Sjogren's Syndrome

Background

1. Definitions
    - Chronic autoimmune disorder characterized by lymphocytic destruction of exocrine glands
    - Frequently results in xerostomia and xerophthalmia
2. General information
    - Underdiagnosed due to insidious onset and varied clinical presentation
    - Associated with HLA-DR

Pathophysiology

1. Pathology of disease
    - Chronic autoimmune response against epithelial cells of exocrine glands
    - B lymphocyte dysregulation / hyperactivity plays major role
    - Histological hallmark is B and T cell lymphocytic infiltration of exocrine glands
2. Incidence/prevalence
    - Second most common rheumatologic disorder in the US behind fibromyalgia (1st) and RA (3rd)
    - Occurrence in association with another connective tissue dz: 50-60%
    - Affects 1-2 million people in US
    - Female-to-male ratio: 9:1
    - Peak incidence in 4th and 6th decades of life
3. Risk factors
    - Female >40 yo
    - Preexisting autoimmune dz
    - Family Hx
4. Morbidity/mortality
    - Morbidity
        - Most cases mild
        - Chronic keratoconjunctivitis
        - Corneal ulcers
        - Extraglandular dz
            - Affects 25-30%
            - Kidney, liver, lung, skin
        - Multiple dental caries, tongue fissures, oral candidiasis
        - Fatigue
        - Non-Hodgkin's lymphoma eventually develops in 2.5-5%
        - Depression, cognitive impairment
    - Mortality
        - Primary dz
            - Normal life expectancy
        - Secondary dz
            - Increased mortality from associated autoimmune disorder

Diagnostics

1. History/symptoms
    - Dryness of
        - Mouth (98%)
            - Difficulty speaking, eating, swallowing
        - Eyes (93%)
            - Dryness, grittiness, pruritus, foreign body sensation
            - Required for clinical Dx
        - Skin
            - Dryness, pruritus
        - Vagina
            - Pruritus, dyspareunia
        - Nose
        - Trachea
        - Cough
    - Fatigue
    - Arthralgias (37-75%)
    - Myalgias, fibromyalgia
    - Raynaud's phenomenon (16-28%)
    - Autoimmune thyroiditis (15-33%)
2. Physical exam
    - Keratoconjunctivitis, conjunctival injection, corneal clouding (severe Dz)
    - Decreased saliva, dry mucous membranes (with fissuring, ulceration) and multiple dental caries
    - Vasculitis
        - Palpable purpura, urticaria or glomerulonephritis
    - Lymphadenopathy
    - Polyneuropathy, peripheral neuropathy
    - Parotid gland enlargement, tenderness
    - Signs of other autoimmune disorders (in 2° SS: RA, SLE)
3. Diagnostic testing
    - Majority of confirmatory tests done outside PCP office
    - Ocular evaluation
        - **Schirmer test**
            - Measures tear production
            - Test strip of # 41Whatman filter paper is placed in lateral third of lower eyelid to measure tear formation
            - Normal test: 15 mm of wet filter paper in 5 min
            - Positive test: < 5 mm in 5 min
        - **Rose bengal staining**
            - Identifies KCS, requires ophthalmologist
            - Instill 1% rose bengal in the eye, slit lamp exam
            - Rose bengal stains devitalized cornea / conjunctiva
    - Oral
        - Dental exam
        - Sialometry
            - Salivary flow rate measured by spitting into test for 15 minutes
            - Abnormal: unstimulated flow rate <1.5 mL/15 min

        - Contrast sialography
            - Visualize salivary glands with injected contrast
        - Salivary scintigraphy
            - Insensitive but highly specific
            - Evaluates salivary gland function
        - Minor (lip) salivary gland biopsy
            - Can confirm SS or exclude other Dx
    - Laboratory
        - Specific (% positive in SS)
            - ANA: 55-97%
            - Anti-SS-A/Ro: 16-70%
            - Anti-SS-B/La: 7-50%
            - RF: 32-90%
        - Systemic
            - CBC, ESR, LFTs, TSH, BUN/Cr, UA
    - Other studies
        - CT scan if progression to lymphoma suspected
4. Revised International Classification Criteria for Sjogren Syndrome
    - Dx requires presence of 4 of 6 criteria below and must include criterion #5 or #6
        1. Ocular symptoms
            - Dry eyes >3 mths
            - Foreign body sensation in the eyes
            - Use of artificial tears >3x per day
        2. Oral symptoms
            - Dry mouth >3 mths
            - Chronic swelling of salivary glands
            - Use of liquids to facilitate swallowing
        3. Ocular signs
            - Schirmer test <5 mm/5 mins, performed without anesthesia
            - Positive vital dye staining
        4. Oral signs
            - Abnormal salivary scintigraphy
            - Abnormal parotid scintigraphy
            - Unstimulated salivary flow <1.5 mL in 15 mins
        5. Positive salivary gland biopsy
        6. Antibody screen (anti-SS-A or anti-SS-B)

        Exclusion criteria
        - Past head and neck radiation Tx
        - Hepatitis C infection
        - AIDS
        - Pre-existing lymphoma
        - Sarcoidosis
        - Graft vs Host Dz
        - Anticholinergic drug use

Differential Diagnosis

1. Dry mouth
    - Diabetes
    - Head / neck irradiation
    - Meds
        - Anti-hypertensive, anti-cholinergic, psychotherapeutic
    - Psychogenic
2. Dry eyes
    - Chronic conjunctivitis or blepharitis, eyelid infections / abnormalities
    - Lifestyle (long driving, reading, computer use)
    - Environment (low humidity, smoke)
    - Meds
        - Anti-hypertensive, anti-cholinergic, psychotherapeutic
    - Hypovitaminosis A
3. Parotid enlargement
    - Viral
        - Mumps, EBV, HIV, HCV, coxsackie
    - Endocrine
        - Acromegaly, hypogonadism, testosterone deficiency / hypogonadism, diabetes
4. Systemic / extraglandular
    - Rheumatoid arthritis, SLE, scleroderma
    - Menopause
    - Multiple sclerosis
    - Lymphoma
    - Hepatitis
    - HIV
    - Sarcoidosis
    - Amyloidosis
    - Anxiety
    - Myopathies
    - Atopic disease

Therapy

1. Ocular dz
    - Moisture preservation and replacement methods
        - Preservative free artificial tears
        - Osmoprotective artificial tears
        - Lubricating ointments and methylcellulose inserts at night
        - Occlusion of puncta: collagen or silicone plugs (temporary), thermal / surgical (permanent)
        - Special goggles and glasses
    - Secretagogues: cholinergics
        - Pilocarpine 5 mg PO BID-QID
        - Cevimeline 30 mg PO TID
            - Contraindicated in asthma, angle -closure glaucoma, pregnancy

- Anti-inflammatory therapy
  - Topical steroids
  - Topical cyclosporine
  - Omega-3 essential fatty acids: topical or oral

2. Oral dz
   - Saliva substitutes: lozenges, rinses, sprays, swabs
   - Frequent dental exams with fluoride treatment
   - Secretagogues
     - Pilocarpine and cevimeline as above
   - Avoid diuretics, antihypertensives, antidepressants, antihistamines
   - Oral hygiene, humidifiers, adequate water intake
   - Sugar-free gum/hard candy with xylitol: 4-5 times per day
   - Treat oral candidiasis
3. Systemic dz
   - NSAIDs (arthralgias, myalgias, parotid pain)
   - Hydroxychloroquine 200 mg PO QD
   - Corticosteroids (severe joint Sx, vasculitis, renal dz)
   - Anxiolytics, hypnotics, antidepressants
   - Secretagogues, humidification, guaifenesin

Follow-Up

1. Referrals
   - Consider referral of patients with known or suspected Sjogren's to rheumatologist
   - Consider referral to ophthalmologist (eye exams) and dentist (oral exams)
   - Consider oral surgery consultation for lip biopsy
2. Admit to hospital
   - Decision based on severity of presenting symptoms

Prognosis

1. Primary dz
   - High morbidity, increased risk of lymphoma, but not in all-cause mortality
2. Secondary dz
   - High morbidity, increased risk of lymphoma, increased mortality
3. Increased risk of lymphoma
4. General
   - Usually stable exocrine function over time

Prevention

1. Early diagnosis and treatment
   - Prevent complications of dental caries, corneal ulceration, chronic oral infection and sialadenitis
   - Clinical surveillance for serious extraglandular / systemic complications
   - Avoid activities that cause dryness to control symptoms

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