Current issues in the Diagnosis and Management of Sjogren’s Syndrome

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Primary Sjogren

A systemic autoimmune disease whose characteristic is ocular and salivary involvement, but also includes other organs such as lung (pneumonitis), kidney (interstitial nephritis), and neurological (central and peripheral) and lymphoproliferative features
Correct therapy depends on correct diagnosis

a) New international criteria
b) Potential pitfalls in diagnosis
Goals-2

Review the use of Topical medications for dry eyes and dry mouth
Goals-3

Review the current guidelines for diagnosis and therapy of extra glandular manifestations
Goals-4

How to empower the patient to participate in their own care
Epidemiology of Sjogren’s

1. Predominately women (9:1) with two ages of median onset
   In the 30’s and 50’s
2. Much of what we call SLE in the older patient is actually Sjogren’s syndrome
What causes Sjogren’s

A combination of Genetic and Environmental Factors

From family and twin studies, approximately 4 genes are required but even then an environmental factor is needed
Genetics

1. Most important is HLA-DR, which correlates closely with ANA and anti-SS-A antibody

2. Genes of B-cell activation similar to SLE patients
Environmental

No single agent identified
Viral candidates may include EBV and coxsackie viruses
Hepatitis C, HIV and HTLV-1 can mimic
There is good agreement about diagnosis for the patient with florid symptoms of keratoconjunctivitis sicca (KCS), parotid swelling, and high titer ANA with SS-A/SS-B.

The issue in these patients will be therapy and the extent of extra glandular involvement.
Typical features of dry eyes, dry mouth and swollen glands
Dryness results in the clinical appearance of keratoconjunctivitis sicca (KCS) characteristic of Sjogren’s syndrome.
Severe Xerostomia with dry tongue
Sjogren’s syndrome
Eye and Oral Features

1. Most of these patients have a positive ANA with positive Anti-Sjogren’s SS-A/SS-B antibodies
2. They have specific needs for the eye and mouth care
Since these patients see many health care professionals (ophthalmologists, dentists, rheumatologists) their care is expensive and fragmented

We must empower them to be part of the therapeutic team and even to educate their health providers
Sjogren’s Syndrome - Cervical Dental Caries
In addition to dry eyes and dry mouth

These patients have signs and symptoms that affect other parts of their body ranging from obvious manifestation of skin vasculitis to vague symptoms of fatigue and cognitive loss.
Diagnostic Issues
In the patient with true Sjogren’s

Sjogren’s syndrome

Extent Of Extra glandular Disease

Therapy And Education
Differential Diagnosis: is the Dryness Due to Other Causes

Non Salivary Gland Disease
- Drugs-esp. BP and cardiac muscle relaxants
- Antidepressants and OTC meds for cold
- Acute anxiety and depression
- Mouth breathing
- Central lesions:
  - Multiple sclerosis
  - Alzheimer’s

Salivary Gland Disease
- Hepatitis C
- Sarcoidosis
- Fatty Infiltrate of Gland
- HIV disease
- Lymphoma
- Cancer of the Salivary Gland
- Infection of gland (TBC, Actinomycosis)
- Head & neck radiotherapy
The most difficult and common questions involve the diagnosis and treatment of the patients with vague complaints of dryness, fatigue, cognitive dysfunction, arthralgias and low titer ANA.
Objective-3
Clinical Issues of Diagnosis of fatigue

- Primary Sjogren’s (high ESR, CRP)
- Hypothyroid
- Drug toxicity
- Sleep disorder (nocturnal myoclonus)
- Fibromyalgia with Low titer ANA and depression
- Depression
Issues in Diagnosis-1

Past confusion over criteria
San Diego criteria (0.5% incidence) versus
Original EEC criteria (5% incidence)
Now clarified
With new proposed international criteria
Issues in Diagnosis-2

Submitted criteria (11/01) by International SS advisory board
Will require either
A positive minor salivary gland biopsy
Or
Antibody against SS-A (Ro)
New international criteria-1

1. Ocular Symptoms
2. Oral Symptoms
3. Salivary gland function
   (flow rate by flow rate, scan, or sialography)
   AND
4. Histopathology (focus score > 1)
5. Autoantibody to SS-A or SS-B
New international criteria-2

New Criteria for SS (cont’d)

Exclusions

- Pre-existing lymphoma, sarcoid
- Hepatitis B or C
- Drugs with Anticholinergic side effects

(measurements of tear/saliva with patient off drug for 3 half lives)
Caution in interpreting studies on clinical associations published during past several years—since results will depend on the inclusion criteria

For example:

A) On disease associations (esp. liver-as hepatitis C now now now an exclusion)
B) “Primary” Fibromyalgia patients now excluded
How good are our tests?

The lip biopsy and the ANA and anti-SS A antibody are often considered “specific” tests but they are not specific.
Pitfalls in diagnosis-1

A) Positive ANA does not mean Sjogren’s or SLE
   These tests are sensitive but not specific
   (only about 1:100 patients with ANA 1:320 will have SS
   or SLE)
B) anti SS-A antibody more specific-but
   differences between detection kits
The ANA is sensitive but not specific

The ANA should not be used as a screen for Sjogren’s or SLE but to confirm a clinical diagnosis. ANA 1:80 present in 20% of normals (esp. in fibromyalgia patients)

This is important since some aggressive physicians have actually treated fibromyalgia patients for their fatigue with cyclophosphamide thinking that it was CNS vasculitis.
Even the Gold standard of lip biopsy is often misread by pathologists.

On review of outside biopsies diagnosed as Sjogren’s syndrome, over half (32/60) were reclassified on review.

Part of the confusion is that patients complain of dry eyes/mouth and rheumatologists talk about antibodies.

Why do patients complain of dry eyes and dry mouth?

It is important to recognize that symptoms can only be interpreted as part of a functional unit that involves a neuroendocrine circuit.
They are describing the sensation of increased friction

As the eyelid traverses the orbit
Or the tongue moves around the buccal mucosa
Normally the upper eyelid glides over the globe on a coating called the tear film composed of water, protein, mucins.
When the tear film is inadequate, The upper lid sticks to the surface of the orbit and Actually pulls off the surface layer of the ocular surface.

The Sjogren’s patient is describing increased friction as the upper lid moves over the globe.
Dryness results in the clinical appearance of keratoconjunctivitis sicca (KCS) characteristic of Sjogren’s syndrome
In Sjogren’s syndrome

A similar deficiency in the saliva increases the friction as the tongue moves around the mouth in order to swallow or talk. The decrease in saliva leads to acceleration of dental decay and other infections such as oral candidiasis.
The Sjogren’s Syndrome with swollen parotid gland

The concern is infection or lymphoma
Sjogren’s Syndrome - Diffuse Submandibular Salivary Gland Enlargement
Sjogren’s Syndrome - Ascending Salivary Gland Infection
Sjogren’s Syndrome - Investigations

MRI
If you order an MRI

1. Ask for MRI-sialography (this is just a fat suppression view to visualize the ducts). It takes only 5 minutes more and no risk

2. Have the MRI printed out on CD and give copy to patient for their record
Although the systemic manifestations can occur in Sjogren’s as in SLE, there are some subtle differences.
### Extraglandular manifestations

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<th>Sjogren’s syndrome</th>
<th>SLE</th>
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<td>Skin-leukocytoclastic vasculitis</td>
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<td>Lung-interstitial pneumonitis</td>
<td>Lung-pleural effusions</td>
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<td>Renal-interstitial nephritis</td>
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<td>Cardiac-pulmonary hypertension</td>
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<td>Hematologic--lymphoma</td>
<td>Hematologic-ITP, hemolytic anemia</td>
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<td>Neurologic-peripheral neuropathy</td>
<td>Neuropathy-mononeuritis multiplex</td>
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<td>Esophageal-dysphagia and tracheal reflux</td>
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Systemic therapy-1

In general, similar to SLE
Steroids work and the question is how to get the patients off steroids
Systemic therapy-2

Usually start with hydroxychloroquine or methotrexate for rash or arthralgias
Systemic therapy-3

For severe visceral vasculitis, still use cyclophosphamide (pulse)
But try to use less than 6 cycles and then try
Leflunomide, mycophenolic acid anti-CD20 (Rituxin)
Recent preliminary report that infliximab (Remicade) Published (Steinberg, 2003) But a larger multicenter trial Presented at American College of Rheumatology Did not show benefit of TNF inhibitor
How can we educate and make the patient part of the therapeutic team

In an era of decreased time for patient contact, we must utilize the internet and support groups as a backbone. The internet can be source of either information or mis-information unless we help create useful sites.
What should be on an Internet site?

We need to ask Patients what they want and need-
   a) medications and procedures
   b) insurance issues
   c) Hot “Links” to other relevant sites
But not all patients are computer literate?

Determine if physicians and patients can work through local libraries, where high school students can fulfill “civic service” by setting up sites and serving as resources to maintain sites.
1. New diagnostic criteria are developed that should diminish confusion in clinical practice and in the research literature.
2. There is variability in reading minor salivary gland biopsies and interpretation of positive ANA’s.
Sjogren’s syndrome has clinical features and treatment that are generally similar to SLE. But the Sjogren’s patient has particular needs in terms of the medications they tolerate and particular disease manifestations.