

# **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

## Diagnosics

### 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 # 41 Whatman 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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