NANOS: Rare Orbital Inflammations

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Relevant Financial Disclosures

- I do not have any financial interests or relationships to disclose.
Differential Diagnosis of Non-idiopathic Orbital Inflammatory Disease

- Sarcoidosis
- Churg-Strauss Syndrome
- Wegener’s Granulomatosis: Granulomatosis with Polyangiitis (GPA)
- Giant Cell Arteritis
- Adult Xanthogranulomatous Diseases
- Rosai-Dorfman
Sarcoidosis

- Demographics: 3rd and 6th decade; M=F
- Incidence: 60/100K Scandinavia; 35/100K in AA’s and 11/100K in US for Caucasians
  - Post-911, the incidence of sarcoid lung disease in NYFD’s responders was 86/100K (primarily pulmonary), suggesting environmental trigger
- Systemic findings: pulmonary > skin > neuroaxis
- Ocular findings: uveitis of any type; lid granulomas
- Orbit: bilateral disease in 50%, systemic manifestations in 70%, lacrimal gland involvement in 55%, discrete mass in 20%, nerve sheath in 20%
- Pathology: non-caseating granulomas, giant cells, Schumann body inclusions, background fibrosis
- Test: ACE, lysozyme, imaging enhances
- Treatment: steroids, cyclosporine, azothioprine systemically; may benefit some patient with steroid injection locally into lesion
Churg-Strauss Syndrome

- Demographics: 5th decade peak
- Incidence:
- Systemic findings: Asthma, rash, pain/numbness in extremities, malaise, night sweats, bleeding
- Ocular findings:
  - Ischemic presentation: amaurosis, ION, BRAO or CRAO
  - Infiltrative presentation: lid swelling, episcleritis, periscleritis, conjunctival granulomas, dacryoadenitis, thickened optic nerve sheaths
- Pathology: eosinophilic infiltration of granulomatous inflammation; vasculitis
- Test: B scan choroidal thickening in macula; weak + ANCA
- Treatment: steroids, methotrexate, cytotoxic drugs for refractory states

Figure 1. Case 1: A 43-year-old man with orbital inflammatory pseudotumor associated with Churg-Strauss syndrome. Magnetic resonance imaging (time inversion [TI], 2000; time echo [TE], 135) of the orbit demonstrated marked enlargement of the lateral rectus muscle bilaterally with increased soft tissue density in the surrounding tissues. Bilateral ethmoid sinusitis was also noted.

Figure 2. Case 1: A 43-year-old man with orbital inflammatory pseudotumor associated with Churg-Strauss syndrome. Extravascular infiltration of eosinocytes was marked in the biopsy specimen of the lacrimal gland (tissue, hematoxylin–eosin). Black bar indicates 100 μm.

Figure 3. Case 2: A 63-year-old man with orbital inflammatory pseudotumor associated with Churg-Strauss syndrome. B-mode echography demonstrated localized thickening of the choroid in the posterior pole.

Figure 4. Case 2: A 63-year-old man with orbital inflammatory pseudotumor associated with Churg-Strauss syndrome. Lymphoplasmacytic and occasional eosinophilic infiltrates are seen around the small vessel wall in the skin biopsy specimen (tissue, hematoxylin–eosin). Black bar indicates 50 μm.
Granulomatosis with Polyangiitis (GPA)

- Demographics: peak 5th-8th decade; M=F, Caucasians
- Incidence: .4-8/100K
- Systemic findings: upper airway including sinus involvement in 90%; classical nasal septal perforation; frequent lung and renal involvement
- Ocular findings: episcleritis, scleritis, keratitis, retinal vasculitis
- Orbit: bilateral dacryoadenitis, orbital fibrosis
- Pathology: fat necrosis with giant cells, free vacuoles, fibrosis
- Test: cANCA + in >90%
- Treatment: corticosteroids plus cyclophosphomide, methotrexate or azathioprine; some anti TNF and anti CD20 monoclonals may be helpful
Wegener's granulomatosis: ophthalmic manifestations and management. Pakrou N¹, Selva D, Leibovitch I.
The antineutrophil cytoplasmic antibody-associated vasculitides. Seo P, Stone JH

Figure 1. Saddle-nose deformity in Wegener’s granulomatosis.
Giant Cell Arteritis

- Demographics: peak 8th decade, Caucasian, M:F = 1:2
- Incidence: rare orbital involvement
- Systemic findings: headache, neck pain, jaw claudication, scalp tenderness, polymyalgia, weight loss
- Ocular findings: AION in 20%, CRAO, amaurosis fugax, diplopia
- Orbit: diffuse orbital inflammation
- Pathology: epithelioid cells, giant cells, round cell infiltration
- Test: CRP, sed rate, biopsy
- Treatment: hi dose corticosteroids, methotrexate, azathioprine, cyclosporine, immunomodulatory drugs (tocilizumab, abatacept, ustakinumab)
Orbital presentations of giant cell arteritis. Lee AG¹, Tang RA, Feldon SE, Pless M, Schiffman JS, Rubin RM, Rao N
Adult Xanthogranulomatous Disease
(AOX, AAPOX; NBX, ECD)

- Demographics: peak in 6th decade; M=F
- Systemic findings:
  - AAPOX is associated with asthma and lymphadenopathy
  - NBX is associated with paraproteinemia/myeloma
  - ECD is characterized by pulmonary, cardiac, and retroperitoneal fibrosis, as well as bone involvement
- Ocular findings: eyelid masses
- Orbit: dacryoadenitis, diffuse infiltrative process
- Pathology: foamy histiocytes (CD68+), Touton giant cells spindle cells, mononuclear infiltrate.
- Test: paraproteins, lymph node biopsy
- Treatment: multi-agent chemo with or without radiation; combo cyclosporine and cyclophosphamide
Rosai-Dorfman

- Demographics: M>F; 80% are <21 years old
- Incidence: rare
- Systemic findings: lymphadenopathy of head and neck; respiratory tract, salivary glands, skin, bone, meninges, CNS, testes
- Ocular findings: rare scleritis, uveitis, marginal corneal ulcers, choroidal mass, lid lesions
- Orbit: often sinus involvement, bilateral dacryadenitis; enhancing homogeneous mass on T1 MRI and only rare bony destruction
- Pathology: Emperipolesis (lymphocytes found phagocytized by large histiocytes; lymph node architecture in extranodal locations; scattered mixed inflammatory reaction
- Test: anemia, polyclonal hypergammaglobulinemia
- Treatment: Excision or debulking of masses. Spontaneous remission possible. Radiation, steroids and chemo for recurrent or unresponsive cases

FIG. 2. A, Clinical photograph of patient 2 demonstrating left proptosis, hypoglobus, and blepharoptosis. Axial (B) and coronal (C) T1 MRI with gadolinium showing homogenous enhancement of a left intracranial orbital apex mass with involvement of the dura and left ethmoid and sphenoid sinuses.

FIG. 3. Histopathology of biopsy specimen from patient 3 demonstrating emperipolesis, (A, touch preparation cytology, ×600), positive immunostaining with CD68, (B, ×400), and positive immunostaining with S-100 (C, ×400).
## Ocular Disease Truth Table

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SUMMARY

Non-idiopathic orbital inflammation should be suspected when:
• The inflammation is bilateral
• There is ocular involvement
• There are systemic symptoms or signs
• There is a characteristic biopsy

Treatment consists of:
1. Biopsy of orbit, skin or other involved organ
2. Corticosteroids (localized or systemic)
3. Immune suppression
4. Targeted biologicals