Case Report

Primary Sjogren’s Syndrome: A Case Report
Sapna Raut Dessai,1* Elaine Barretto2
1-Consultant Maxillofacial Radiologist, Omkar X-ray and Ultrasound Clinic, Margao – Goa, India. 2- Lecturer in Department of Paediatric Dentistry, Goa Dental College and Hospital, Bambolim – Goa, India.

Abstract
Sjogren’s syndrome is a chronic autoimmune disorder characterized by xerostomia, xerophthalmia, and lymphocytic infiltration of the exocrine glands. It is named after the Swedish ophthalmologist Henrik Sjogren who first described it as a triad of keratoconjunctivitis sicca, xerostomia and rheumatoid arthritis. Besides this triad there are various other systemic conditions which may be frequently associated with this syndrome. Besides presenting a case review, this article also reviews in detail these various other systemic conditions related and found associated with this syndrome.

Keywords
Sjogren’s syndrome, xerostomia, sicca complex, sialography, lymphoma.

*Author for correspondence:
Consultant Maxillofacial Radiologist, Omkar X-ray and Ultrasound Clinic, Margao – Goa, India. Email: dr.sapnasrd@yahoo.com

Submitted: Nov’ 2014; Accepted: Jan’ 16
Introduction

Complete description of Sjogren’s syndrome was first given by Danish Ophthalmologist, Henrik Sjogren in 1933 [1]. Its association with other autoimmune conditions was then reported by Bloch et al in 1956. Sjogren’s disease is now known to be one of the most common autoimmune diseases of the world. Most people are in the 4th or 5th decade of life at the time of diagnosis. This condition is frequently seen in females with male to female ratio of 1: 9 [2]. Sjogren’s syndrome may be considered primary when it includes sicca complex (dry eyes and dry mouth) and extra glandular symptoms without any additional connective tissue disorder. It may be called Secondary Sjogren’s syndrome when another autoimmune rheumatic disease such as; rheumatoid arthritis, systemic lupus erythematosus, polyarthritis nodosa, scleroderma, primary biliary cirrhosis is present besides the sicca complex [2]. Secondary Sjogren’s syndrome may be manifested long after the onset of other associated autoimmune disorder. This syndrome is believed to have genetic, hormonal, infectious and immunologic etiology which will lead to induction of immune dysregulation and loss of tolerance [2].

Case Report

A 40-year-old female patient reported with the chief complaint of dryness of oral cavity and eyes since 1 year. She recollected having recurrent episodes of bilateral parotid swelling with associated dull aching pain and difficulty in eating in the past, since two years. Patient denied history of associated fever and weight loss during these episodes. Most recent swelling was 2 months prior on left side of face.

Patient previously had undergone multiple investigations and treatment. One of it even included serologically diagnosed tuberculosis that was treated with AKT (there was no improvement in the condition). She was also diagnosed with hypothyroidism seven years prior, for which she is on levothyroxine since then. Fine Needle Aspiration Cytology of the parotid gland was performed which revealed the presence of large and small lymphocytes dispersed with predominance of small lymphocytes. Clusters of benign acinar epithelial and myoepithelial cells were seen. Patient was advised sugar free chewing gums and antibiotics in the past.

On reviewing the systems, there were no major signs or symptoms except mild stiffness of joint in the morning. On examination patient had dry lips, angular cheilitis, wrinkled oral mucosa which used to stick to the instrument during examination. On palpation of the salivary duct openings, no pus discharge or inflammation was noted. Tongue showed atrophy of the filiform papillae, prominent fungiform papillae and fissures and pigmentation on the dorsum (Figure 1. A & B). Cervical caries of mandibular anterior teeth was noted with fixed maxillary prosthesis (Figure 1 C & D).

Figure 1 A & B: Extraoral views showing dry lips & intraoral view showing atrophy of tongue papillae.
Primary Sjogren’s Syndrome: A Case Report

Ultrasound of both parotids showed enlarged glands with heterogenous echotexture. No solid or cystic areas were noted within and no evidence of calculus (Figure: 2).

Retrograde irrigation with metrogyl twice every week for a period of 4 weeks, was carried out to clear any infection present in the glands. Sialography was performed after 4 weeks which showed multiple globular collection of the contrast that were fairly uniform in size and distribution (Snow storm appearance) (Figure 3 and 4). No evidence of salivary calculi. In the frontal post evacuation films after 30 min, there was residual contrast within the gland with good drainage of the main ducts.

Figure 1 C&D: Intraoral view showing atrophy of tongue papillae and multiple dental treatments.

Figure 2: Ultrasound image of parotid glands showing heterogenous echotexture.

Figure 3: Lateral oblique radiographs of parotid region showing multiple globular collection of the contrast on sialography.
Routine blood investigation values were within normal limits. Erythrocyte sedimentation rate was 50 mm/hr (N= 0 to 20 mm/hr). Fasting and post prandial blood sugar levels were normal. Liver function tests and renal functions tests were also within normal limits. No evidence of abnormality was noted on Abdominal Ultrasound.

Antibodies to extractable nuclear antigen SS-A was positive and to extractable nuclear antigen SSB was negative. ANA was positive and Anti ds DNA was negative. Thyroid stimulating hormone level was above normal (17.16 µIU/ml).

Sialometry showed absolutely no saliva production even on stimulation over a period of fifteen minutes. Histological examination of the sublabial salivary gland tissue showed numerous salivary gland acini and a dense chronic inflammatory cell infiltrate (Figure 5). Schirmer's test was abnormal with less than 0.3 mm of wetting of the strip.

Based on the history, clinical presentation and above investigatory findings, a confirmatory diagnosis of Primary Sjogren's syndrome was given. Patient was evaluated for any signs of systemic involvement. She was advised adequate
Primary Sjogren’s Syndrome: A Case Report

water intake, in between sips of lemon juice, multivitamin supplement, artificial saliva for oral dryness and eye drops for ocular dryness. The restoration of the carious teeth was advised with diet modification. Patient reported with significant reduction in oral and ocular dryness.

Discussion

Sicca complex (dry eyes and dry mouth) which is the hallmark of Sjogren’s syndrome may be a symptom of many other conditions like patients on medications, multiple sclerosis, alzheimers disease, sarcoidosis etc. To arrive at a diagnosis of Sjogren’s syndrome, one needs to systematically evaluate the revised criteria proposed in 2002 by the American European Consensus Group criteria (AECC).

The revised criteria suggests evaluation of ocular symptoms and signs which includes; dryness of eyes for more than 3 months, ocular discomfort, sensation of gravel in the eyes, positive Schirmer’s test (< 5 mm in 5 min) or Rose bengal score of > 4 (according to van Bijsterveld’s scoring system). Presence of oral symptoms is the second criteria to be assessed, which includes dry mouth for more than 3 months or recurrent swelling of salivary glands. Further criteria are, histopathology of minor salivary gland showing focal lymphocytic sialoadenitis with a focus score >1 (number of lymphocytic foci per 4 mm2 of glandular tissue) and unstimulated whole salivary flow of <1.5 mL in 15 min. Parotid sialography showing the presence of diffuse sialectasis (punctate, cavitory or destructive pattern), without evidence of obstruction in the major ducts, salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer. Presence of serum autoantibodies to Ro(SSA) or La (SSB) or both should also be considered in the evaluation of patients for Sjogren’s syndrome [1, 2].

In order to be diagnosed with Primary Sjogren’s one must have 4 of the 6 diagnostic criteria positive. Patients with previous head and neck radiation, Hepatitis C, AIDS, a pre-existing lymphoma or sarcoidosis, a graft vs. host disease or on anticholinergic drugs cannot be diagnosed with Sjogren’s syndrome [2].

Other diagnostic tests for Sjogren’s Syndrome:

Besides all the above criteria, Histopathology of major salivary gland may show intense lymphocytic infiltration of gland replacing all acinar structures preserving the lobular architecture and ‘epimyoepithelial islands’. Third alteration may be atrophy of glands sequential to the lymphocytic infiltration.

Both Sjogren’s syndrome types show marked hyper-gammaglobulinemia, elevated sedimentation rates, with persistent rheumatoid factors and low WBC counts [3]. Immunofluorescence technique may show demonstration of antialimentary duct antibodies. Sialochemistry may show elevated levels of IgA, potassium and sodium.

Ultrasound examination of the salivary glands is the simplest confirmatory test and has the added advantage of being non-invasive with no complications. Shimizu et al stated that multiple hypoechoic areas in salivary gland represent multiple cystic areas. Hypoechoic changes in the gland parenchyma decrease in gland size and obscuration of the gland configuration is seen in patients with Sjogren’s syndrome [4].

Multiple, small hypoechoic lesions noted in the gland parenchyma of Sjogren’s syndrome patient, indicate lymphocytic infiltrates. Grading of ultrasonography of salivary glands is given by Salaffi et al which includes 0 for normal glands, 1 for small hypoechoic spots, 2 for multiple scattered hypoechoic areas (< 2 mm), 3 for multiple
Primary Sjogren’s Syndrome: A Case Report

hypoechoic areas (2 - 6 mm) and 4 for multiple hypoechoic areas (> 6 mm). Grade 3 or higher is considered Sjogren’s syndrome [5]. Extra-nodal lymphomas can also be detected as larger 1-4 cm hypoechoic areas.

Magnetic resonance imaging is another noninvasive examination for the salivary glands. The normal parotid gland shows homogeneous signal intensity on T1 weighted MR images. On the other hand, the parotid gland in patients with Sjogren’s is characterized by a loss of homogeneity in signal intensity on T1-weighted MR image. Izumi et al performed quantitative analysis of the changes in signal intensity patterns on T1 weighted MR images of the parotid gland. Focal high signal intensity areas in these cases represent fat deposits which increase with the progression of Sjogren’s disease [6]. MR imaging can be also useful in locating lymphoma within glands affected by Sjogren disease.

Sjogren’s syndrome patients often presents with multiple systemic manifestations either at the time of diagnosis or later. In the present case, patient besides complaining of the symptoms of dryness of mouth was previously diagnosed with hypothyroidism (on medication).

Various systemic manifestations associated with Sjogren’s syndrome include, Ocular manifestations of dryness, inflammation (keratoconjunctivitis sicca), decreased lacrimal flow, conjunctival damage and corneal ulceration [1, 2]. Gastrointestinal symptoms include xerostomia, angular cheilitis, burning sensation over oral mucosa, papillary atrophy of tongue, persistent salivary gland enlargement, frequent oral infections, rapidly progressive dental caries, difficulty in mastication and swallowing, esophageal spasms, atrophic gastritis, celiac disease, primary biliary cirrhosis, active autoimmune chronic hepatitis and pancreatitis. Pulmonary manifestations include hoarse voice, epistaxis, nasal crusting, xerotrachea, dyspnea, interstitial lung disease, lymphoma, bronchiolitis obliterans organizing pneumonia and pleural involvement. Thyroid abnormalities like thyroid dysfunction are frequent in primary Sjogren’s syndrome [7].

Skin and mucosal changes like xerosis, nasal and vaginal dryness, pruritis and subcutaneous nodules also may be noted. Musculoskeletal conditions like arthritis, arthralgias, myalgias, morning stiffness, intermittent synovitis and chronic polyarthritis, which may sometimes lead to Jaccoud’s arthropathy. Genitourinary manifestations like renal tubular necrosis secondary to hyper-gammaglobulinemia and interstitial nephritis from lymphocytic infiltration of kidneys. Vasculitis and Reynaud’s phenomenon also may be evident. Lymphadenopathy, lymphoma, thrombocytopenic purpura, and petechiae may also be associated with this condition. Neurologic manifestations include peripheral and central neuropathy. Other manifestations like fatigue, malaise and decreased hearing also may be experienced.

There are multiple case reports showing association of this syndrome with other systemic manifestations. Some of them have been listed in Table 1.

Management:

This syndrome requires multidisciplinary management by oral and general medicine, rheumatology, immunology, ophthalmology, otolaryngology, pathology and microbiology department.

Treatment of Oral Symptoms: Involves, oral hygiene maintenance, fluoride application, treatment of dental caries, use of artificial saliva, abundant water intake, multivitamins and lemon drops. Medications like Muscuranic agents (Pilocarpine and Cevimelin) to increase saliva secretion from residual healthy gland tissue.
Table 1: Multiple case reports showing association of the syndrome with other manifestations

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Authors</th>
<th>Associated systemic condition in patient with Sjogren’s syndrome</th>
<th>Possible theories for the association</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Suzuki H et al [8]</td>
<td>Cryoglobulinemic glomerulonephritis, congestive cardiac failure, pericardial and pleural effusion.</td>
<td>Cryoglobulin deposits within glomerular capillary lumen, immune complex deposition in the pleura and pericardium.</td>
</tr>
<tr>
<td>2</td>
<td>Kobayshi H et al [9]</td>
<td>Nodular pulmonary amyloidosis</td>
<td>Lymphocyte infiltration into the bronchiolar wall which induced prominent immunoglobulin production and amyloid deposition.</td>
</tr>
<tr>
<td>3</td>
<td>Koh MS et al [10]</td>
<td>Sensory and motor demyelinating polyneuropathy.</td>
<td>Cerebral infarct possibly from autoimmune related vasculitis.</td>
</tr>
<tr>
<td>5</td>
<td>Choi W et al [12]</td>
<td>Necrotizing keratocleitis</td>
<td>Corneoscleral perforation developed from previous corneoscleral thinning due to recurrent inflammation.</td>
</tr>
<tr>
<td>6</td>
<td>Tazi I et al [13]</td>
<td>IgA-lambda-type Multiple myeloma</td>
<td>Chronic inflammation may represent a stimulus in the development of Multiple Myeloma.</td>
</tr>
<tr>
<td>7</td>
<td>Chen SF et al [14]</td>
<td>Rhomboencephalitis</td>
<td>Cerebral vasculitis has been considered to be the pathologic mechanism of CNS manifestation of primary Sjogren’s syndrome.</td>
</tr>
<tr>
<td>9</td>
<td>Choi YM et al [16]</td>
<td>Remitting seronegative symmetric synovitis with pitting edema</td>
<td>Either incidental association or an early manifestation of Sjogren’s syndrome.</td>
</tr>
<tr>
<td>10</td>
<td>Krstic M et al [17]</td>
<td>Iron deficiency anemia, watermelon stomach or gastric antral vascular ectasia</td>
<td>From small cutaneous vasculitis with cryoglobulinemia.</td>
</tr>
</tbody>
</table>
Cevimeline has less of the cardiac side effect of muscarinic therapy [18, 19].

**Treatment of ocular symptoms:** This involves use of artificial tears, and punctual plugs to help retain tears on the ocular surface for a longer time and use of goggles to increase local humidity. Cyclosporine eye drops which decrease inflammation in the eye and allows the gland’s function to recover. Medications like Pilocarpine may also be used [20, 21].

**Treatment of other symptoms:** Skin, nose, and vaginal dryness often can be relieved with topical treatments using skin creams or lotions and saline nasal sprays. Hydroxychloroquine, methotrexate, cyclophosphamide may be helpful in reducing joint and muscular symptoms. NSAIDS may also be used to treat musculoskeletal symptoms. IV immunoglobulin like mycophenolate mofetil and monoclonal antibodies like the anti-CD20 rituximab and the anti-CD22 epratuzumab can also be tried [22, 23].

**Prognosis**
Due to its constant systemic involvement, Sjogren’s syndrome can damage vital organs of the body with symptoms that may regress or worsen. Some patients can develop multiple system involvements. Sjogren’s syndrome also highly increases the risk of parotid lymphoma. Therefore, any dominant mass in a Sjogren’s affected parotid gland must be investigated further by aspiration or biopsy.

**Conclusion**
The American European Consensus Group criteria, ultrasonography grading and MRI evaluation of the salivary glands are the best for evaluating Sjogren’s’ syndrome. Sicca complex and other symptoms of this syndrome cause chronic discomfort to the patient. The syndrome being associated with other systemic conditions, can compromise lifestyle of patients to a major extent.

Patients should be given complete knowledge of the progress of disease, its various signs and symptoms and methods to treat these symptoms. This will definitely help patients to live a tension free life.

**References**