Sjogren’s Syndrome

Overview

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Coordinator, Multidisciplinary Sjogren’s Clinic
Toronto Western Hospital
Sjogren’s Syndrome is Defined by Criteria

It is an autoimmune disease that causes dryness of eyes and mouth.
It can cause systemic problems as well.
There is no specific test for Sjogren’s Syndrome. In fact, there is no specific test for any autoimmune disease. The diagnosis has to be made by criteria.
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria (Annals of Rheumatic Diseases 2002)

I. Ocular symptoms: a positive response to at least one of the following questions:

a. Have you had daily, persistent, troublesome dry eyes for more than 3 months?
b. Do you have a recurrent sensation of sand or gravel in the eyes?
c. Do you use tear substitutes more than 3 times a day?
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria (Annals of Rheumatic Diseases 2002)

II. Oral symptoms: a positive response to at least one of the following questions:
   a. Have you had a daily feeling of dry mouth for more than 3 months?
   b. Have you had recurrently or persistently swollen salivary glands as an adult?
   c. Do you frequently drink liquids to aid in swallowing dry food?
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria (Annals of Rheumatic Diseases 2002)

III. Ocular signs—defined as a positive result for at least one of the following two tests:

a. Schirmer’s I test, performed without anaesthesia (5 mm in 5 minutes)
b. Rose bengal score or other ocular dye score (4 according to van Bijsterveld's scoring system)
Sjogren’s Syndrome
What does it look like?

- Schirmer’s Test for dry eyes:
Sjogren’s Syndrome
What does it look like?

- Rose Bengal Test for surface damage:
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria
(Annals of Rheumatic Diseases 2002)

IV. Histopathology: In minor salivary glands with a focus score 1.

defined as a number of lymphocytic foci containing more than 50 lymphocytes) per 4 mm² of glandular tissue
Lip glands in Sjögren’s syndrome

Left panel: High power view showing lack of inflammatory infiltrates. Middle panel: Low power view showing focal areas of lymphocytic infiltration (arrows). Right panel: High power view showing extensive infiltration by lymphocytes with glandular and ductal atrophy. Courtesy of Samuel L Moschella, MD and Cynthia Magro, MD.
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria (Annals of Rheumatic Diseases 2002)

V. Salivary gland involvement: objective evidence defined by a positive result for at least one of-

a. Unstimulated whole salivary flow (1.5 ml in 15 minutes)
b. Parotid sialography showing the presence of diffuse sialectasias
c. Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer
Sjogren’s Syndrome
What does it look like?

- Unstimulated Salivary Flow:
Salivary Scan
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria
(Annals of Rheumatic Diseases 2002)

VI. Autoantibodies: presence in the serum of the following autoantibodies:

a. Antibodies to Ro(SSA) or La(SSB) antigens, or both
# Sjogren’s Syndrome and Anti-Ro antibody

<table>
<thead>
<tr>
<th></th>
<th>Sjogren’s</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-Ro</strong></td>
<td>52 kD</td>
<td>60 kD</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>normal</td>
<td>Photosensitive Rash</td>
</tr>
<tr>
<td><strong>Congenital Heart Block</strong></td>
<td>yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Neonatal Lupus</strong></td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>
Sjogren’s Syndrome and Neonatal Lupus Rash
Sjogren’s Syndrome and Anti-Ro

Congenital Heart Block

8 weeks; 2.95 kg

5 years; 17.2 kg
Sjogren’s Syndrome can be Primary or Secondary

- **Primary** means it occurs alone and everything that happens is due to that disease.

- **Secondary** means that it is only one manifestation of another autoimmune disease such as *Lupus*, *Rheumatoid Arthritis* or *Scleroderma*.
Sjogren’s Syndrome Diagnosis

*European-American Consensus Criteria (Annals of Rheumatic Diseases 2002)*

**Primary** SS may be defined in patients without any potentially associated diseases as:

- *a.* The presence of any four of the six items as long as either histopathology (IV) or serology (VI) is positive or
- *b.* The presence of three of the four objective criteria (i.e. items III, IV V or VI).
Sjogren’s Syndrome Diagnosis

European-American Consensus Criteria
(Annals of Rheumatic Diseases 2002)

Secondary SS is defined as:

a. the presence of item I or item II plus
b. any two items from III, IV and V in patients with a potentially associated disease (e.g., another connective tissue disease).

Sjogren’s Syndrome

Sjogren’s can occur secondary to other diseases:

- Systemic Lupus Erythematosus 15-20%
- Scleroderma 25%
- Rheumatoid Arthritis 25%
- Mixed Connective Tissue Disease 4%
American College of Rheumatology Classification Criteria for Sjögren’s Syndrome:

For a formal diagnosis of Sjögren's syndrome, patients must meet two of the following three criteria:

- **Positive serum autoantibodies**, either anti-SSA and/or anti-SSB; or positive rheumatoid factor and a titer of antinuclear antibody (ANA) ≥1:320

- **Labial salivary gland biopsy** showing inflammation with focal lymphocytic sialadenitis and a minimal focus score of ≥1/4 mm²

- **Ocular staining score** ≥3 for keratoconjunctivitis sicca

  93% sensitivity, 95% specificity, using AECG as gold standard in an external group
Sjogren's Syndrome... an immunological storm
1. ETIOPATHOGENIC BACKGROUND

3. ESTABLISHMENT

T-cell dysfunction
B-cell hyperractivity

4. PERPETUATION

− cytokines
+ − chemokines

5. EPITHELIAL DAMAGE

Apoptosis
Altered epithelial repair
Proteolysis

2. INITIATION

Autoantigens + Viruses

Genetic background
Neurohormonal factors
Sjogren’s Syndrome is like an iceberg.....
What you see.....

Local signs of dry eyes and dry mouth
Corneal Ulcer
Sjogren’s Syndrome Case: Mr. VM

- Dry furrowed tongue:
  - Angular cheilitis
  - Monilia overgrowth
Cervical caries
Fragmentation
Gingivitis
Loss
Information from our Multidisciplinary Sjogren’s Clinic (263 patients)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age</strong></td>
<td>52.5 years</td>
</tr>
<tr>
<td></td>
<td>(39-66)</td>
</tr>
<tr>
<td><strong>Mean duration</strong></td>
<td>7.34 years</td>
</tr>
<tr>
<td></td>
<td>(0-15)</td>
</tr>
<tr>
<td>Abnormal saliva production in</td>
<td>82%</td>
</tr>
<tr>
<td><em>(a quarter of these patients had normal saliva with gum or candy)</em></td>
<td></td>
</tr>
<tr>
<td>Mean severity of dry mouth /10</td>
<td>6.77</td>
</tr>
<tr>
<td></td>
<td>(4.37-9.17)</td>
</tr>
<tr>
<td>Mean severity dry eye /10</td>
<td>6.25</td>
</tr>
<tr>
<td></td>
<td>(3.55-8.95)</td>
</tr>
</tbody>
</table>
Information from our Multidisciplinary Sjogren’s Clinic (263 patients)

Oral Complaints:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean DMF</td>
<td>20.56 (max. is 32)</td>
</tr>
<tr>
<td>Hx Parotid Swelling</td>
<td>109 (42.4%)</td>
</tr>
<tr>
<td>Hx Parotitis</td>
<td>49 (19%)</td>
</tr>
<tr>
<td>Oral Candidiasis</td>
<td>63 (23.8%)</td>
</tr>
</tbody>
</table>
Second: Often this condition does not occur alone.

There are associated diseases.....
Sjogren’s Syndrome

U. of Toronto Sjogren’s Clinic......Family History CTD 47 (17.8%)

Sjogren’s can associate with other diseases:
- Systemic Lupus Erythematosus 15-20%
- Scleroderma 25%
- Rheumatoid Arthritis 25%
- Mixed Connective Tissue Disease 4%
Sjogren’s Syndrome

Primary Sjogren’s can overlap with:

- Primary Biliary Cirrhosis
  - 46 (17.9%) had AMA; 15 had PBC (5.7%)
- CREST Syndrome (Limited Scleroderma)
  - 6 had ACA (2.35%)
## Sjogren’s Syndrome Systemic Complications

<table>
<thead>
<tr>
<th>System</th>
<th>Literature (%)</th>
<th>Sjogren’s Clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint Pain</td>
<td>37-96%</td>
<td>137 (52.3%)</td>
</tr>
<tr>
<td>Raynaud’s</td>
<td>16-54%</td>
<td>83 (31.8%)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>14.8-50%</td>
<td>9 (3%)</td>
</tr>
<tr>
<td>Intrstitl Neph.</td>
<td>20-73%</td>
<td>18 (6.8%)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>20-68%</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>5-30%</td>
<td>16 (6%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>4-7%</td>
<td>18 (6.8%)</td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>17%</td>
<td>45 (17.9%)</td>
</tr>
</tbody>
</table>
Sjogren’s Syndrome and Raynaud’s Phenomenon
Sjogren’s Syndrome and Pneumonitis
Sjogren’s Syndrome and Vasculitis
Sjogren’s with Non-Hodgkins B-Cell Lymphoma
Lymphoma Salivary Gland

Occur in 14% of Bx with Germinal Centres, 0.8% of those with no Germinal Centres after mean 7 year follow-up

## Sjogren’s Clinic
### Significant Systemic

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Primary SS</th>
<th>Sicca Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>19.47 ± 8.41</td>
<td>12.27 ± 3.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgA</td>
<td>3.24 ± 2.61</td>
<td>2.32 ± 1.17</td>
<td>0.002</td>
</tr>
<tr>
<td>WBC</td>
<td>4.78 ± 1.97</td>
<td>5.69 ± 1.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% with Pos RF</td>
<td>58.6</td>
<td>13.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% with high TSH</td>
<td>18.9</td>
<td>9.2</td>
<td>0.029</td>
</tr>
<tr>
<td>% with incr SMA</td>
<td>35.4</td>
<td>19.0</td>
<td>0.009</td>
</tr>
<tr>
<td>% Raynaud’s</td>
<td>32.6</td>
<td>13.6</td>
<td>0.001</td>
</tr>
<tr>
<td>% Candidiasis</td>
<td>33.8</td>
<td>19.3</td>
<td>0.042</td>
</tr>
</tbody>
</table>
Third, Sjogren’s is not easy to take like chicken soup……

Patients are very unhappy
Quality of Life Assessment in Sjogren’s Syndrome and Sicca

Abbey S, Stewart D, Devins G, Bookman A
Sicca

- Refers to people with dry eyes and/or dry mouth
- Who do not meet criteria for primary or secondary Sjogren’s Syndrome
<table>
<thead>
<tr>
<th>ITEM</th>
<th>SS (35)</th>
<th>SICCA (25)</th>
<th>%ILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role Phys</td>
<td>44.1</td>
<td>38.0</td>
<td>25</td>
</tr>
<tr>
<td>Body Pain</td>
<td>59.2</td>
<td>42.5 (p.018)</td>
<td>25</td>
</tr>
<tr>
<td>Vitality</td>
<td>41.8</td>
<td>37.8</td>
<td>25</td>
</tr>
<tr>
<td>Role Emot</td>
<td>69.7</td>
<td>69.7</td>
<td>50</td>
</tr>
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</table>
### DEVINS ILLNESS INTRUSIVENESS SCALE

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>MEAN SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Tx Recipients</td>
<td>24</td>
</tr>
<tr>
<td>CAPD</td>
<td>31</td>
</tr>
<tr>
<td>Dialysis in Centre</td>
<td>36</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>43.5</td>
</tr>
<tr>
<td>SJOGREN’S SYNDROME</td>
<td>42.5</td>
</tr>
</tbody>
</table>
Quality of Life: Sjogren’s and Sicca experiences with medical profession

<table>
<thead>
<tr>
<th></th>
<th>Sjogren’s</th>
<th>Sicca</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. mos. to get dx</td>
<td>27.3</td>
<td>31.8</td>
<td>ns</td>
</tr>
<tr>
<td>No. MD’s seen prior to dx</td>
<td>2.9</td>
<td>3.2</td>
<td>ns</td>
</tr>
<tr>
<td>Satisfctn with med profn (0-7)</td>
<td>3.7</td>
<td>3.8</td>
<td>ns</td>
</tr>
</tbody>
</table>
So what can you do about it?

Local Management
Management Options for Xerostomia

- Fluid sips
- Xylitol gum or candy
- Biotene products
- Moi-Stir spray
- Salagen
- Evoxac
- Ketoconazole cream, Nystatin
Management Options for Dental Decay

- Chlorhexadine rinse
- Fluoride preparations: Prevadent, Oral B
- Fluoride trays
- Amalgam fillings (not composite)
- Caps
- Implants
Some people need drugs

Systemic Management
Systemic Management

- **Prednisone**…minimal effect on parotomegaly, no effect on xerostomia, exhaustion, xerophthalmia

- **Hydroxychloroquine**…..ineffective for xerostomia, xerophthalmia or most systemic features. Helpful for cutaneous vasculitis.

- **Immunosuppressants**: Imuran ineffective. Most others untried.

- **TNF inhibitors** (Infliximab) ineffective.
Rituximab

- A chimeric anti-CD20 monoclonal antibody.
- Destroys mature B-cells
- Leaves intact immunoglobulin producing plasma cells
- Leaves intact stem cells.
Around the corner….

- Benlysta
- Stromal Stem Cell Infusions (fetal umbilical cords)
Sjogren’s Syndrome
Conclusions:

- An uncommon, not a rare disease
- Diagnosed by Criteria
- Can affect the entire body
- Not just a nuisance: major impact on QoL
- Women
- Treatment is becoming more effective
Multidisciplinary Sjogren’s Clinic

- Oral Pathologist, Dr. John McComb
- Otolaryngologist, Dr. John Rutka
- Ophthalmologist, Dr. Allan Slomovic
- Optometrist, Dr. Barbara Caffery
- Pathologist, Dr. Denis Bailey
- Rheumatologist, Dr. Arthur Bookman (Coordinator)