



SECONDARY SJOGREN'S SYNDROME: CASE REPORT AND A BRIEF REVIEW

Dental Science

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ABSTRACT

Sjögren's syndrome, either primary or secondary, has been defined as an autoimmune epithelitis characterized by lymphocytic glandular infiltration and various extraglandular manifestations. It shows an intense T lymphocyte mediated autoimmune process in the glands as one of its most prominent components, owing to dry eyes (xerophthalmia) and dry mouth (xerostomia). It can exist by itself (Primary Sjogren's syndrome or Sicca syndrome) or develop in association with another connective tissue disorder (Secondary Sjogren's syndrome). The syndrome has many dental implications that are important for the dentists. We present a case on secondary sjogren's syndrome and a brief note on its etiopathogenesis.

KEYWORDS

Sjogren's syndrome, Sicca syndrome, Xerophthalmia, Xerostomia.

Introduction:

Sjogren's syndrome (SjS) is an autoimmune destruction of exocrine that produces the clinical manifestations of dry mouth, dry eyes. [1] SjS is estimated to affect 1–3% of the general population. Whilst all ages can be affected, it is generally seen in menopausal women in the fourth and fifth decades of life, with women to men ratio of 9:1.1. Interestingly, approximately one-third of patients with some form of autoimmune disorder (AID) concurrently suffer from SjS. [2]

Descriptions of the patients with what we now call SjS began to appear in the medical literature during the latter half of the 19th century. [3] However, the first to suggest they could be attributed to a systemic disease was the Swedish ophthalmologist Henrik Sjögren, in 1933. [2]

Case report:

A female patient aged 56 years, walked into the department of Oral medicine and radiology, with a chief complaint of dryness of the mouth and eyes for the past 1 year and recurrent painful oral ulcers.

Patient gives a history of visiting a private hospital 2 years back for painful joints of knee, ankle and wrist. Laboratory investigations were performed and the report revealed a higher erythrocyte sedimentation rate (ESR) and positivity for IgM Rheumatoid factor (RF) while antinuclear antibody (ANA) was negative. The patient was diagnosed with Rheumatoid arthritis (RA) and was advised to take steroid injections and non-steroidal anti-inflammatory drugs (NSAIDs) since then.

Extra-oral examination revealed dryness in the eyes, which has been assessed by fluorescein staining (Figure: 1). On intra-oral examination, there was decreased salivation and the consistency of the saliva was thick and ropy, other sites of the oral cavity, like buccal mucosa and tongue appeared pale and dry with depapillation on the tongue.

Biopsy from the minor salivary gland of the lower lip was performed and the tissue specimen was sent to the department of oral pathology for microscopic examination.

Microscopically, the stained H & E sections revealed the presence of salivary gland tissue consisting of mucous acini and intralobular ducts along with dense lymphocytic infiltrate in the lobules. The lymphocytic infiltration into the mucous acini destroyed the parenchyma sparing the lobular and ductal architecture. (Figure: 2) With the above mentioned clinical features and microscopic findings along with the previous history of associated RA, the lesion was diagnosed as secondary SjS.



Figure 1: Note the filamentary keratitis in a moderate dry eye secondary to keratoconjunctivitis sicca where in the degenerated epithelium and mucous strands are visible taking up fluorescein stain due decreased aqueous tear production.

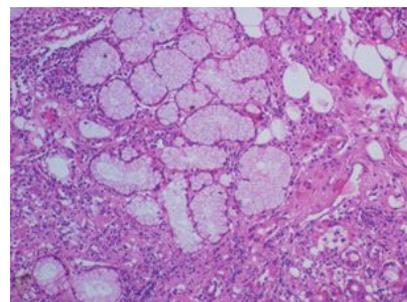


Figure 2: The above H & E stained section shows numerous minor salivary gland acini with dense lymphocytic infiltration (10x)

Discussion:

SjS is a chronic, systemic AID characterized by lymphocytic infiltration of the exocrine glands (mostly lacrimal and salivary glands) leading to the formation of keratoconjunctivitis sicca and xerostomia. SjS may occur in two forms: Primary SjS, when the clinical manifestations of the syndrome are seen alone and Secondary SjS, when associated with another AID, most commonly RA. [4]

The etiopathogenesis of SjS is controversial; however the recent clinical studies suggest that the disease process involved in SjS has genetic, immune, and neuroendocrine components. [5]

Firstly, the genetic basis of SjS is expected to be as complex as that of other AID including systemic lupus erythematosus (SLE) and RA and its genetic architecture still remains unexplained. Genome-wide association studies have shown strong associations between SjS and human leukocyte antigen (HLA) class II molecules, of which HLA-DR genotype being more predominant. HLA-DR3 is normally present in about 25% of the population, but it occurs in 66% of patients with primary SjS and with normal frequency in those with secondary SjS. The difference in frequency of occurrence of these gene products identify difference between primary and secondary SjS.^[5]

Secondly, considering neuroendocrine factors in the etiopathogenesis of SjS, many studies have suggested that the patients with SjS have 50-60% of their glandular structure being destroyed and 40-50% of the remaining structure being viable. The dysfunction of the remaining glandular tissue clearly plays a role in SjS pathogenesis. Proinflammatory cytokines released by epithelial cells and lymphocytes seem to impair the neural release of acetylcholine.^[2] In addition, antibodies to acetylcholine (muscarinic) receptors may interfere with the neural stimulation of local glandular secretion perhaps by interfering with aquaporin.^[5]

Lastly, immunopathogenesis in SjS is considered one of the most commonly accepted theories. The theory termed auto-immune epithelitis suggests that the epithelial tissue is inflamed in SjS. Epithelial cells thus acts as central regulators of the autoimmune response by acting as atypical antigen presenting cells (APC). Salivary gland epithelial cells (SGECs) have been shown to constitutively express a plethora of immune-competent molecules, which helps in infiltration of lymphocytes.^[6] Additional T cells and B cells with autoantibody-secreting capabilities are recruited.

Most reports on the subject are in agreement that infiltrating mononuclear cells in SjS express Bcl-2. Expression of the pro-apoptotic Bax protein appears to be significantly elevated in SjS patients, with an increase in the ratio of Bax to Bcl-2. This shift in the balance between pro- and anti-apoptotic regulators could indicate a predisposition in favor of apoptosis in the salivary epithelia of these individuals.^[5]

The criteria for diagnosing SjS, according to the international guidelines, the “focus” must be composed of at least 50 lymphocytes infiltrating the periductal area; one focus must be detected in a tissue area of at least 4 mm². The criteria from the SICCA revised in 2012 is as follows:^[7]

1. Ocular symptoms - not included
2. Oral symptoms - not included
3. Ocular signs - positive Schirmer's test/rose Bengal score/BUT
4. Histopathology in minor salivary gland biopsy - Focal lymphocytic sialadenitis with focus score >1 (a focus is defined as >50 lymphocytes per 4 mm² of glandular tissue adjacent to normal appearing mucous acini)
5. Salivary gland involvement - not included
6. Autoantibodies - positive serum anti-SS-A/Ro or anti-SS B/La or RF or ANA titer.

Secondary SjS is the presence of another AID, the presence of item 1/item 2, plus any two from items 3, 4, 5. (Figure 3)

The clinical presentation of the present patient was very typical of secondary SjS. The patient initially had symptoms of arthralgia, then dry eyes followed by dry mouth. Dentists are the first health care providers to encounter the early stage. Therefore, dentists should be familiar with the manifestation of disease and be prepared to take an active role in diagnosis, management, and treatment of oral complications associated with the disease.

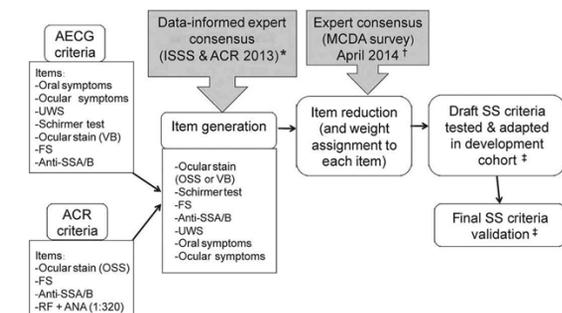


Figure 3: Overview of the methodology used for the definitive set of SjS classification criteria. American-European Consensus Group (AECG); American College of Rheumatology (ACR); Unstimulated whole saliva flow rate (UWS); van Bijsterveld (VB); Focus score (FS); Ocular Staining Score (OSS); RF; ANA;. *International SS Criteria Working Group meetings held during the 2013 International Symposium on Sjögren's Syndrome (ISSS) in Kyoto, Japan and the 2013 ACR Annual Meeting in San Diego, California. †The multi-criteria decision analysis (MCDA) ‡Disease case and non-case status was derived from expert clinical judgment based on clinical vignettes.^[7]

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