Sjögren's Syndrome: A Case Report and Review of the Literature

M Öğütcen-Toller[1], R Gedik[2], S Gedik[3], F Göze[4]

ABSTRACT

The manifestations and complications of Sjögren's syndrome are important to know, and dentists can play an important role in the detection of this disease. This report highlights such a case.

Keywords: Autoimmunity, salivary disease, Sjögren's syndrome

El Síndrome de Sjögren: Reporte de Caso y Revisión de la Literatura

M Öğütcen-Toller[1], R Gedik[2], S Gedik[3], F Göze[4]

RESUMEN

Es importante conocer las manifestaciones y complicaciones del síndrome de Sjögren, y los dentistas pueden jugar un papel importante en la detección de esta enfermedad. Este reporte documenta este caso.

Palabras claves: Autoinmunidad, enfermedad salival, síndrome de Sjögren

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INTRODUCTION

Sjögren's syndrome (SS) is a chronic systemic disorder characterized by polyglandular tissue destruction that causes keratoconjunctivitis sicca (KCS) and xerostomia (dry mouth). Patients with primary SS have KCS and xerostomia, whereas those with secondary SS have KCS, xerostomia and an autoimmune disease. Sjögren's syndrome can affect any age but the onset is most common in middle age or older, and 2−5% of people aged 60 years and above have primary SS (1, 2). The prevalence of SS is 4 cases per 100 000 of population with nine times as many females as males affected. The disease affects predominantly middle-aged women in the peri- or post-menopausal period. In addition to the primary syndrome, 30% of patients with rheumatoid arthiritis, systemic lupus erythematosus and systemic sclerosis suffer secondary SS (3−8).

Signs of salivary gland dysfunction should be sought through careful examination. There is a consensus among most investigators that unstimulated whole saliva flow rates of less than 1.5 mL per 15 minutes or stimulated whole saliva rates of less than 0.5 mL per minute are abnormally low. Changes in salivary cytokines and other protein levels may have diagnostic significance (9, 10).

The aetiology and pathophysiology of SS are still unknown. Autoimmunologic factors such as multiple autoantibodies particularly SS-A and SS-B, and a genetic predisposition are associated with SS. Some human leukocyte antigens also increase the risk of SS. Viral infection could be involved in the induction of SS. Epstein-Barr virus, human T-lymphotrophic virus-1, human herpes virus, human immunodeficiency virus-1, hepatitis C virus, and cytomegalovirus may play a role (6, 10−14). The prognosis of SS is generally better than that of other autoimmune diseases. Early clinical manifestations of SS are primarily decreased tear and saliva secretion, leading to dry eye and dry mouth syndromes. It may develop into salivary and extrasalivary B cell lymphomas at later stages (4, 7, 8, 13, 15−17).

Dry mouth can be brought on by autoimmune dysfunction, resulting in lymphocytic infiltration leading to acinar destruction, resulting in atrophy of the salivary glands (18). Glandular atrophy causes reduced amount of saliva and also causes increased rate of bacterial infections in the mouth and the need for medications. People with xerostomia often have a very high rate of tooth decay and mucosal infection. There is no consistently effective treatment for Sjögren

[1]Department of Oral and Maxillofacial Surgery, [2]Department of Oral and Maxillofacial Radiology, Dental Faculty of Cumhuriyet University, Sivas, Turkey, [3]State Hospital, Sıvas, Turkey and [4]Department of Pathology, Medical Faculty of Cumhuriyet University, Sivas, Turkey.

Correspondence: Dr M Öğütcen-Toller, Department of Oral and Maxillofacial Surgery, Dental Faculty of Cumhuriyet University, Sivas, Turkey. E-mail: melahattoller@hotmail.com

syndrome. The current therapy is primarily symptomatic. Dentists should know how to recognize and treat this condition. Proper brushing, flossing and use of alcohol-free mouth washes should be recommended (2, 10−12, 14, 18).

CASE REPORT

A 55-year old woman was referred to clinic complaining of dry mouth, difficulty in wearing dentures and her tongue sticking to the roof of her mouth, complicating speaking, eating and swallowing food. There was burning and itching of the eyes with foreign body sensation. There was no glandular enlargement. Intraoral examination revealed red, dry and smooth mucosal surface on the dorsum of the tongue and buccal mucosa and gingiva, dry, scaly lips and cracks at the corners of the mouth (Figs. 1, 2). The patient had received medical treatment for dryness of the eyes in the past. She was put on lubricant eye drops by an ophthalmologist.

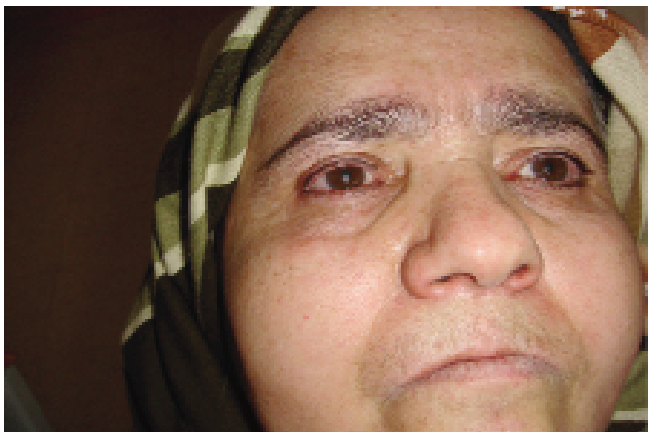

Fig. 1: Extra-oral view of the patient showing signs of keratoconjunctivitis as redness and dryness.

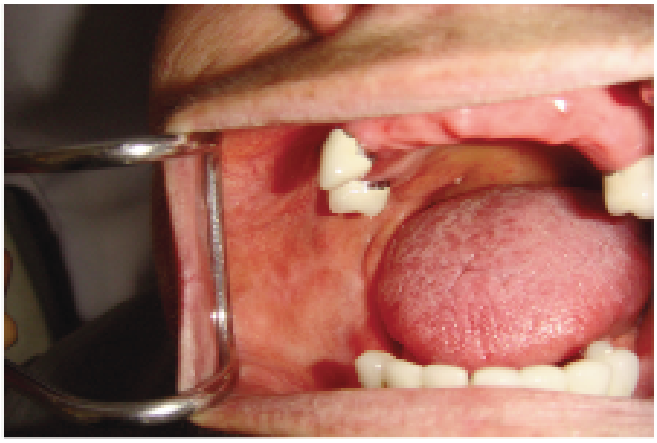

Fig. 2: Intra-oral view of the patient showing redness and dryness indicating atrophic changes of the mucosa including dorsal surface of the tongue. Dry, scaly lips and cracks at the corners of the mouth are also seen.

The submandibular and parotid glands took up very little radioisotope, technetium 99 m, on scintigraphy indicating glandular dysfunction and atrophy (Fig. 3). High uptake of the radioisotope in the thyroid gland was noticed and she was referred to the Endocrinology department for any thyroid pathology. Thyroid hormone levels were found within normal limits. A lip biopsy from the lower lip showed, on histology, characteristic focal periductal and mononuclear cell infiltrate with acinar cell loss in the labial minor salivary glands (Figs. 4, 5). She had received medical treatment for rheumatoid arthritis in the past. She was positive for rheumatoid factor (RF). The diagnosis of secondary Sjögren's syndrome was made. She was reassured and recommended to use lubricant mouth rinse which did not contain alcohol and consume water in sips during the day.

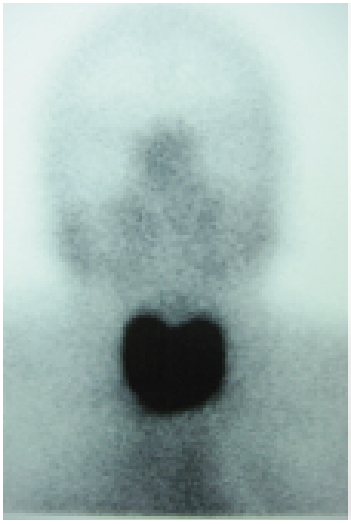

Fig. 3: Scintigraphy of the glands with isotope, technetium 99 m. The lack of uptake of theisotope by the salivary glands show dysfunction and atropy. The uptake of the isotope by the thyroid gland is clearly seen.

DISCUSSION

Sjögren's syndrome is often diagnosed on the basis of symptomatic dryness of mucous surfaces including the oral cavity (xerostomia) and the eyes [keratoconjunctivitis sicca] (2). Our case was in accordance with the literature, except for glandular enlargement. The syndrome may be divided into primary and secondary forms, where the latter, in addition to sicca symptoms, also includes another autoimmune connective tissue disease. Most commonly, this autoimmune disease is rheumatoid arthritis. Another disease that is occa-

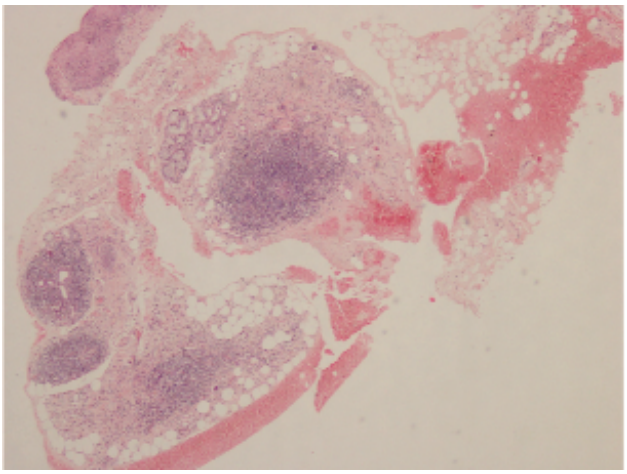

Fig. 4

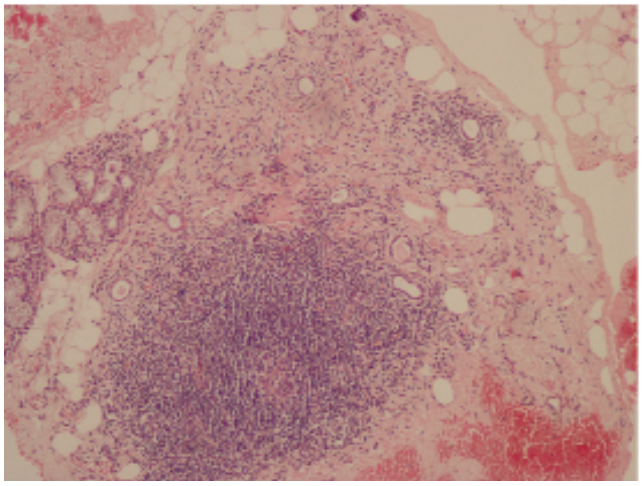

Fig. 5

Figs. 4 and 5: Histopathologic view of the minor labial salivary gland, typical for Sjögren's syndrome. Dense, well defined foci of lymphocytes replacing acini indicating acinar atrophy. A small island of residual salivary parenchyma remains around the periphery of the lobule.

sionally associated with SS is autoimmune thyroiditis (Hashimoto's thyroiditis), which can lead to abnormal thyroid hormone levels. Uncommonly associated with SS is primary biliary sirrhosis. Other associated states are graft *versus* host disease, sarcoidosis and Raynaud's disease (1, 5). The differential diagnosis was made according to the literature in the case presented. The other key features are evidence of an autoimmune reaction usually shown by serum autoantibodies and sometimes confirmed by demonstrating mononuclear cell infiltrates in a labial salivary gland biopsy (13), as was the case with the case presented. Salivary gland infiltration by polyclonal CD4 lymphocytes leading to acinar destruction is characteristic. Recent studies on pathogenesis of SS in human and animal models have examined the clonality of the T-cell infiltrates and the production of cytokines by lymphocytes and glandular epithelial cells. Neuroendocrine and other hormonal factors that affect glandular secretion and the fine structure of antigens recognized by T cells and B cells could play a role in the development of acinar destruction in SS (8, 15−17, 19).

There is a consensus among most investigators that unstimulated whole saliva flow rates of less than 1.5 mL per 15 minutes or stimulated whole saliva rates of less than 0.5 mL per minute clearly are abnormally low. Recent work in Sjögren syndrome is beginning to identify changes in salivary cytokine and other protein levels that may have diagnostic significance (1, 5). Sonography is another proven method for investigation of the major salivary glands. The ongoing development of ultrasonographic procedures has resulted in a fundamental change in the spectrum of diseases affecting the large salivary glands that can be diagnosed by imaging techniques. As a result, sonography has supplemented sialography in many instances as the preferred method for imaging of the major salivary glands. It has been suggested that radionuclide salivary gland imaging, scintigraphy, should replace conventional contrast sialography as the primary imaging modality in sialodenitis, duct occlusion and SS (19). Salivary gland scintigraphy not only accurately identifies ductal obstruction, but also reflects the functional status of the gland. It is less invasive than contrast sialography and less dependent on technical expertise (20). Glandular hypoactivity as a sign of diminishing functional and secretory capacity of the gland resulting from chronic inflammatory change leads to reduction in the acinar mass. Scintigraphy and plain films are recommended as the primary imaging complex in patients presenting with acute or episodic painful swelling of the salivary glands. Conventional contrast sialography can be reserved for patients with scintigraphic evidence of obstruction but no calculi on plain films. Besides, scintigraphy has a lower morbidity than sialography, assesses all major salivary glands at one sitting, and is not so operator dependent. For this reason, scintigraphy was used as a diagnostic tool in the patient presented (21). The scinti-graphic evaluation showed that the submandibular and parotid glands were dysfunctional as a result of the acinar atrophy of the glands, which confirmed the preliminary diagnosis. Scintigraphy is also useful in excluding any thyroid pathology at the same time when indicated (2, 19−25). However, not all patients will agree to lip biopsy, and scintigraphy may be an insensitive test. Magnetic resonance imaging (MRI) provides better contrast resolution, exposes the patient to less harmful radiation, and yields detailed images on several different planes without patient repositioning. This technique therefore is preferred in the evaluation of parapharyngeal space masses, especially in discriminating between deep lobe parotid tumours and other pathology, such as schwannoma and/or glomus vagale. Chronic inflammation of the salivary glands and calculi are not indications for MRI (9).

The treatment of patients with SS is directed toward the particular areas of the body that are involved and complications, such as infection. Dry mouth can lead to an increased rate of bacterial infections in the mouth and the need for medications (1−3, 14). Although artificial saliva and pilocarpine tablets are recommended, optimum oral hygiene and patient motivation are essential to prevent dental decay and oral mucosal infections. Dryness of the mouth can be relieved to some degree by providing artificial saliva. Cholinesterase inhibitors such as pilocarpine are sometimes recommended to stimulate salivary secretion but any benefits may be conterbalanced by side-effects such as nausea, diarrhoea and bradycardia. Dryness of the eyes is treated with artificial tears such as methyl cellulose solution. In dentate patients, sweet-eating should be prohibited, and a high standard of oral hygiene should be maintained (2, 18).

CONCLUSION

Dentists may often be the first to identify patients suffering from Sjögren's syndrome. In general, SS is an autoimmune disorder characterized by reduced activity of the salivary glands and the tear ducts. Patients with SS have a chronically dry mouth and may experience difficulty in chewing, swallowing and speaking. There are two types of SS. Patients with primary SS have KCS and xerostomia, whereas those with secondary SS have KCS, xerostomia, and an autoimmune disease. Most commonly, this autoimmune disease is rheumatoid arthritis.

REFERENCES

1. Daniels TE. Sjögren's syndrome: clinical spectrum and current diagnostic controversies. Adv Dent Res 1996; **10:** 3−8.
2. Scully C, Felix HD. Update for the dental practitioner, dry mouth and disorders of salivation. British Dental Journal 2005; **199:** 423−7.
3. Lynch MA, Brithman VJ, Greenberg MS. Burket's oral medicine, diagnosis and treatment Philadelphia: JB Lippincott Co; 1994: 425−9.
4. Sjogren's syndrome: a community-based study of prevalence and impact. Br J Rheumatol 1998; **37:** 1069−76.
5. Zandbelt MM, van den Hoogen FH, de Wilde PC, van den Berg PJ, Schneider HG, van de Putte LB. Reversibility of histological and immunohistological abnormalities in sublabial salivary gland biopsy specimens following treatment with corticosteroids in Sjögren's syndrome. Ann Rheum Dis 2001; **60:** 511−3.
6. Nikitakis NG, Rivera H, Lariccia C, Papadimitriou JC, Sauk JJ. Primary Sjögren syndrome in childhood: report of a case and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003; **96:** 42−7.
7. Carsons S. Sjögren's Syndrome. In: Harris ED, Budd RC, Firestein GS, Genovese MC, Sergent JS, Ruddy S et al, eds. Kelley's textbook of rheumatology. Philadelphia: Saunders; 2005: 1105−24.
8. Mathews SA, Kurien BT, Scofield RH: Oral manifestations of Sjögren's syndrome. J Dent Res 2008; **87:** 308−18.
9. Moutsopulos HM, Tzioufas AG. Sjögren's syndrome. In: Kliple JH, Dieppe PA, eds. Practical Rheumatology. London: Mosby; 1995: 394−6.
10. Kassan SS, Moutsopoulos HM. Clinical manifestations and early diagnosis of Sjögren syndrome. Arch Intern Med 2004; **164:** 1275−84.
11. Dry eye and dry mouth in the elderly: a population-based assessment. Arch Intern Med 1999; **159:** 1359−63.
12. Pedersen AM, Nauntofte B. Primary Sjögren's syndrome: oral aspects on pathogenesis, diagnostic criteria, clinical features and approaches for therapy. Expert Opin Pharmacother 2001; **2:** 1415−36.
13. Soto-Rojas AE, Kraus A. The oral side of Sjogren syndrome. Diagnosis and treatment. A review. Arch Med Res 2002; **33:** 95−106.
14. Manthorpe R. Sjogren's syndrome criteria. Ann Rheum Dis 2002; **61:** 482.
15. Manganelli O, Fietta P. Apoptosis and Sjögren syndrome. Semin Arthritis Rheum 2003; **33:** 49−65.
16. Hayashi Y, Arakaki R, Ishimaru N. The role of caspase on the development of primary Sjögre's syndrome. J Med Invest 2003; **50:** 32−8.
17. Hayashi Y, Arakaki R, Ishimaru N. Apoptosis and estrogen deficiency in primary Sjögren syndrome. Curr Opin Rheumatol 2004; **16:** 522−6.
18. Papas AS, Sherrer YS, Charney M, Golden HE, Medsger Jr TA, Walsh BT et al. Successful treatment of dry mouth and dry eye Symptoms in Sjogren's syndrome patients with oral pilocarpine: A randomized, placebo-controlled, dose-adjustment study. J Clin Rheumatol 2004; **10:** 169−77.
19. Schmelzeisen R, Milbradt H, Reimer P, Gratz P, Wittekind C. Sonography and scintigraphy in the diagnosis of diseases of the major salivary glands. J Oral Maxillofac Surg 1991; **49:** 796−803.
20. Pilbrow JW, Brownless SM, Cawood IJ, Dynes A, Hughes DJ, Stockdale RH. Salivary gland scintigraphy – a suitable substitute for sialography. The British Journal of Radiology 1990; **63:** 190−96.
21. Ino C, Matsuyama K, Ino M, Yamashita T, Kumazawa T. Approach to the diagnosis of sialadenosis using sialography. Acta Otolaryngol (Stockh) 1993; (**Suppl. 500):** 121−25.
22. Jonsson R, Kroneld U, Backman K, Magnusson B, Tarkowski A. Progression of sialadenitis in Sjögren's syndrome. British Journal of Rheumatology 1993; **32:** 578−81.
23. Hughes MP, Carson K, Hill J, Hastings D. Scintigraphic evaluation of sialadenitis. The British Journal of Radiology 1994; **67:** 328−31.
24. Saito T, Sato J, Kondo K, Horikawa M, Ohmori K, Fukuda H. Low prevalence of clinicopathologic and sialographic changes in salivary glands of men with Sjögren's syndrome. J Oral Pathol Med 1999; **28:** 312−6.
25. Primary Sjögren's syndrome: current and emergent aetiopathogenic concepts. Rheumatol 2005; **44:** 1354–367.