ACHING JOINTS, FATIGUE AND SJÖGREN’S

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WHAT IS SJÖGREN’S SYNDROME?
Major women’s health problem, largely underdiagnosed and undertreated

Increasingly recognized among younger women.

Multiracial, multiethnic, men and pediatric populations.
It is characterized by dryness of the mouth and eyes. Featuring the production of abnormal antibodies in the blood directed against glands that produce tears and glands that produce saliva.
Sjögren’s syndrome is the most common autoimmune disorder among women.

Predominately women (9:1) with median ages of onset in the 30’s and 50’s.

2nd most common autoimmune rheumatic disease with a prevalence of 2-3 million Americans (RA is 1st)
Usual Presentations:

- Ocular and Oral signs and symptoms (Only 80% of patients with SS present with classical sicca symptoms)
- 20% of patients present in an atypical fashion (minimal symptoms at time of presentation)
- So the diagnosis of SS can be easily missed.
  - High level of suspicion
Unusual Presentations:

- Seropositive polyarthritis
- Polymyalgia Rheumatica
- Fever of unknown origin
- Chronic fatigue syndrome
- Peripheral neuropathy
Unusual Presentations:

- Isolated CNS disease
- Inflammatory myositis
- Elevated ESR
- Positive ANA or RF in an Asymptomatic Patient
- Salivary gland swelling
Differential Diagnosis of the Sjögren’s syndrome:

- Amyloidosis
- Chronic Sialadenitis
- Diabetes Mellitus
- Eosinophilia-myalgia syndrome
- Fibromyalgia
- Medication related dryness
- Multiple sclerosis
- Hepatitis C
Extraglandular Manifestations

- Joint pain or inflammation,
- Raynaud’s phenomenon
- Lung inflammation
- Lymph node enlargement
- Kidney, nerve and muscle disease
- Vasculitis.
- Autoimmune thyroiditis
- GERD
- PBC
- Lymphoma
WHAT CAUSES SJÖGREN'S SYNDROME?
Aching Joints, Fatigue and Sjögren’s

- The exact cause is unknown
- Growing scientific support for genetic (inherited factors)
- Environmental factors (viral candidates may include EBV and Coxsackie viruses)
- Hormones?
WHAT ARE THE MUSCULOSKELETAL MANIFESTATIONS?
Aching Joints, Fatigue and Sjögren’s

- Joint, Muscle, Bone, Periarticular
- Nonarticular, Soft tissue
- Arthralgias, Myalgias
- Inflammatory Arthritis
- Fibromyalgia Syndrome (FMS)
- Hypothyroidism
- Osteoarthritis (OA)
### Aching Joints, Fatigue and Sjögren’s

<table>
<thead>
<tr>
<th>SYSTEMIC MANIFESTATIONS</th>
<th>MEAN %</th>
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<tbody>
<tr>
<td>Musculoskeletal</td>
<td>58%</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>53%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>7%</td>
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<tr>
<td>Myalgias</td>
<td>22%</td>
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<tr>
<td>Myositis</td>
<td>12%</td>
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# Aching Joints, Fatigue and Sjögren’s

<table>
<thead>
<tr>
<th>SIGNS AND SYMPTOMS</th>
<th>%</th>
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<tbody>
<tr>
<td>Hypergammaglobulinemia</td>
<td>80</td>
</tr>
<tr>
<td>Dry Skin</td>
<td>55</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>53</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td>50</td>
</tr>
<tr>
<td>Esophageal dysmotility</td>
<td>40</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>40</td>
</tr>
<tr>
<td>Pulmonary- CT changes</td>
<td>30</td>
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<tr>
<td>Raynaud’s</td>
<td>30</td>
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Primary Sjögren’s Arthritis

- Usually non-deforming, non-erosive
- Often early symptom
- Antinuclear antibody +
  - Similar in distribution to RA (non-erosive)
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Sjögren's Arthritis
(Inflammatory Musculoskeletal Pain)

- Targets the synovium and periarticular structures
- Arthralgias (joint pain),
- Myalgias (muscle Pain),
- Arthritis (joint inflammation, i.e.- pain, stiffness, redness, warmth)
- Polyarticular ($\geq 4$), oligoarticular (2-3) or monoarticular (1)
Pain, morning stiffness

Symmetrical small joints (hands, wrist, feet, ankles)

Shoulders, elbows, hips, knees,

Carpal tunnel syndrome
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Sjögren's Arthritis

Goals of Treatment

• Control of Disease activity
• Alleviate pain
• Restore and Maintain function
• Maximize quality of life
• Prevent structural damage
Hypothyroidism

- **Common in SS patients** (decrease thyroid hormone production, high TSH)
- **Multiple Symptoms** (slow heart rate, fatigue, dry skin/hair, hoarseness, constipation, facial swelling, muscle weakness, weight gain, cold intolerance)
- **Musculoskeletal manifestations** (arthralgias, muscle weakness, carpal tunnel syndrome, polyarthritis similar to RA)
- **Mimicker**
Muscle Disease

- Weakness vs. Fatigue
- Steroid Myopathy
- Myositis (Inflammatory muscle disease, EMG, NCV, Muscle biopsy)
Fibromyalgia

- Common (30% of patients with Sjögren's)
- Coexists with other comorbidities (not a dx of exclusion)
- Diagnosis based on Patient HX and PE
Fibromyalgia

- Chronic Widespread pain ≥3mo
- 4 Quadrants, Axis
- 11/18 tender points
- Manual Tender Point Survey (MTPS)
- Dysfunctional Pain syndrome Decreased stimulus, Increased sensitivity (hyperalgesia, allodynia)
  - Nonrestorative sleep, Fatigue
Osteoarthritis

- Most common type of Arthritis
- Disease of the Cartilage
- Not SS Specific
- Small joints of hands, knees, hips, spine
Osteoporosis

- Affects over 8 million women in US
- Silent (until fx), progressive
- Not SS Specific
- Risk factors (female, advancing age, postmenopausal, family history, chronic corticosteroids)
- 50% of women over age 50
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DIAGNOSIS AND MEASUREMENTS
Diagnosis

- History and Physical examination
- Pain assessment (location, duration, limitation)
- Laboratory Evaluation
Measurements

Blood tests: ESR, CRP, SPEP, B2 microglobulin, TSH, low free T4

Radiographs: X-rays, Bone Scan, DEXA, MSK Ultrasound

Arthrocentesis: Inflammation vs. Infection, vs. Crystals
WHAT ARE THE TREATMENT GOALS?
Non Pharmacological Intervention:

- Education
- Energy conservation
- Hydration
- Exercise (Isotonic, Isometric, Aerobic)
- Nutrition (Weight maintenance)
- Relaxation
- Dental Health
Pharmacological Intervention:
Inflammatory Arthritis

- Topical agents (Methyl Salicylate, Diclofenac)
- NSAIDS
- Acetaminophen, Tramadol
- Corticosteroids (Most potent anti-inflammatory, lowest dose, shortest course)
Pharmacological Intervention:
Inflammatory Arthritis

- **DMARDS:** Hydroxychloroquine, Methotrexate, Azathioprine, Sulfasalazine
- **Muscarinic agents:** Pilocarpine, Cevimeline
- **Biological agents:** Entanercept, Adulimumab, Infliximab, Rituxan (Not FDA approved-investigational)
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Treatment

Pharmacological Intervention:

Fibromyalgia

• Neurostimulatory inhibitors (Pregabalin decreases Substance P and Glutamates)

• Serotonin & Norepinephrine reuptake inhibitors (Duloxetine, Milnaciprin)
Treatment
Pharmacological Intervention:

Osteoarthritis

- Topical Agents (Methyl Salicylate, Diclofenac)
- NSAIDs (good first line, balance safety and efficacy)
- Acetaminophen (e.g. 4000mg/day)
- Nutrapharmaceuticals (glucosamine sulfate), Medical Foods (Limbrel)
Treatment
Pharmacological Intervention:

Osteoporosis (Calcium, Vitamin D, HRT, Antiresorptive Anabolic Therapies)

Hypothyroidism (Thyroid replacement)
Fatigue in Sjögren's Syndrome
Definition

The feeling of extreme tiredness or exhaustion (mental or physical) often involving muscle weakness that can result in difficulty performing tasks.
Sjögren's Quality of Life Study

- SSF membership Survey (1998)
- Concerns: Major symptoms, comorbid illnesses, demographics, disease impact on QOL & patient health self-assessment
- 3386 responders (~50%)
- 95% female
Sjögren's Quality of Life Study

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<th>MOST TROUBLING SYMPTOMS</th>
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<tr>
<td>Dry Eyes (90%)</td>
<td>Disturbed Sleep (52%)</td>
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<tr>
<td>Dry Mouth (88%)</td>
<td>Vaginal Dryness (49%)</td>
</tr>
<tr>
<td><strong>Fatigue (77%)</strong></td>
<td>GI Dysfunction (47&amp;)</td>
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<tr>
<td>Dry Skin (68%)</td>
<td>Tooth Decay (44%)</td>
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<tr>
<td><strong>Joint Pain (67%)</strong></td>
<td>Mouth Sores (35%)</td>
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Fatigue is a prominent symptom and can be profound.
Evidence exists for substantially reduced health-related QOL.
Characterizing and measuring fatigue severity and general discomfort is important to effectively assess and treat.
Questionnaire tools are sensitive and effective (self administered).
Causes:

- Systemic inflammation
- Poor Sleep
- FMS
- Depression
- Medication adverse effects
- Hypothyroidism
- Myositis
- Steroid Myopathy
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Systemic Inflammation:

• Upregulation of cytokines (IL-1, IL-6, TNF)
• Elevated Acute Phase Reactants (ESR, CRP)
  - Autoimmunity (RF, ANA, Anti-SSA, Anti SSB)
  - Elevated Inflammatory Proteins (Cryoglobulins, serum B2 microglobulins, IgG, IgM, IgA)
• Association with other organ involvement (Lungs, CNS, Kidneys)
Systemic Inflammation:

Clinical Features

- Fatigue
- Anemia
- Decrease in appetite
- Weight loss
- Fever
Systemic Inflammation:

Laboratory Evaluation

- CBC with differential, CMP
- ESR, CRP
- Serum Protein Electrophoresis (SPEP)
- Beta-2 microglobulin
- Autoimmune panel (e.g. ANA, SSA, SSB, RF, CCP)
Treatment

- Corticosteroids
- Hydroxychloroquine
- Methotrexate
- Biologics
Poor Sleep

- Common in autoimmune disorders
- Sjögren's (dry mucosal membranes, musculoskeletal symptoms, urinary frequency)
- Nonrestorative Sleep
- Sleep Hygiene
- Restless leg syndrome, Sleep Apnea
Treatment

- Darkness
- Ocular Lubricants
- Oral Lubricants (Salivary stimulants: e.g. pilocarpine)
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Recommendations

• Keep regular sleep schedule
• Consistent (personalized) exercise regimen
• Quiet, tranquil environment
• Warm bath
• Avoid caffeine, alcohol, tobacco (bedtime chocolates)
• Reserve bedroom for sleep and intimacy
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Recommendations

• Keep a daily schedule
• Organize each day
• Prioritize activities
• Energy conservation measures
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GOALS

- Control of Disease activity
- Alleviate pain
- Restore and Maintain function
- Maximize quality of life
- Prevent recurrent symptoms and structural damage
CONCLUSIONS

- Multiple causes of aching joints and fatigue
- Thorough evaluation is imperative
- Patient History and Physical examination
- Exercise patience evaluating the DDX
- Establishing the diagnosis is essential for instituting safe and effective treatment
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References:


