Ocular Inflammations associated with Systemic Diseases

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Anterior Segment

ATOPIC DERMATITIS (ECZEMA)

Background
- 10 to 12% children and 1% adult population
- Men > women slightly
- More common in Caucasians
- History of childhood atopy (IgE mediated)
- Etiology remains unclear
- 42% ocular manifest.
Systemic manifestations
- peanuts, eggs, milk, soya, fish, and seafood.
- pruritic, ichthyosis
- eczematous inflammation: face-cheeks, neck, diaper area. (crawling: knees and hands)
- xerosis
- fissuring/scaling of the hands/feet (lichenification)
- hypo/hyper skin pigmentation
- pulmonary problems (dyspnea, wheezing)
- Young manifest vs older

Ocular manifestations
- pruritic/inflamed peri-ocular tissue
- chronic rubbing – brown discoloration of upper eyelids (lichen-simplex chromium: women/Asians)
- Dennie Morgan folds (lower lid)
- eyelid manifestations of inflammations blepharitis very common
- corneal involvement varies: SPK – atopic keratoconjunctivitis, pannus, HS, RD
- higher risk of keratoconus
- Cataracts

Work Up
1. Systemic
   - FH,
   - Patch, Scratch testing
   - Blood Levels show increased eosinophils
2. Ocular
   - Allergic Eye disease with above evidence
Systemic therapy

- Moisturization of skin
- Oral and Topical Antihistamines
- Doxepin cream 5% / Protopic 0.03%
- Topical anti-pruritis medications
- Topical steroids
- Immunosuppression for severe cases

Ocular therapy

- CC for lids
- Topical anti-histamines/mast cell stabilizers
- Topical steroids (flare-ups)
- Topical NSAIDS (late stage inflammation)
- Topical cyclosporine
- AT CC “Optimize Ocular Surface”
- Monitor for secondary complications
- Referral for cataract extraction

Anterior Segment

FACIAL / OCULAR ROSACEA
Systemic manifestations

- Occurs as oculo-facial rosacea and as ocular rosacea; the dermatologic condition usually has mild eye signs occurring simultaneously with skin signs
- Unknown etiology, but a combination of two broad processes
  - disorder of sebaceous glands and function
  - disorder of superficial capillaries

Systemic manifestations

- Facial rosacea exists as three broad types
  - Mild: simple redness, with scattered telangiectasias ("ruddy complexion")
  - Moderate: telangiectasias, redness, with scattered papules and pustules
  - Severe: telangiectasias, redness, papules and/or pustules, and sebaceous degeneration of the nose (rhinophyma)
- Facial rosacea typically presents with facial flushing and no more than 10 eruptions at any one time
- Women affected 2 to 3x > men

Possible Rosacea Food Trigger Factors (TF)

- dairy including yogurt, sour cream, cheese (except cottage cheese);
- alcohol including red wine, beer, vodka, gin, bourbon, and champagne;
- chocolate;
- soy sauce;
- yeast extract;
- eggplants, avocados, spinach;
- some beans and pods, including lima, navy or peas;
- citrus fruits, including tomatoes, bananas, red plums, raisins, or figs;
- spicy and temperature hot foods.
Possible Cosmetic Trigger Factors (TF)

- Alcohol
- Witch hazel
- Peppermint
- Eucalyptus oil
- Clove oil
- Fragrance
- Menthol
- Salicylic acid

Ocular signs

- Non-specific signs of ocular rosacea
  - Meibomitis
  - Frequent chalazia
  - Chronic blepharitis
  - Lid margin telangiectasias
  - Conjunctival hyperemia
    - Telangiectasias
    - Non-specific redness
    - Exacerbated by meibomitis and dry eyes

Ocular signs

- Prominent limbal arcades; later vessel abnormalities are pannus and neovascularization
- Nodules near limbus, resembling phlyctenules
- SPK
- Peripheral epithelial basement membrane disorders (EBMD), peripheral epithelial edema, microcysts
Ocular signs

- Specific corneal signs of ocular rosacea
  - process of advancing pannus followed by neovascularization
  - infiltration follows neovascularization
  - peripheral corneal thinning
  - risk of corneal perforation (rare)

Treatment - Facial Rosacea

- Oral tetracycline (DRUG OF CHOICE)
  - Tetracycline 250 mg, PO, QID, up to 8 weeks
  - should stay on full dose of tetracycline for one full month after maximal improvement
  - slow taper, possibly reducing daily dose by 250 mg each month to 250 mg daily or on alternate days
  - less traditional, short-term regimen: 250 mg, PO, TID X 3 weeks, then 250 mg, PO, QD X 3 weeks

- Doxycycline is a possible alternative / Minocycline / Erythromycin / Clarithromycin
  - improves compliance since BID dosage
  - dairy products interfere less with doxycycline, which should be taken with milk if G.I. upset occurs
**Treatment - Facial Rosacea**

- Metro-Gel
  - oral and topical metronidazole (Flagyl) is both an antibiotic and antiprotozoan agent / Amoxicillin 250-500 mg BID
  - Metro-Gel is mainly for skin eruptions; also reduces erythema
- Isotretinoin (Accutane) (0.5-1mg / kg/d) 28 wk – may succeed where other measures fail
- Home remedies: Dilute Vinegar and Green tea soaks

**Treatment - Ocular Rosacea**

- Most of the manifestations of ocular rosacea are non-specific and are managed with standard lid hygiene therapies for:
  - non-specific blepharitis
  - meibomitis
  - chalazia
  - hordeola
  - tear film disruption, dry eye symptoms
  - map-dot dystrophy (peripheral EBMD)

**Treatment - Ocular Rosacea**

- Conjunctival manifestations of ocular rosacea
  - usually non-specific conjunctivitis with telangiectatic vessels
  - unusual self-limiting gray nodules
  - systemic management of rosacea may improve the conjunctival presentation
Treatment - Ocular Rosacea

- Corneal thinning
  - very mild steroid
  - 0.12% prednisolone acetate, BID
  - stronger steroids are felt to be very risky, with the chance of perforating the cornea

Treatment

- Likelihood of relapse is over 50% in 6-18 months; may need indefinite maintenance therapy vs. tetracycline "pulses"

TEMPORAL ARTERITIS (AKA: Giant Cell Arteritis / Cranial Arteritis)

- Temporal arteritis is a disease of unknown etiology characterized by the inflammation of large and medium sized arteries, by constitutional complaints, and be a frequent association with
  - POLYMYALGIA RHEUMATICA (PMR)
2. Elderly patients of both sexes are affected (usually >65 y.o.) (women slightly more than men) Average age: 71

3. Pathologically multinucleated giant cells and other inflammatory cells infiltrate the walls of these arteries in a segmental distribution

Clinical Manifestations

- Polymyalgia rheumatica characterized by pain and stiffness of shoulder and pelvic girdle (lasting 1 month or more w/o any other explanation)
- Fever (low grade)
- Headache
- Neck Pain
- Night Sweats / Anorexia
- Joint swelling (minimal)
- Patients commonly around age 70 (71.5 highest)
- Jaw Claudication (90% or greater) **
- Temporal artery tenderness or pulse-less artery
- Mononeuritis complex (less common)

Ocular Manifestations

- Devastating vision loss (20/20 → CF or worse)
- TVL or Amaurosis Fugax
- Color Vision loss
- (+) APD of affected eye
- Swollen disc with flame hemorrhages
- Altitudinal Visual Field loss
Other Ocular Signs

- 6th nerve palsy (possible)
- CRAO (possible)
- PION (Posterior Ischemic Optic Neuropathy)
- Iritis with possible iris neovascularization
- Hypotony
- Cataract
- Posterior segment ischemia signs in one eye > other eye (CWS, IRMA, Venous Beading)
- Occipital Lobe Stroke

Laboratory Testing

- Immediate Westergren ESR
  \[ \text{men} = \frac{\text{age}}{2}; \quad \text{women} = \frac{\text{age} + 10}{2} \]
- C-reactive protein
- CBC w/differential
- CD4 and CD8 lymphocytes
- Anticardiolipin AB
- Temporal artery biopsy (done within 1 week of starting steroids)
- Possible ocular pneumoplethysmography
  - (OPG)
  - Color Doppler Ultrasonography

Treatment

- Medical:
- Steroids (methylprednisone 250 mg IV q6h for 12 doses in the hospital)
  - then switch to oral prednisone 80-100 mg, p.o. daily (4 weeks)
- WITHOUT STEROIDS – THE CONTRALATERAL EYE CAN BECOME INVOLVED IN 24 TO 72 HRS!!
- Oral steroids should be given for 6 months to 1 year (smallest dose that suppresses dz is used)
- Ocular Tx: NONE
SYSTEMIC LUPUS ERYTHEMATOSIS

Introduction

• S.L.E. is an inflammatory, autoimmune disease of unknown cause characterized by inflammatory lesions of many organ systems

• Epidemiologically women and blacks are affected more frequently, and the age of onset is generally between 15 and 40 - favors women (8:1)

• Syndrome may be drug induced (esp. procainamide/hydralazine) the brain/kidney is spared

Pathogenesis:

• Antibodies to DNA and other nuclear constituents are found in the serum of patients with S.L.E.

• Viral infection has been suggested as the event which prompts antibody formation against these host antigens

• Complexes of these antinuclear antibodies (ANA) and their respective antigens are entrapped by vascular and glomerular basement membranes initiating inflammation
Clinical manifestations:

- Constitutional symptoms include:
  - fever (low grade)
  - weight loss
  - malaise
  - myositis
  - alopecia (baldness)
  - myocarditis
  - pericarditis
  - vasculitis
  - lymphadenopathy
  - glomerulonephritis

Arthritis and Arthralgias

Skin eruptions:

- Malar “butterfly” erythematous rash is the most characteristic, but the form and location of the eruption may be quite variable
- Discoid lupus is a special form of the disease with manifestations limited to the skin

Cardiopulmonary involvement

Renal involvement is a major cause of morbidity and mortality (either by hypertension or kidney dysfunction)**

- Neurologic abnormalities are highly variable and a serious consequence of the disorder
- Hematologic changes include anemia, leukopenia, thrombocytopenia, and clotting abnormalities (very common)
OCULAR MANIFESTATIONS:

- Dermatologic abnormalities may affect the lids (discoid lupus)
- Neurologic involvement may affect extraocular motion
- Conjunctivitis
- Keratitis (K. sicca syndrome #1)
  - (most common ocular condition)

Episcleritis

Retinopathy:
- Cotton Wool Exudates / Spots are the MOST characteristic retinal abnormality
- Vasculitis (inflammation of retinal arteries and veins) produces these abnormalities: hypertension when present due to renal involvement may exacerbate the retinal changes

Superficial hemorrhages (flame shaped)

Retinal edema and pseudopapilledema

Arteriolar narrowing and A-V crossing abnormalities

Miscellaneous abnormalities:
- proptosis, cranial n. palsies and lupus optic neuropathy.

Ocular side effects of systemic treatment (i.e., Placquenil)
We have seen no cases of toxicity when the 6.5mg/kg/qd threshold was honored.

Diagnosis:
Clinical criteria suggest the diagnosis, 4 or more of the following 11 criteria must be present:
- macular rash
- discoid rash
- photosensitivity
- oral ulcers
- arthritis
- serositis
- renal disease
- (+) ANA test
- hematologic disorders
- neurologic disease
- immunologic disease (antibodies to DNA)

Serologic tests confirm the presence of S.L.E.
- antinuclear antibody (ANA) test
- ESR
- RF
- Immunoglobulin Electrophoresis
- Lupus Erythematosis Cell Prep
Treatment:

- Medical therapy
- NSAIDs (ibuprofen, 800 mg 3 X/day) **
- Aspirin (1 gram 4 X/day)
- Methotrexate 7.5 mg
- TNF (entercept, infleximab, adalimumab)
- Anti-malarials (Hydroxchloroquine 200 - 400 mg/day)
- Corticosteroids (60-100 mg/day)
- Cyclophosphamides (severe cases)
- More recently: Mycophenolate mofetil (Cellcept)
- Azathioprine (severe cases)

We have seen no cases of toxicity when the 6.5mg/kg/qd threshold was honored.

Ocular therapy

- Dry Eye ( #1 Ocular prob.)
- Retinopathy – no treatment (resolves w/sys. tx.)
- Conjunctivitis – topical antibiotic
- Keratitis / Episcleritis – topical antibiotic / steroid combo.
Treatment Regimen for K. Sicca Patients
- AT Substitutes
- Gels/ointments
- Topical CsA and corticosteroids, Omega III FA
- Tetracyclines
- Plugs
- Secretagogues
- Serum
- Contact Lenses
- Systemic Immunosuppressives
- Surgery

Adjunct. Tx
- withdraw offending agent if drug induced
- avoid sun exposure, sunblocks, stress
- bed rest

Anterior Chamber / Orbit
ANKLYLOSING SPONDYLITIS
Systemic manifestations

- Disease of the axial skeleton
- Males (3x) > females (1x)
- Ages 20-40
- Affects 0.1% of Caucasian adults
- Lower back pain in morning lasting 15 min. > 3 months (relieved by activity)
- Other complaints are "pain in the chest cavity and difficulty with chest expansion"
- Anorexia, fever, malaise - systemic signs

Ocular presentation

- Anterior uveitis - usually unilateral
- Recurrence in same or other eye
- Rapid onset of pain and photophobia
- Flare may be heavy
- Posterior synechiae form quickly
- Episodes last 2-6 weeks

Investigations / lab testing

- X-ray of sacroiliac joints
- ESR ↑/ C-reactive protein ↑
- Family Hx of AS
- HLA B27 tissue typing
- Alkaline phosphotase levels
Ocular therapy

- Topical steroids (q1h to Q2h - initially)
- Topical cycloplegic agents (QD or BID)
- Periocular steroid injections for more severe cases
- NSAIDS, COX-2 drugs, steroids, final resort is radiotherapy to the spine - main stay for systemic treatment & physical therapy

Anterior Chamber / Orbit

SARCOIDOSIS

Etiology

- Usually African-American (blacks 10X > whites)
- Multisystemic disease: hallmark, noncaseating granulomas
- Accounts for 3-10% of all uveitic cases
- 50% patients develop ocular sequellae
- Most commonly seen in the Atlantic Gulf Coast states
- Ages 20-40
- Disease has anterior and posterior involvement
- Systemic symptoms: fever, fatigue, dyspnea, weight loss
Ocular presentation

- Bilateral iridocyclitis
- Dense posterior synechiae
- Mild pain and photophobia
- Palpebral conjunctiva may manifest sarcoid granulomas (17%)
- Lacrimal gland enlargement
- KPs are extremely large (mutton-fat)
- Iris nodules are usually present (20%)
- Cataracts and glaucoma are complications

Ocular presentation

- Posterior segment: (involvement is less frequent)
  - Vitreous snowballs (vitritis)
  - "Candle wax drippings" - venule involvement
  - Perivenous sheathing
  - Choroidal lesions (Dalen-Fuch's nodules)
  - Choroidal granuloma (rare)
  - Chronic cystoid macular edema
  - Neovascularization of the disc (15%)
  - Optic disc swelling (40%)

Ocular presentation

- Skin lesions - erythema nodosum or sarcoid nodules under the skin
- Lungs are frequently affected
- Facial nerve palsies are possible as well
Investigations

- Chest X-ray (hilar adenopathy) (paratracheal adenopathy)
- ACE (↑)
- Serum lysozyme (↑)
- PPD (-)
- Anergy panel

Investigations

- Gallium scan of the head and neck
- Biopsy of conjunctiva or skin or lacrimal gland nodule
- ACE and gallium scan will give false negative if patient is taking steroids
- Pulmonary function tests

Differential diagnosis

- Sickle cell disease
- TB
- Idiopathic pars planitis
- Histoplasmosis/coccidiomycosis
Ocular treatment

- Topical cycloplegics (BID or QD)
- Topical steroids (Q1h to Q2h) depends on activity
- Periocular steroids if topicals are ineffective
- Oral steroids and histamine H2 blocker if treating posterior uveitis, facial nerve palsies, pulmonary problems
- Cyclosporin A - effective in patients intolerant to oral steroids

Ocular treatment

- Anti-glaucoma meds (topical and oral) for 2° complications
- Panretinal photocoagulation for neovascularization
- Patients need to be re-examined in 3-7 days
- Asymptomatic patients seen Q 6 months
- Steroid treated patients need to be seen Q 3 months
- Children with sarcoid need to be seen Q 1-3 months

Anterior Chamber / Orbit

Miscellaneous

SJOGREN’S SYNDROME
Introduction

- Sjogren's syndrome is a disorder without known cause characterized by keratoconjunctivitis sicca, xerostomia (dry mouth) or salivary gland enlargement (sicca complex), and often an association with other connective tissue diseases or rheumatoid dz
- Post menopausal women > 55 yrs. are affected much more frequently than men

Clinical manifestations

- Destruction of exocrine glands leading to mucosal dryness
- Dry mouth (xerostomia)
  - Difficulty in eating/talking
  - Sticking of gums
- Parotid enlargement
- Severe dental caries (lipstick sign)
- Loss of taste and smell

Clinical manifestations

- Associated with might include:
  - Nephritis
  - Vasculitis
  - Pancreatitis
  - Pleuritis
  - Polynuropathy
  - Thyroid disease
  - Cardiac conduction defects
Ocular manifestations
- keratoconjunctivitis sicca
- lacrimal gland dysfunction causing ↓ aqueous layer (dry eye symptoms) stringy discharge
- filamentary keratitis secondary to dry eye
- corneal ulcers secondary to dry eye
- blepharitis

Connective tissue diseases associated w/Sjogren’s
- rheumatoid arthritis (#1)
- SLE
- systemic sclerosis (scleroderma)
- polymyositis
- polyarteritis

Laboratory testing
- ANCA (serum anti-neutrophilic cytoplasmic antibody)
- anti-Ro (SS-A)
- anti-La (SS-B)
- RF
- ANA
- Lyme titer
Treatment

- Medical
  - Creams/ointments for skin dryness
  - Treat the connective tissue disease
  - Antifungal creams for vaginal yeast infections
  - Patients should be evaluated for lymphoma (5%)

- Ocular
  - Lacrimal gland dysfunction: (artificial tears, oral pilocarpine, punctal plugs, surgical intervention)
  - Filamentary keratitis: topical antibiotic after removal of filaments
  - Corneal ulcers: topical antibiotics

- Adjunct Tx
  - Chewing gum or frequent drinking (H2O) for dental caries
  - Avoidance of sugar containing candies
  - Mucomyst
  - Saline nasal sprays
  - Humidifiers