Sjögren's Syndrome: A Difficult Diagnosis to Make

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Sjögren's Syndrome ***is*** a difficult diagnosis to make and there are several reasons for this:

1) A syndrome and not a disease
2) The limitations of the classification criteria used to define the syndrome
3) Not recognizing the systemic nature of the syndrome
4) Lack of education of patients, healthcare providers and the public in general.

Syndrome

The word syndrome is defined as "a group of symptoms commonly occurring together" and a syndrome is not as well defined as a disease where there is frequently a characteristic pathology that helps to define the cause of the disease i.e. inflammation, infection, malignancy, vascular abnormalities or degenerative changes.

Criteria

The most recent classification criteria, the American European Consensus (AEC) Criteria have contributed significantly to defining a specific group of signs and symptoms indicative of Sjögren's Syndrome as well as excluding other diseases that could be confused with Sjögren's Syndrome. They also specify the methods used to test for the dry eyes and dry mouth complaints which means a more uniform way of defining the syndrome. These criteria have also contributed another significant step in the right direction and now a patient can be classified as having primary Sjögren's Syndrome without having either dry eye or dry mouth *subjective* complaints. However, despite numerous attempts to develop criteria to help define this syndrome, there is still a problem with recognizing the full clinical spectrum of this systemic disease. The main focus of the criteria are on the sicca complaints pertaining to the mouth and eyes and in this regard classification criteria are not necessarily adequate for the diagnosis of individual patients.

The AEC criteria also require either a positive lip biopsy or the presence of antibodies to either Ro or La antigens for the diagnosis of primary Sjögren's Syndrome. The requirement of a fairly specific pathology helps to move this syndrome more towards being a disease. The requirement of a fairly specific autoantibody profile helps us to categorize this syndrome more appropriately in the spectrum of the connective tissue diseases. The problem that remains is the specificity of these antibodies is not 100% and efforts to identify a more specific autoantibody profile indicative of Sjögren's Syndrome continue. This point is even more important now that we know that the presence of specific auto antibodies can be associated with the presence of a specific pathology, for example the association of antibodies to phospholipid/protein complexes with a predisposition to develop blood clots.

The diseases that are excluded by the AEC criteria can produce a pathology that is very similar to that found in the, so called, idiopathic Sjögren's Syndrome. Some of these excluded diseases are chronic viral disease states and they serve to remind us that viruses have been implicated in the pathogenesis of Sjögren's Syndrome and other connective tissue diseases.

Systemic Nature of the Syndrome

Sjögren's Syndrome is a systemic syndrome that can occur alone (primary Sjögren's Syndrome) or in association with numerous other rheumatic diseases; rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, CREST and mixed connective tissue disease (secondary Sjögren's Syndrome). Sjögren's Syndrome therefore helps us to understand more about the connective tissue diseases in general in that it crosses boundaries, including the next step into malignancy. It is these features that make Sjögren's Syndrome so interesting as it is quite unusual for other diseases such as rheumatoid arthritis and systemic lupus erythematosus to coexist in the same patient, yet it has been estimated that more than 50% of classical rheumatoid arthritis patients also have Sjögren's Syndrome. Ro antibodies, that are now a required criteria for the classification of Sjögren's Syndrome, are also found in patients with Systemic Lupus Erythematosus and not in patients with rheumatoid arthritis.

Primary Sjögren's syndrome patients also develop arthritis but usually there is no associated deformity with this arthritis. Approximately 30% of Sjögren's patients also have raynauds phenomenon and it has been estimated

that 70% of patients with primary biliary cirrhosis also have sicca complaints.

The spectrum of clinical complaints is enormous (table 1). In fact, every organ in the body can be affected by this disease including the peripheral and central nervous systems. Fatigue is probably one of the most disabling features of this disease. It is therefore not surprising that this syndrome is difficult to diagnose when the classification criteria do not include any of these other systemic manifestations.

Lack of Education

Patients, Healthcare Providers and Public in General

Patients presenting to a rheumatologist's office for their joint complaints and fatigue are unlikely to volunteer the information that they also have dry eyes and dry mouth unless they are specifically asked about these complaints. The presence of antibodies to Ro may raise a few eyebrows but unless the physician is thinking about this diagnosis the test may never be ordered. Very few rheumatologists routinely evaluate patients for adequate salivary flow and the patient may think it inappropriate to mention their caries problem unless they are at the dentist. So overall Sjögren's syndrome is missed, primarily because it is not looked for and there is still the misconception that nothing can be done to help these patients so there is no urgency to make this diagnosis.

The other problem that contributes to the difficulty of making this diagnosis and difficulty of living with this disease is that often there is very little to see on examination. There is generally no facial rash, hair loss or deforming arthritis. It has been estimated that it can take up to 9 years for the correct diagnosis to be made even in the patients who do present with the classical signs and symptoms. Sjögren's patients are often just considered to be depressed and to have nothing wrong with them. This concept is also a consequence of ignorance. Generally, the lay pubic has not heard of Sjögren's Syndrome and if they have not heard of it, it cannot be very common and it cannot be very important. This needs to be changed.

Conclusion

Sjögren's Syndrome *is* a difficult diagnosis to make.

Table 1 Clinical manifestations of Sjögren's Syndrome

Mouth	Dryness, dental caries, oral candidiasis, glandular swelling
Eyes	Dryness, corneal ulcers
Skin	Dryness, purpuric rash
Lungs	Dry airways, Lymphocytic infiltrates, pulmonary nodules,
Gastro intestinal tract	Atrophic gastritis Adult onset celiac disease Liver disease, chronic active autoimmune hepatitis, Primary biliary cirrhosis Pancreatitis and pancreatic insufficiency
Renal and urogenital	Interstitial nephritis with renal tubular acidosis Renal stones Glomerular nephritis Interstial Cystitis Vaginal dryness
Cardiac	Heart block in infants born to Ro positive mothers
Neurological	Peripheral neuropathy Autonomic neuropathy CNS with optic neuritis Autoimmune deafness
Thyroid	Autoimmune thyroid disease
Vascular	Vasculitis, Raynauds phenomenon
Malignancy	Lymphoma and lymphadenopathy