Eye Diseases with Deadly Consequences

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Financial Disclosure

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Goals

Discuss several conditions where ophthalmic signs and symptoms can be manifestations of significant systemic disease

Present clinical cases where taking a thorough history aided in the diagnosis of life-threatening disease

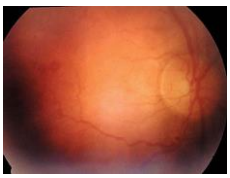
Recognize that early recognition may allow for the institution of life saving treatment

72 yo female c/o fatigue

HPI:
- Fatigue x one month
- Persistent cough with minimal sputum
- Fever to 100 degrees
- 5 pound weight loss

PMH:
- HTN
  - Meds – HCTZ, Clonidine, Estrogen

Physical Exam:
- Normal VA's, pupils, IOP's, slit lamp
- Fundus:



Giant Cell Arteritis

WORKUP

CBC with differential – normal with mild reduced hematocrit

Blood cultures/ urinalysis negative

ESR – 90

CRP – 9.0

Alk Phos - 228

CLINICAL COURSE

Temporal artery biopsy performed – positive for GCA – giant cells, intimal hyperplasia

Patient started on Prednisone 60 mg/day

Symptoms improve and after 4 months, tapering of Pred to 10 mg/day is attempted, but symptoms return and ESR increases

Slower taper takes place over 2 years with diabetes developing while on Pred

Pt. dies of ischemic CVA one year later

Giant Cell Arteritis

Systemic, inflammatory, vascular syndrome affecting the temporal arteries

Associated with polymyalgia rheumatica (PMR)
- ½ of patients with GCA have PMR
- 15% of patients with PMR develop GCA

Criteria for GCA
- > 50 years old
- New onset temporal headache
- Temporal artery tenderness
- ESR of > 50 mm/h
- Abnormal biopsy specimen with granulomatous inflammation

GCA Presentation often coexists with PMR

CONSTITUTIONAL SYMPTOMS

Fatigue, malaise

Weight loss

Fever
- PMR – mild
- GCA – may be high with night sweats

Anorexia and weight loss

PROXIMAL MYALGIAS

Joint and muscle aching soreness and stiffness
- Shoulders, neck, pelvis
- Worse in the morning
- Muscle tenderness leads to disuse atrophy, weakness

Patients treated for PMR who develop new headache may have occult GCA

GCA Presentation often coexists with PMR

JOINT SYMPTOMS

Tenderness over joints and hips

Synovitis of knees, shoulders or wrists

Carpal tunnel syndrome and synovitis may be present in patients with PMR

SYMPTOMS RELATED TO VASCULITIS OF EXTERNAL CAROTID BRANCHES

Headache and scalp pain – most common symptom
- Dull, boring, burning
- Temporal location, sometimes occipital – scalp tenderness
- Pain in ear canal, pinna, or parotid gland
- Jaw claudication – pain in masseter muscles – highly specific for GCA

GCA: Presentation

SYMPTOMS RELATED TO AORTIC ARCH AND THORACIC AORTA INVOLVEMENT

Frequency of involvement between 9 and 18%

88% occurs in women

Younger age at onset

Fewer constitutional symptoms

Mostly arm or leg claudication

Brain ischemia

Abdominal aortic aneurysm

GCA: Genetic factors

PMR and GCA may aggregate in families

More common in Caucasians, less common in Blacks

Infectious etiology may trigger GCA

GCA: Differential diagnosis

Atherosclerosis

Cluster headache

Migraine headache

Polymyalgia rheumatica

Rheumatoid Arthritis

Takayasu arteritis

Trigeminal neuralgia

GCA workup

ESR of 50 – 100 mm/h
- ESR of 20 – 30 does not exclude GCA
- Visual ischemic events typically with ESR > 70

CRP (C-reactive protein)

Normocytic normochromic anemia, thrombocytosis
- Anemia – good negative predictive value for severe complications

Alkaline phosphatase levels elevated in 1/3 of patients

Temporal artery biopsy

What are the lethal complications?

PMR morbidity/mortality relates to treatment complications associated with long-term steroid therapy
- Hypertension, diabetes, osteoporosis (hip fractures), increased risk of infection

GCA morbidity/mortality causes are similar to PMR but also at risk for blindness (26%)

GCA mortality

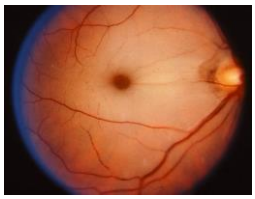
Rarely involves the CNS
- When it does, seizures, CVA's are possible
- GCA affects vessels with an elastica – intradural vessels do not have an elastica
- May cause aneurysms, dissections, stenosis of aorta
- Subclavian steal with brain ischemia

78 yo female c/o sudden, painless loss of vision OD

HPI
- Developed upon awakening today
  - Vision loss is severe
  - Preceded by episodes of transient loss of vision lasting 5 – 10 minutes

PMH
- HTN, high cholesterol, atrial fibrillation

Physical exam
- VA – 20/30 OD, CF OS
- + APD OS
- Fundus exam



Central Retinal Artery Occlusion

Acute, painless loss of vision from counting fingers to light perception
- Some central vision is maintained if there is a cilioretinal artery
- Possible history of amaurosis fugax lasting seconds to minutes

Central Retinal Artery Occlusion

Possible temporal arteritis symptoms
- Sudden, painless loss of vision with headaches, jaw claudication, scalp tenderness, proximal muscle/joint pain

Medical problems such as:
- Atrial fibrillation
- Endocarditis
- Coagulopathies
- Atherosclerotic or hypercoagulable states

CRAO ophthalmic findings

+APD

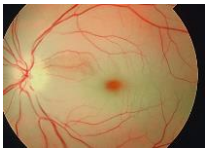
Cherry red spot

Pale/swollen optic nerve with splinter hemorrhages

Emboli in 20%

Boxcar segmentation of arteries and veins

Carotid bruits, heart murmurs



CRAO causes

Systemic hypertension in 2/3 of patients

Diabetes mellitus

Cardiac valvular disease in ¼ of patients

Embolism
- Cholesterol (most common), calcific, bacterial or talc
- Cardiac emboli – most common cause of CRAO <40 yo
- Coagulopathies from sickle cell common cause of CRAO in patients <30 yo

CRAO causes

Carotid atherosclerosis – seen in 45% of CRAO, with 60% stenosis seen in 20% of cases
- Leading cause of CRAO in 40 – 60 yo

Giant cell arteritis – consider in patients > 65 yo

Hypercoagulable states
- Oral contraceptives

Polycythemia

Polyarteritis nodosa

Syphilis

Sickle cell disease

Migraine

Increased IOP from prolonged direct globe pressure

CRAO work-up

CBC
- Anemia, polycythemia, platelet disorders

ESR, CRP for giant cell

Fibrinogen, antiphospholipid antibodies, PT/PTT, serum protein electrophoresis for coagulopathies

Fasting blood sugar, cholesterol, triglycerides, lipid panel for atherosclerotic disease

Blood cultures for bacterial endocarditis

CRAO work-up

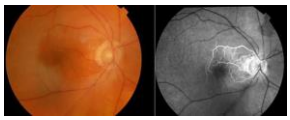
Carotid ultrasound imaging for atherosclerotic disease

Magnetic resonance angiogram (MRA) – more sensitive

Fluorescein angiogram

Electrocardiogram for possible atrial fibrillation

Echocardiogram for valvular disease, wall motion abnormalities



CRAO treatment

IOP lowering with diamox, topical meds

Digital massage

Anterior chamber paracentesis

Carbogen

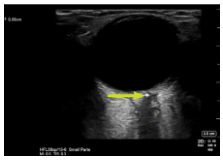
Hyperbaric oxygen

Intra-arterial tPA (tissue plasminogen activator)

Lethal complications of CRAO

Patients with visualized retinal artery emboli, whether or not obstruction is present
- 56% mortality rate over 9 years, compared to 27% for an age-matched population without retinal artery emboli

Life expectancy of patients with CRAO
- 5.5 years compared to 15.4 years for an age-matched population without CRAO

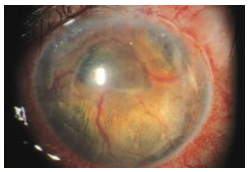


80 yo male c/o gradual vision loss, red eye OD

HPI
- Gradual worsening of vision over the past several weeks, with throbbing and achy brow pain and redness OD

PMH
- HTN, MI, CVA x 2

Physical exam
- VA – 20/400 OD, 20/50 OS
- +APD OD
- Cornea – mild edema
- AC – trace cell and flare

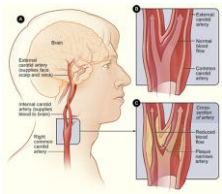


Ocular Ischemic Syndrome

Chronic vascular insufficiency

Severe unilateral or bilateral atherosclerotic disease
- Internal carotid – high grade stenosis results in ophthalmic artery insufficiency
- Bifurcation of the common carotid

Giant cell arteritis



Ocular Ischemic Syndrome

History
- Loss of vision in 70-90%
  - 20/60 or worse in 2/3
  - CF or worse in 1/3
- Pain in 40 % - dull ache
- Amaurosis fugax in 10%

Physical
- Pulses, carotid and cardiac auscultation

Ophthalmic exam

Anterior segment
- Corneal edema, hypotony, rubeosis iridis, neovascular glaucoma, AC reaction in 20 %, asymmetric cataract

Posterior segment
- Narrowed retinal arteries
- Midperipheral hemorrhages in 24-80%
- CW spots
- Neovascularization
- Optic disc pallor

Ocular Ischemic Syndrome

Workup
- IVFA – prolonged circulation times, decreased choroidal filling, capillary nonperfusion
- Color Doppler imaging
- MRA
- Carotid angiography
- ERG – reduced a and b waves

Treatments
- PRP for neovascularization
- IOP lowering meds
- Steroids
- Glaucoma filtering procedures
- Antiplatelet therapy
- Thrombolytic therapy
- Carotid endarterectomy

Ocular Ischemic Syndrome: Lethal complications

5 year mortality rate is 40 %

Leading cause of death – cardiac disease

Stroke

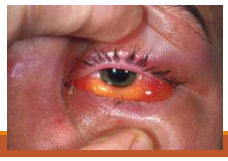
Cancer
- Predisposing atherosclerosis risk factors are significantly higher in patients with OIS than in age matched populations

30 yo male c/o eye pain

HPI
- Painful, red right eye for 2 days
- Mild blurring of vision
- General fever and malaise
- Nasal discharge

PMH
- Noncontributory
- No past ophthalmic history
- Recent dental procedure

Physical Exam
- VA – 20/25 OD, 20/50 OS
- Conj – chemosis
- EOM – limited ductions, painful movements
- Lids – edematous, reddish



Differential diagnoses

Thyroid ophthalmopathy

Orbital pseudotumor, myositis

Cavernous sinus thrombosis

Orbital cellulitis

Leukemia

Metastatic carcinoma

Retinoblastoma, rhabdomyosarcoma

Sarcoidosis

Workup

CBC – significant leukocytosis

Blood cultures

Swab of purulent material, if any

CT scan of head and orbits – axial and coronal views

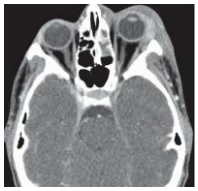
Diagnosis?

Orbital cellulitis treatment

Hospitalization for IV antibiotics, monitoring
- Vancomycin, cefotaxime, clindamycin; Bactrim for gram positive, possibly methicillin resistant sinus flora

Surgical drainage of subperiosteal abscess if inadequate response to antibiotics

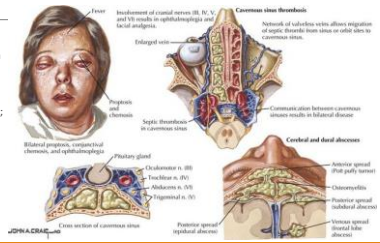
ENT consultation



What are the lethal complications of orbital cellulitis?

Cavernous sinus thrombosis

Late complication of infection of the central face or sinuses
- Also bacterial sepsis, trauma, ear or dental infections
- Staph aureus 70% of the time; also strep, gram negatives, anaerobes, fungi



Cavernous sinus thrombosis mortality

Prior to advent of effective antimicrobials, mortality rate was effectively 100%

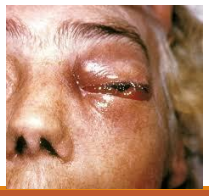
Death due to sepsis or CNS infection

With aggressive antibiotic management mortality rate is 30%
- Many who live have residual vision impairment, cranial nerve deficits.

Delayed diagnosis, delayed surgical drainage, improper antibiotics lead to morbidity/mortality

Same patient, with poorly controlled DM…

Think **orbital mucormycosis**



Orbital mucormycosis

Infection of the sinuses, nasal passages, oral cavity, orbit, and brain caused by fungi – rhizopus, absidia, mucor

- Diabetics with elevate blood sugars
- Immunocompromised state
- Infection spreads along vascular and neuronal routes
- Erode through bones of sinus into orbit and brain
- Cavernous sinus, carotid, and jugular vein thrombosis

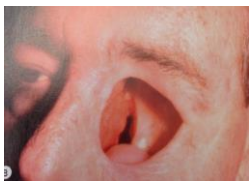
Orbital mucormycosis

Workup –

- CT /MRI of head/orbits
- Biopsy, surgical exploration

Treatment

- Amphotericin B (extremely nephrotoxic) – IV and local
- Debridement of sinus and orbit
- Orbit and sinus exenteration



Orbital mucormycosis

Mortality rate - >80% with spread to brain

- Death may occur within 2 weeks if poorly treated

Survival improves with:

- rapid diagnosis
- early management with antifungal therapy, surgery
- reversal of underlying risk factors

Orbital tumors

Orbital tumors

The orbit –

- Small in volume (30 cc)
- Densely packed with globe, muscles, fat, blood vessels, nerves, connective tissue
- All anatomic structures can give rise to neoplasia

Space occupying lesions will result in proptosis and affect adjacent structures

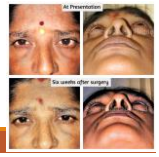
- Proptosis of less than 4 mm can easily go undetected

Most common pediatric orbital tumors

- Capillary hemangiomas
- Dermoid cysts
- Rhabdomyosarcoma

Most common adult orbital tumors

- Lymphoid
- Cavernous hemangiomas
- Meningiomas

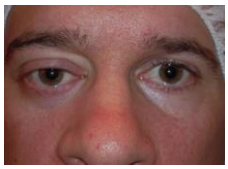


Orbital tumors

Considerations when taking a history in patient with proptosis
- Concomitant sinus disease
- Duration and rate of progression of proptosis
- Pain
- Diplopia
- Pulsation
- Change with positional change or Valsalva
- Changes in vision

Orbital tumors

Physical exam considerations
- Eyelid lesions or edema
- Conjunctival chemosis, enlarged conj vessels
- Lagophthalmos
- Proptosis – AP protrusion, but also downward, lateral
- Palpation for tenderness, resistance to retropulsion, pulsations
- Auscultation for high flow states – e.g.., CC fistula



Orbital tumors

Physical exam considerations
- Decreased VA
- Pupil abnormalities
- Change in refraction
- EOM dysfunction with diplopia
- IOP elevation
- Optic disc edema or pallor
- Retinal detachment
- Choroidal folds
- Vascular engorgement or shunt vessels

Orbital tumors with lethal potential

Metastatic tumors
- Reach the orbit by hematogenous route
- Usually carcinomas; rarely melanomas and sarcomas
- Breast, lung, GI, GU, cutaneous – most common primaries
- Women 40 to 60 yo
- Rapid onset of unilateral proptosis
- Simultaneous mets to uvea and orbit in 2 to 9%
- Pain, diplopia, blurred vision

Orbital tumors with lethal potential

Metastatic tumors
- Prognosis depends on the primary and extent of disease
- Median survival time from diagnosis to time of death ranges from 7.4 to 15.6 months
- 1-year survival rate
  - 57% with breast cancer mets
  - 20% with lung cancer mets
- Therapy is palliative
  - Usually chemo alone, radiotherapy if vision threatening

Orbital tumors with lethal potential

Secondary orbital tumors
- Reach the orbit by direct extension from adjacent structures
  - Sinuses, nasal cavity, conjunctiva, eyelid, globe
  - Conjunctival squamous cell and melanoma
  - Eyelid basal cell, squamous cell, sebaceous cell, melanoma
  - Nasopharyngeal carcinoma
  - Sphenoid wing meningioma – temporalis fossa fullness, proptosis, anosmia, personality changes, papilledema
- Orbital exenteration is indicated

Orbital tumors with lethal potential

Rhabdomyosarcoma
- Most common primary malignant orbital tumor in kids
- Mean age at diagnosis is 8 yo
- Rapid onset, with proptosis, globe displacement, eyelid edema, and conj chemosis
- Skeletal muscle markers on immunohistochemistry
- Isolated orbital involvement – mortality rate is 4%

Orbital tumors with lethal potential

Myelogenous leukemia (chloroma)
- Usually occurs in young children
- Systemic disease is usually present before orbital disease
- Treatment – systemic chemotherapy for leukemia

Burkitt's lymphoma
- Highly aggressive
- Most common childhood malignancy in Africa
- Often seen in AIDS patients – Epstein Barr virus in 25-40%
- Treatment – chemotherapy for systemic disease, radiation

Periocular skin cancer

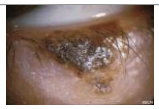
Periocular skin tumors

Basal cell carcinoma
- Usually lower lid
- Metastasis is rare
- Local invasion

Squamous cell carcinoma
- Keratoacanthoma
- Squamous intraepithelial neoplasia (Bowen's disease)
- Actinic keratosis

Periocular skin tumors

Melanoma
- Rare
- Lentigo maligna, dysplastic nevus – precursors
- Prognosis depends on depth of invasion



Sebaceous gland carcinoma
- More prevalent in Asians
- Upper lid in 67%
- Elderly females
- Masquerades as chronic chalazion, blepharitis

Periocular skin CA mortality rates

Squamous cell CA –
- 9% of all eyelid tumors
- Sun exposure
- Metastasis in 1-5% , mortality rate – 15%

Sebaceous cell CA –
- Orbital extension in 6 to 35% with 70% mortality rate
- Overall 5 year mortality rate – 15%

Periocular skin CA mortality rates

Melanoma – risk graded by depth of invasion and presence of nodal or distant metastasis

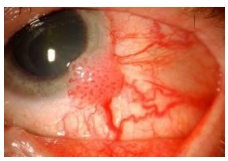
- Localized, confined to dermis – 95% 10 year survival
- With distant metastasis – 50% 10 year survival
- Risk factors – UV light, fair skin or hair
- Treatment – local excision with chemo for palliation

Conjunctival tumors

Conjunctival tumors

Squamous cell –

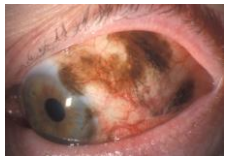
- Occurs at limbus in prexisting carcinoma in situ
- From longstanding UV exposure or irritation
- Nutritional disorders, chronic infection
- Whitish, rough, dry
- Telangiectatic, gelatinous
- Invades intraocularly in 10%
- Orbital or distant spread in 10%
- Treatment – local excision, brachytherapy



Conjunctival tumors

Malignant melanoma

- May arise in primary melanosis or nevi
- Middle aged white patients
- First, superficial pigmentation that enlarges and invades, then metastasizes
- 5 year survival – 83%, 10 year – 69%
- Higher risk in palpebral conj, caruncle, evidence of distant spread



Intraocular malignancies

Uveal melanoma

The most common primary ocular tumor in adults

Occurs in blue eyes, rare in dark pigmented eyes; older persons

Nevus of Ota

UV exposure

Uveal melanoma

Clinical presentation – 4 stages
- Asymptomatic
- Symptomatic – glaucoma, inflammation
- Extrascleral growth
- Distant metastasis

Usually detected on routine exam, occasionally after sudden vision loss
- Retinal detachment

Glaucoma – pupil block, infiltrating the trabecular meshwork

Induced hyperopia

Diagnosed with indirect ophthalmoscopy, IVFA or ICG, ultrasound, CT, MRI, fine needle biopsy

Uveal melanoma

Mortality rate – 80%

Mortality rate after enucleation –
- 30% at 5 yrs
- 40% at 10 yrs

Factors affecting survival –
- Larger tumor size
- Extrascleral extension
- Mixed cell type

Extrascleral extension may present as
- Epibulbar nodule
- Proptosis
- Phthisis
- Orbital mass

Uveal melanoma

Spreads through bloodstream
- Metastasis to liver (90%), lung (24%), and bone (16%)
- 50% with distant mets die within 1 year

Therapy –
- Enucleation, radiotherapy – plaque brachytherapy
- Radiation retinopathy causes a loss of useful vision
- Local resection for smaller tumors

Retinoblastoma

Most common intraocular tumor of childhood

Clinical presentation – leukocoria
- Strabismus, pupil block glaucoma
- Differential diagnosis
  - Toxocariasis, PHPV, Coat's disease, ROP, RD, VH, cataract coloboma

Mortality rate –
- 25% with minimal choroidal invasion
- 78% with optic nerve invasion

Retinoblastoma

Extrascleral extension through aqueous outflow pathways, or through sclera

Metastasizes to lung, bones, brain

Enucleation for staging

Survivors of bilateral RB develop a 2nd tumor

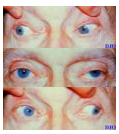
RB patients often develop pineal gland tumors

64 yo male with diplopia

HPI - Diplopia is intermittent –
- 2 weeks earlier pt awoke with horizontal diplopia that changed to diplopia in lateral gaze only, then returned to normal
- No headache, eye pain, weakness, ptosis

PMH
- Negative

Physical examination
- VA – 20/20 OU
- Pupils – normal, no APD
- Lids – mild ptosis OS



Myasthenia Gravis

Differential diagnosis includes brainstem stroke, MS

Fatigability of striated muscle after repeated contraction – improves with rest

Antibodies to Ach receptors

Suspect with any EOM abnormality

Anti-Ach antibodies

Often begins with ocular involvement only, then systemic involvement
- Extremity weakness
- Difficulty swallowing
- Difficulty breathing
- Treatment is with acetylcholinesterase inhibitors (pyridostigmine), plasmapheresis, steroids, immunosuppresives, IV immune globulin, thymectomy

Myasthenia gravis lethal complications

Impairment of muscle strength causes
- Aspiration
- Increased incidence of pneumonia
- Respiratory failure (myasthenic crisis)

15-20% experience myasthenic crisis

Mortality is 4%

44 yo woman with headaches

HPI - Headaches began several months ago, now increasing in severity
- Mild glare, photophobia
- Occasional diplopia

PMH - negative

Physical examination
- Abnormal Hirschberg test
- Pupils sluggish – no APD
  - Anisocoria
- MRD unequal
- EOM – poor upgaze, downgaze, abduction
- Fundus - normal

3rd cranial nerve palsy

Causes
- Infarction
- Aneurysm
- Pituitary tumor expansion
- Neoplastic infiltration
- Inflammation
- Cavernous sinus hemorrhage

Workup
- MRI/MRA (MRA – 97% effective in detecting aneurysm)

Treatment
- Directed toward specific cause

Mortality associated with 3rd nerve palsy

13 – 30% of 3rd nerve palsies are due to aneurysm (PCA)

Isolated 3rd nerve palsy with **pupil** involvement is aneurysmal until proven otherwise

Average time from onset of 3rd nerve palsy to subarachnoid hemorrhage from ruptures of PC aneurysms – 29 days
- Aneurysmal subarachnoid hemorrhage – 30 day mortallity rate of 45%
- Half of survivors – irreversible brain damage

Conclusion

Many ocular conditions can give rise to systemic involvement with high mortality rates

Your observations and good history taking can save a patient's life!

Thank you!

Questions?

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Credits

- All images were stock images from the internet
- I take no credit for nor do I own any of the images