvement of ethmoid sinus (43% to 75%) is more than maxillary sinuses, while in adolescents and adults, frontal sinus disease is more common.

**Subperiosteal and orbital abscesses**

Subperiosteal abscess results when orbital infection spreads between the periosteum and the orbital walls. Presence of subperiosteal abscess is heralded by severe pain. In orbital abscesses, there occurs collection of pus in the extraconal or intracanal compartment of the orbit, due to progression of orbital cellulitis. Posterior abscesses spread faster due to incomplete fascia between the recti.

The symptoms and signs of orbital cellulitis and orbital abscesses are similar, but with increased severity in the abscess stage. All patients with orbital cellulitis who do not improve in 24-48 hours of intensive antibiotic treatment, should undergo radiological evaluation (Suneetha et al., 2000).

On contrast enhanced computed tomography (CT) scan of orbits, a subperiosteal collection appears as a hypodense lesion adjoining to the orbital wall, bounded by a thick enhancing wall (Figure 3a). Orbital abscesses in all other sites of the orbit have a wall around the hypodensity (Figure 3b). Lesions may be uni or multiloculated.

![Figure 3(a): CT scan (axial section) showing a medial orbital subperiosteal abscess on the right side; (b)- CT scan (axial section) showing multiple thick walled cavities (abscesses) in the left medial and lateral extraconal compartment of the orbit.](image-url)
Other sequelae of systemic spread of orbital infections include meningitis, subdural empyema, septicaemia and toxic shock (Verity et al., 2018).

**Laboratory studies**

- Complete blood count (CBC); Leukocytosis >15,000 with a left shift is present.
- Blood cultures (to establish organisms for bacteraemia).
- Purulent material assessment - Gram stain and culture in both aerobic and anaerobic media

**Commonly reported bacteria** - Most common infective organism is *Staphylococcus aureus* in adults, and *Streptococcus species* in paediatric population (Wu 2010; Lee et al., 2011). Most intracranial abscesses are polymicrobial, with anaerobes being the most common pathogens (Hartstein et al., 2001). Infections due to *Haemophilus influenzae* are now less common following the introduction of the Hib vaccine. No growth is present in up to 25% of abscesses (Ambati, 2000).

**Radiology in orbital infections**

- **X-ray** - In an abscess cavity, air-fluid levels can be visualised on X-ray. Abscesses which are gas-free, are not easily distinguishable (Hornblass et al., 1984).
- **Ultrasonography** - This is an office-screening procedure when orbital abscesses are suspected in cases with orbital cellulitis. It shows low internal reflectivity. Ultrasonography is 90% efficient in detecting anterior orbital abscesses.
and abscesses along the medial orbital wall (Chaudhry et al., 2012). It has low sensitivity for acute abscesses (Schramm et al., 1978).

**Computerised tomography scan**- It is the investigation of choice for diagnosing orbital infections and involvement of paranasal sinuses. It can also demonstrate abscess in the orbit and any intracranial extension. Plain and contrast CT (axial, coronal, and sagittal) with thin sections (2 mm cuts) are ideal.

**Magnetic resonance imaging (MRI)**- MRI is more helpful in complications of orbital cellulitis such as delineating orbital abscesses and in evaluating the possibility of cavernous sinus disease.

**Treatment of orbital cellulitis and abscesses**

Hospital-based, empirical Intravenous broad spectrum antibiotics therapy is the mainstay of treatment. Oral anti-inflammatory (NSAID +/- Corticosteroid) therapy is simultaneously initiated. Role of steroids is controversial. This reduces the inflammation-induced sequelae. Oral antibiotics are continued after discharge from hospital. Often, children with age less than nine years, have been found to respond well to medical therapy. Concurrent sinusitis is treated by head elevation, nasal decongestant, mucolytics, and nasal saline irrigation.

Supportive therapy includes multivitamin supplementation, treatment of concurrent systemic illness or predisposing illnesses and cessation of smoking.

Orbital abscesses are surgically drained. Canthotomy with or without cantholysis is required for Orbital Compartment Syndrome.

Surgical drainage of intraorbital or subperiosteal abscesses is warranted if there is poor response to appropriate antibiotic therapy within 24-48 hours, especially in adults. Decision to initiate surgical therapy for orbital abscesses is also influenced by visual status, size of orbital abscess and intracranial complications.

**Harris and Garcia recommendations** for surgical drainage of orbital abscesses (Tanna et al., 2008).

- Compromised optic nerve or retinal function
- large abscesses
- intracranial complications

**Inter-speciality consultation:**

Otorhinolaryngology consultation for co-existing sinusitis, neurosurgical consultation in cavernous sinus thrombosis or brain abscesses are warranted. Other consultations include paediatrics, infectious disease specialist, and radiologist.

**Follow-up**

Preseptal and uncomplicated orbital cellulitis have favourable prognosis following prompt medical treatment. Patients developing complications of orbital cellulitis often follow a lengthened course. Few cases may require repeat surgical drainage of abscesses. Patients are observed regularly until ocular and systemic symptoms subside and white blood cells count and orbital imaging confirm the same.
ORBITAL TUBERCULOSIS

Orbital tuberculosis (TB) is rare, even in endemic regions, though it has shown resurgence in patients with acquired immunodeficiency syndrome (AIDS). Incidence varies from 1.4% to 18% in various studies (Agrawal et al., 1977). Orbital TB is more frequent in children than adults, with a slight female preponderance. Involvement of left orbit is more than right orbit due to direct origin of left common carotid artery from aorta, suggesting a haematogenous source of infection. The involvement is mostly unilateral, insidious in onset and slowly progressive.

Clinical presentations

Patients commonly present with cicatricial ectropion with or without periocular discharging sinus (Figure 4). Other presentations are eyelid or periocular mass, proptosis with or without displacement of eyeball or unexplained visual loss (base of skull TB).

Signs of tubercular involvement of orbit and ocular adnexa are-

- Orbit- periostitis, periorbital cold abscess, bony destruction, base of skull granuloma invading orbit.
- Lacrimal gland – Inflammatory lacrimal gland mass, cold abscess.
- Eyelid - Chronic blepharitis, recurrent chalazion, diffuse infiltration mimicking cellulitis (Dalvin and Smith, 2016).

Investigations

- Radiology demonstrates periostitis, bone lysis, cold abscesses, inflammatory lacrimal gland enlargement and inflammatory masses in the orbit.

Figure 4: Clinical presentation of orbital tuberculosis - (a) periocular discharging sinus (left upper eyelid) (b) cicatricial ectropion (right upper eyelid) (c) Periocular mass (right side) (d) Lacrimal gland enlargement (left side).
Sputum acid-fast bacilli (AFB) and culture for cases with history of cough with sputum.

- Mantoux skin test in all patients (Positive if induration: >5 mm in human immunodeficiency virus (HIV) -infected patient, >10 mm in high-risk persons and >15 mm for normal population)
- Interferon gamma testing (QuantiFERON Gold test for screening only in patients who have been vaccinated with Bacille Calmette-Guerin (BCG) or in those who are unlikely to return for skin test reading)
- Orbital biopsy - characteristic histopathology (chronic granulomatous reaction with giant cells and caseation necrosis and AFB)
- Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) should be the first diagnostic test in patients with extra-pulmonary TB, children and HIV infection.
- Adenosine deaminase (ADA) – In TB patients, the activity of ADA enzyme is found to increase (ADA is an index for cellular immunity) (Ahmed et al., 2016)

**Treatment**

Orbital TB is treated with standard six-month Anti-tubercular treatment (ATT) as per directly observed therapy short course (DOTS) Category I in accordance with World Health Organisation (WHO) and Revised National Tuberculosis Control Programme guidelines. DOTS Category I treatment is an effective therapeutic protocol for orbital TB in both HIV and non-HIV infected patients according to latest Centres for Disease Control and Prevention (CDC) guidelines. In HIV patients, antiretroviral therapy should ideally be initiated within the first two weeks of TB treatment for patients with clusters of differentiation (CD)4 cell counts <50/mm³ and by 8-12 weeks of TB treatment initiation for patients with CD4 cell counts ≥50/mm³.

Most paediatric patients respond well to medical therapy. Cases that do not show adequate response in the early phase need debridement and removal of sequestrum. Sequelae like cicatricial ectropion need specific surgical correction.

**Fungal Infections of Orbit**

Fungal infections of the orbit are rare. It mostly affects immunocompromised patients. Orbital fungal infections may either be Mucormycosis (order Mucorales, species Rhizopus) or Aspergillosis (order Eurotiales genus Aspergillus).

Initial site of infection is the paranasal sinus with secondary involvement of the orbit.

**Mucormycosis**

Also known as phycomycosis and zygomycosis, it is an aggressive and opportunistic infection. Rhinocerebral, the commonest form, has several subtypes, namely, rhinonasal, rhinoorbital or rhinoorbitocerebral (Roden et al., 2005). Upon inhalation of fungal spores, germination occurs in the nasal mucosa with formation of hyphae. These fungal hyphae finally invade the nasal mucosa, causing sinusitis upon reaching paranasal sinuses. Fungal hyphae may also invade through the orbital walls, spreading into the orbit (Yohai et al., 1994).
Clinical picture

Patients with orbital mucormycosis present with fever, lid swelling and redness, forward protrusion of eyeball with pain and vision loss. Signs include lid oedema, erythema, ophthalmoplegia and proptosis. Facial hypoesthesia may also be present (Karadeniz et al., 2015). Swelling, erythema, and dark scabbing is mostly observed (Figure 5a). Imaging of the orbit shows involvement of paranasal sinus with secondary involvement of orbit (Figure 5b).

Diagnosis

Clinical features and imaging in cases of mucormycosis may be non-specific. Diagnosis is made by biopsy. Broad, irregular, non-septate hyphae with branching at right-angles establishes diagnosis of mucormycosis. Special stains required are Grocott-Gomori methenamine, silver nitrate, periodic acid Schiff, and calcofluor white stains.

Angioinvasion and infarction of tissue may also be observed (Ribes et al., 2000).

Treatment

Medical- First-line medical treatment is Amphotericin B. Initial test dose of 1 mg is given. The dosage is slowly increased from 0.7 to 1 mg/kg I.V. (cumulative dose of 2-4 g). Lipid based are newer and safer formulations (Petrikkos, 2009). Systemic posaconazole, a triazole- adjunctive or alternative treatment (Skiada et al., 2011; Mukherjee et al., 2016).

Surgical- Early aggressive surgical debridement is important with endoscopic or open approach. All necrotic tissue is removed till fresh bleeding tissue is seen. Repeat debridement may be required if there is little clinical improvement.
Orbital exenteration and affected sinus removal may be required in cases with extensive spread. Vascular obstruction, a feature of mucormycosis, may affect drug delivery at the target site. Such cases require local irrigation with amphotericin B in addition to surgical and systemic treatment therapy (Seiff et al. 1999).

**Hyperbaric oxygen therapy**

Hyperbaric oxygen is given every 12 hourly, two hours of 100% oxygen at two atmospheres absolute for three days. Then daily treatments of two hours duration is given, the total number of treatments depending on patient response. However, it is expensive, cumbersome, and not readily available (John et al., 2005).

**Prognosis**

Pre-amphotericin B mortality rate was 90%. Patients who begin treatment within six days have a better survival rate (76-81%). Delayed treatment (>12 days) drastically reduces the survival rate (36-42%). Surgery alone has a survival rate of 57% while it is 70% with combined surgery and amphotericin B therapy (Pillsbury et al., 1997; Revankar et al., 2007).

**ASPERGILLOSIS**

Aspergillosis is an uncommon disease, can affect both immunocompromised and immunocompetent patients. Orbital infection spreads due to direct extension from the adjacent sinuses.

Aspergillus spores may gain entry include the respiratory tract, ear, cornea, and wounds on skin (Denning et al., 1998). Immunocompromised hosts develop subsequent disease. Risk factors include total neutrophil count of <1000/mm³, low T-cell counts (e.g., AIDS), diabetes mellitus, prosthetic devices, advanced age, burn patients, and tight, occlusive dressings.

**Clinical features**

Non-invasive aspergillosis is either allergic sinusitis or sinonasal fungal ball with no histological evidence of tissue or bony invasion. Invasive aspergillosis often starts in paranasal sinuses with spread to adjacent orbit or intracranial cavity (Figure 6a). Multiorgan involvement is a common feature of fulminant form. Invasive aspergillosis affects immunocompromised patients.

**Investigations**

- **Anterior rhinoscopy** for evaluating extent of nasal pathology
- **Examination of the hard palate and gingiva.**
- **Imaging-** CT scans show heterogeneous soft tissue masses with calcification and bony erosion (Figure 6b).
- **Neuroimaging-** localised soft tissue densities with bony destruction are observed. Abscesses are hypodense. MRI provides superior information of posterior orbit and cavernous sinus (Sivak-Callcott, 2004).
- **Biopsy-** Tissue culture is the gold standard for identification of aspergillosis. Microscopic appearance of aspergillus is haemotoxophilic with 45° branching septate hyphae that are 2–4 μm wide, best seen on Gomori methenamine silver and periodic acid Schiff stains (Denning, 1997).
Treatment

Early diagnosis and treatment form an effective treatment strategy of orbital aspergillosis. Specific treatment includes oral Voriconazole, Posaconazole, and Itraconazole. Surgical treatment includes debridement with oral voriconazole therapy.

ORBITAL INFESTATIONS

Orbital infestations refers to parasitic diseases of the orbit. Orbital cysticercosis is the most common followed by orbital hydatid (less encountered) disease and myiasis (Bodh et al., 2012).

CYSTICERCOSIS

Cysticercosis is the commonest ocular infestation in humans. It is caused by encystment of the larvae (cysticercus cellulosae) of the tapeworm Taenia solium.

Life cycle

Humans are definitive hosts while pigs are intermediate hosts in the life cycle of T. solium. Pigs are the main host for the larval stage. When humans ingest raw or undercooked pork containing viable cysticerci, these larvae reach the human intestine, where the scolex attach and grow. Human cysticercosis occurs when eggs released by the adult tapeworm from the human intestine are ingested via faecal-oral route. The human thus becomes an accidental intermediate host. The oncospheres are primary larvae and invade the intestinal mucosa to enter systemic circulation.

Systemic spread to nerves, muscle and ocular tissues is reported. Inside these tissues, the oncospheres get encysted and form secondary larvae (cysticerci) (Markell et al., 1999).
Clinical presentation

Clinical presentation depends upon the location of the cyst. No part of the orbit is exempt from cysticercosis. Subcutaneous cysticercosis, on the eyelid, presents as painless, mobile mass with varying degrees of mechanical ptosis. Subconjunctival cysticercosis may present as a painless or painful yellowish, nodular subconjunctival mass with surrounding conjunctival congestion (Pushker et al., 2001) (Figures 7a and b). Extraocular myocysticercosis presents as recurrent pain, redness, proptosis with or without displacement of globe, diplopia, and ptosis. More than one extraocular muscle may be simultaneously involved, but superior rectus and levator muscle (Figure 7c) complex and lateral rectus muscle is commonly involved (Sundaram et al., 2004). Live cysticercous cyst shows constant motility, due to which it may erode the tissue containing it. It can spontaneously expel out from the conjunctiva and from extraocular muscles, it can reach the orbit (Pushker et al., 2001).

Cysticercous cyst may also compress the optic nerve and result in decreased vision, disc oedema and painful ocular motility. Large cysts tend to produce axial proptosis with or without restricted ocular motility (Goyal et al., 2007).

Diagnosis

Symptoms and signs are site specific.

CT scan and / or MRI is useful in identification of orbital cysticercosis. Cystic lesion with scolex with or without surrounding inflammation or calcification is seen, depending upon the location of the cyst.

Treatment

Oral albendazole (15 mg/kg/d) is given for three weeks with oral steroids (1.5 mg/kg/d) for the initial one week. Identification of the source of contamination should be attempted, if possible. Treatment of the family with anti-helmenthics is also essential.

Follow-up

Symptomatic improvement should be noted with repeat radiology after one month.

Figure 7(a) Clinical presentation of subcutaneous cysticercosis: discrete, mobile mass with mechanical ptosis (left side) (b) Clinical presentation of subconjunctival cysticercosis: nodular, cystic subconjunctival mass (right side) (c) CT scan (coronal section) of the orbits shows cysticercous cyst of superior rectus muscle (left side).
In case of persistence of cyst, excision or repeat drug therapy can be planned. In case of persistence of sequelae, oral anti-inflammatory treatment and corrective surgery can be planned.

**ORBITAL ECHINOCOCCOSIS**

Orbital echinococcosis or hydatid cyst is a parasitic disease caused by *Echinococcus granulosus* (*E. granulosus*). Liver (60–70%) followed by lungs (20%) are the most common sites of hydatid cysts in humans (Ergun et al., 1997). Hydatid cysts rarely involve the orbit, less than 1% of all systemic involvements of hydatid cysts (Turgut et al., 2004).

**Life cycle**

The *E. granulosus* is a small tapeworm. Dogs and other canines are definitive hosts while ungulates (sheep, goats, pigs, horses, etc.) are intermediate host. Eggs are released from the gut of definitive host and they are consumed by the intermediate host. Larval form is known as metacestode, and it develops and grows in the intermediate host. Upon maturation, each metacestode forms multiple protoscoleces. Each protoscolex can form an adult worm upon ingestion by the definitive host. Accidental ingestion of eggs by humans results in human echinococcosis. Mostly cysts are unilocular, however, in some cases, small daughter cysts may form inside larger mother cysts. Mixed infections with *E. granulosus* and *E. multilocularis* are rare.

**Clinical features**

Patients present with lid oedema, chemosis and slowly progressive painless proptosis (Figure 8a) with or without exposure keratopathy. Diplopia and restriction of extraocular motility are also present. Hydatid cyst of the orbit (Figure 8b) usually involves the retrobulbar tissues either within the muscle cone or outside in the superolateral or superomedial angle (Benazzou et al., 2010; Gomez et al., 1988).

![Figure 8(a): Clinical picture of echinococcosis: lid oedema, chemosis, proptosis with ophthalmoplegia (left side); (b)- CT scan (axial section) of the orbits shows hydatid cyst in intraconal compartment of left eye with daughter cysts and bowing of medial orbital wall.](image-url)
Definitive treatment is surgical, removal of cyst in toto. Albendazole treatment is useful, especially if begun 14–28 days before surgery and is used as an adjunctive therapy to surgery (Cooney et al., 2004; Xiao et al., 1999). Rupture of cyst during excision causes spread. In such cases, alcohol irrigation with oral antihelminthic treatment is given.

ORTITAL MYIASIS

Myiasis is defined as infestation of human tissues or organs by Diptera larvae. Orbital myiasis is very rare. Usually, immunocompromised, old and debilitated patients are affected. Progression of orbital myiasis is so rapid that complete destruction of orbital tissues can occur within a few days. (Figure 9). Most common initial presenting features are itching, foreign body sensation, and chemosis, which resembles conjunctivitis. Larvae grow rapidly within the ocular tissues with subsequent destruction and erosion of ocular and periocular tissues (Sucilathangam et al., 2013).

**Treatment**

Oral Ivermectin 12 mg single dose is given. The 1% Ivermectin solution can also be given as drops. Manual removal of maggots should be done several times a day, initially following turpentine wash (Bologna et al., 2008).
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