

Secondary Sjogren's Syndrome Associated with Rheumatoid Arthritis: A Case Report

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ABSTRACT

Sjögren's syndrome is a chronic autoimmune disorder of the exocrine glands with associated lymphocytic infiltrates of the affected glands. Sjogren's syndrome can be classified as primary and secondary. Sicca symptoms (dry eyes, dry mouth) – The features of Sjogren's syndrome increases with age due to normal aging process or due to systemic illness or medication. Therefore, Sjogren's syndrome can be easily overlooked or misinterpreted, and diagnosis can be delayed. This article highlights the importance of proper history and early diagnosis of secondary Sjogren's syndrome. This can pave the way for a comfortable life style and delay the disease process. Here is a case of secondary Sjogren's syndrome associated with rheumatoid arthritis approached as a team with all related specialists.

Keywords: Autoimmune, Rheumatoid arthritis, Sjogren's syndrome, Xerophthalmia, Xerostomia

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INTRODUCTION

Sjögren's syndrome is a chronic autoimmune disorder of the exocrine glands with associated lymphocytic infiltrates of the affected glands. This eventually involves multiple other organs including lungs, kidneys, and nervous system.¹ Extra glandular involvement in Sjogren syndrome falls into two general categories: Periepithelial infiltrative processes and extra epithelial extra glandular involvement. Periepithelial infiltrative process include interstitial nephritis, liver involvement and bronchiolitis which generally follow a benign course.² Extra glandular involvement in Sjogren syndrome is related to B-cell hyper reactivity, hyper gammaglobulinemia, immune complex formation including palpable purpura, glomerulonephritis, and peripheral neuropathy. These are latter manifestations that occur in the course of the disease and are associated with higher risk of transformation to lymphoma.² Dr. Henrick Sjogren, an ophthalmologist, first described it in 1933.³ Sjogren's syndrome can be classified as primary and secondary. Primary Sjogren syndrome occurs by itself and not associated with other diseases. Secondary Sjogren's syndrome develops as a result of an underlying

connective tissue disease, mostly rheumatoid arthritis or systemic lupus erythematosus and scleroderma. This mainly affects the women in the fourth and fifth decade with female to male ratio 9:1.⁴

The etiology of Sjogren's syndrome is controversial however it is multifactorial. Although it is not completely understood, the following events occur in all the patients with this syndrome: Initiation by an exogenous factor, disruption of salivary gland epithelial cells, T-lymphocyte migration and lymphocytic infiltration of exogenous glands, B-lymphocytic hyper reactivity and production of rheumatoid factor and antibodies to Ro (SS-A) and La (SS-B).⁴ This is one of the three most common autoimmune disease. The hall mark symptoms of the disorder are dry eyes and dry mouth also referred to as xerophthalmia (Keratoconjunctivitis sicca) and xerostomia.⁵ The most serious complication of Sjogren's syndrome is salivary gland and gastrointestinal tumors mostly B-cell lymphoma which develop in approximately 5% of patients.⁶

Diagnostic criteria are currently being reassessed as they tend to miss the patients with early disease who are most amenable to beneficial therapies.⁶ The symptoms

of Sjogren's syndrome are vague and may be mistakenly attributed to other diseases or medications taken by the patient. Misdiagnosis of the condition is, therefore, common and it is estimated that approximately half of the sufferers are undiagnosed.⁴ The diagnosis and management of secondary Sjogren's syndrome is challenging and requires co-operative approach between oral physicians, otolaryngologist, rheumatologist, and ophthalmologist.

Here is a case of secondary Sjogren's syndrome. This patient was managed by a rheumatologist and an ophthalmologist, and further the oral physicians joined the team. The effective management of oral manifestations and minimization of oral diseases resulted in improved quality of life. A team approach to multisystem disorders is always prudent.

CASE REPORT

A 46-year-old female patient was referred from the Department of Internal Medicine to the Department of Oral Medicine and Radiology with the chief complaint of dry mouth for past 3 months. Her complaint started 7 years ago with arthralgia, followed by the dryness of eyes since 5 years and dryness of mouth for 3 months. She had a sensation of foreign body in the eyes and Schirmer's test was done to confirm xerophthalmia and refresh tear drops (carboxy methyl cellulose) was prescribed. Her medical report revealed that she is under the following medication for rheumatoid arthritis: Methotrexate once daily, deflazacort twice daily, analgesics (indomethacin) and, pantoprazole. She is also under glibenclamide medication for diabetics since 3 months. On general examination, she appeared fit and healthy with normal vital signs. Intraoral examination revealed restorations and carious tooth. Laboratory studies documented positive rheumatoid factor (44 IU/ml). Considering the history and from medical reports, she was provisionally diagnosed as secondary Sjogren's syndrome associated with rheumatoid arthritis. Minor salivary gland biopsy was done to confirm the diagnosis as shown in Figure 1. Minor salivary gland biopsy showed moderate infiltration with chronic inflammatory cells suggestive of inflammation of the salivary gland. The histopathological section is shown in Figure 2. According to the Sjogren's International Collaborative Clinical Alliance (SICCA) revised in 2012 the final diagnosis of secondary Sjogren's syndrome in the initial stage without the destruction of acinar cells was given. The treatment was carried out to relieve symptoms of the patient in order to lead a comfortable and productive life. Xerostomia was symptomatically managed by rehydrating oral cavity with small sips of water throughout the day and use of salivary substitutes/mouth coating products. The importance



Figure 1: Minor salivary gland

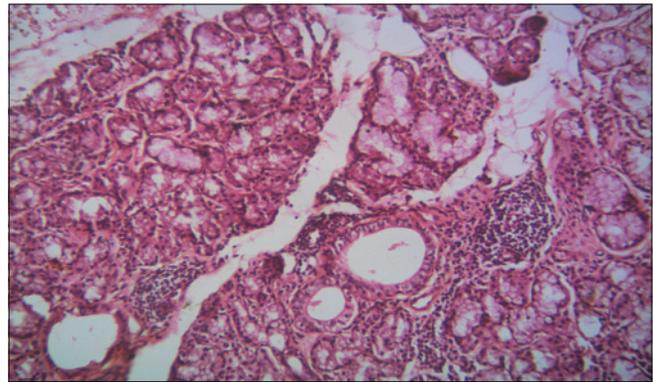


Figure 2: Histopathological view of minor salivary gland

of oral hygiene and topical fluoride application was mentioned clearly. A periodic review with the three specialists (rheumatologist, ophthalmologist, oral physicians) is essential.

DISCUSSION

Autoimmune disease refers to a disorder in which the body's immune system, which usually fights infection attacks the body's own tissues.³ Sjogren's syndrome is a chronic autoimmune disease characterized by symptoms of oral and ocular dryness, exocrine dysfunction and lymphocytic infiltration, and destruction of the exocrine glands. This mainly affects women in the fourth and fifth decade with female to male ratio 9:1.⁷ The etiology of Sjogren syndrome is obscure. A viral etiology has been suspected, the virus implicated are cytomegalovirus, Epstein-Barr virus, hepatitis C virus, and HIV virus. Genetic influences are also associated with pathogenesis. The HLA-DR alleles (DRB1 genes) including DR3, DR5, DRw11, and DRw53. There is B-cell activation and elevated serum autoantibody levels suggesting autoimmune etiology.⁸ The hallmark symptoms of Sjogren syndrome are dry eyes and dry mouth. Dry eyes are manifested as dry, gritty sensation or recurrent sensation of sand or gravel in the eyes.⁶ Complication of xerophthalmia include corneal ulceration and infection

of eyelids. The tests of choice to diagnose dry eye include break-up time (BUT), Schirmer's test and ocular surface staining with rose bengal, fluorescein, and lissamine green stain.⁹

Dryness of the mouth makes swallowing of food and even talking difficult. The sudden development of pain in the mouth is due to angular cheilitis or candidiasis.¹ Dryness of the mouth cannot simply be attributed to the total destruction of the gland, the local environment of the inflamed gland leads to dysfunction of the residual glandular units owing to release of cytokines, metalloproteinases, and autoantibodies.¹ The patient often have dry cracked lips, sore mouth, depapillation of the tongue, unpleasant taste. Intra orally the mucosa is pale and dry, minimal salivary pooling can be noted and the saliva present is thick and ropy.⁸ Xerostomia predisposes to smooth surface caries, oral mucosal inflammation, erythematous mucosa, and traumatic ulcer. There can be gingivitis and recession due to poor lubrication and less clearance of plaque and debris.⁴ The pathological hallmark of Sjogren's syndrome is a chronic inflammatory infiltrate in the exocrine glands, mainly constituted by activated T- and B-cells. In the early stages of disease, focal aggregates of lymphocytes appear in the glandular lobules.⁹

Initially, the lymphocytes infiltrate the space around small ducts, and finally the atrophic involution of the acina. The lymphocytes initiate the damage to the ducts with the formation of epimyoeptithelial lesions, described as "epimyoeptithelialoadenitis."

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 mm.²⁹ The criteria from the SICCA revised in 2012 is as follows:⁹

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 rheumatoid factor or anti-nuclear antibody titer.

Secondary Sjogren syndrome is the presence of another connective tissue disease, the presence of item 1/item 2, plus any two from items 3, 4, 5.

Rheumatoid arthritis is frequently associated with both sicca symptoms and true secondary Sjogren's syndrome. Rheumatoid arthritis patients with high titers of a rheumatoid factor were reported to be more likely to have secondary Sjogren syndrome.⁹ The clinical presentation of our patient was very typical for the early stage of secondary Sjogren syndrome. The patient initially had symptoms of arthralgia, then dry eyes followed by dry mouth. The histopathological report shows the early stage of lymphocytic infiltration. The most serious aspect of Sjogren's syndrome, however, is the increased risk of developing non-Hodgkin's lymphoma which is approximately 44 times greater than the risk of the general population, and a 1000-fold increased risk of parotid gland marginal zone lymphoma, and diffuse large B-cell and follicular lymphomas. The risk of lymphomas is closely related to B-cell hyperreactivity.¹⁰ Any parotid focus of lymphoma is treatable with radiotherapy and any change in size color, or architecture of involved gland mandates repeat biopsy. The management of dry mouth aims to prevent infections, periodontal disease, and dental caries.⁸ Adequate hydration remains the simplest yet the most effective means to treat xerostomia. Frequent sips of water not only rehydrate the oral cavity but also cleanse and reduce microbial load. Salivary stimulants are available both topical to systemic therapies. Xylitol is an acceptable artificial sweetener and has been shown to reduce caries. Oral pilocarpine and cevimeline have also been recommended. Fluoride carriers and remineralization solutions are necessary for caries control.¹¹ Sjogren syndrome is a common and underdiagnosed inflammatory disease with significant impact on oral health. Oral physicians are the first health care providers to encounter the early stage. Therefore, oral physicians should be familiar with the manifestation of disease and be prepared to take an active role in diagnosis, management, and treatment of oral complication associated with the disease. Secondary Sjogren syndrome associated with Rheumatoid arthritis, especially should be managed as a team comprising of rheumatologist, an ophthalmologist, and oral physicians.⁸

CONCLUSION

Sjogren syndrome is slow in its course. The risk of lymphomas is high and concern for mortality of the disease. Early diagnosis is imperative so that oral complication can be minimized, and appropriate management is instituted both medically and dentally. Appropriate management requires cooperative approach between all health professionals involved. Oral Physicians must be fully aware of the clinical signs and symptoms as well as management of these patients.

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