©Operative Dentistry, 2009, **34-3,** 359-364

Diagnosis of Sjögren's Syndrome From a Xerostomia Case Accompanied by Multiple Dental Caries

D-G Seo • J Kim
C-Y Lee • S-H Park

Clinical Relevance

This paper presents a comprehensive and systemic approach for determining the etiology of patients with xerostomia and the rapidly progressing potential systemic diseases that can result. Dentists must be reminded of their role in the early diagnosis and treatment of some systemic diseases, because the oral environment may show early symptoms that are relatively easy to detect.

INTRODUCTION

Sjögren's syndrome is a chronic, systemic auto-immune disorder of the salivary and lacrimal glands that leads to xerostomia and kerotoconjuctivitis sicca.[1-3] This process is the result of the characteristic infiltration of lymphoid cells into the exocrine glands and the gradual destruction of these organs.[1-2,4] The condition was first reported in the 19th century, and it was given its current term of Sjögren's syndrome in 1933 based on the scientific investigation by Henrik Sjögren, a Swedish ophthalmologist.[5] Two forms of the disease are currently recognized: primary Sjögren's syndrome, if it is not accompanied by other connective tissue disorders, and secondary Sjögren's syndrome, if it is accompanied by other connective tissue disorders.[2-3,5] The incidence of Sjögren's syndrome is estimated to be approximately 1%, with almost 90% of cases occurring in females older than 50 years of age.[1,3,5-6]

The cause of the disease is unknown, and the prognosis is not good. Patients have an increased risk of malignant lymphoma, up to 40 times greater than the normal population. The disease may also be accompanied by other conditions, such as Raynaud's phenomenon, primary biliary cirrhosis, diffuse interstitial lung disease, interstitial nephritis, chronic atrophic gastritis and peripheral neurophathy.[1,5]

In the following case, a patient presented with multiple dental caries and xerostomia. Sjögren's syndrome was diagnosed while investigating the cause of the problems. This report discusses the importance of appropriate diagnostic approaches to resolving the chief complaint.

Deog-Gyu Seo, DDS, MSD, Department of Conservative Dentistry, Yonsei University, Seoul, Korea

Jin Kim, DDS, PhD, professor, Department of Oral Pathology, Yonsei University, Seoul, Korea

Chan-Young Lee, DDS, PhD, professor, Department of Conservative Dentistry, Yonsei University, Seoul, Korea

*Sung-Ho Park, DDS, PhD, professor, Department of Conservative Dentistry, Yonsei University, Seoul, Korea

*Reprint request: 134 Shinchon-Dong, Seodaemun-Gu, Seoul, Korea; e-mail; sunghopark@yuhs.ac

DOI: 10.2341/08-71

CASE REPORT

In August 2002, a 20 year-old female patient was referred from a local clinic to the Department of Conservative Dentistry, Yonsei Dental Hospital, due to multiple dental caries in the mandibular anterior region. She complained of sensitivity to cold in the lower anterior teeth and dryness in her mouth.

Her prior medical history and familial history were non-contributory, and she did not show any external abnormalities, such as facial asymmetry or swelling (Figure 1). She had received restorative treatment three years earlier. The clinical oral examination revealed teeth #3,9,10,11,14,21,22,23,24,25,26,27,28 and 30 with moderate dental caries (Figures 2 and 3). The mandibular anterior teeth and premolars showed moderate sensitivity to cold. There was a generalized tendency toward decreased salivary flow. Therefore, a tentative diagnosis of xerostomia accompanied by multiple dental caries was made.

A treatment plan of resin composite restorations was made, considering both the esthetics and durability, followed by fluoride application and regular follow-ups four times a year. The patient was also referred to the Department of Oral Medicine for saliva flow and fungus smear tests to confirm the diagnosis of xerostomia. The examination at the Department of Oral Medicine revealed a saliva flow of 0.03ml/minute when not stimulated (normal 0.3-0.5ml/minute) and 0.1ml/minute (normal 1-3ml/minute) when stimulated, which is one-tenth of the normal saliva flow, thus confirming the diagnosis of xerostomia. In addition, candida was detected in the fungus smear test. The Oral Medicine Department prescribed artificial saliva and nystatin suspension in addition to regular follow-ups.

Table 1: *Possible Causes of Xerostomia*

Medication
Radiation Therapy
Primary Biliary Cirrhosis
Chronic Active Hepatitis
HIV
AIDS
Bone Marrow Transplantation
Graft vs Host Disease
Renal Dialysis
Anxiety & Depression
Diabetes Type I or Type II
Primary Sjögren's Syndrome
Secondary Sjögren's Syndrome

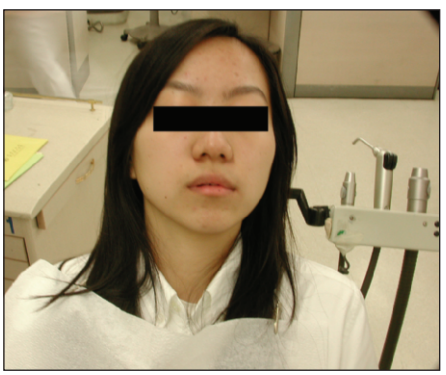

Figure 1. *Clinical photo showing the facial aspect.*

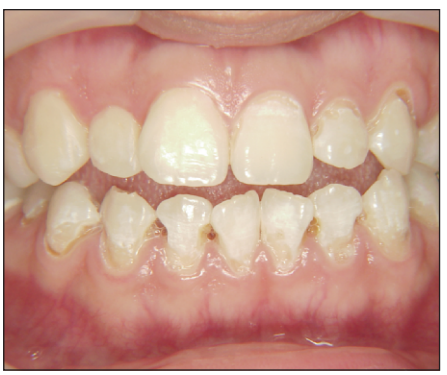

Figure 2. *Clinical photo showing multiple dental caries.*

After confirming xerostomia, the patient was referred to the Department of Hematology for a complete blood count (CBC) test and urinalysis to determine the etiology (Tables 1 and 2). Most of the results were within the normal range, but the hemoglobin level was low and iron deficiency anemia was diagnosed (Table 3).

Through these examinations and differential diagnoses, it was deduced that the xerostomia was caused by the iron deficiency anemia. Iron supplements were prescribed by the Department of Hematology, and the multiple dental caries were restored with resin composite at the Department of Conservative Dentistry. In addition, a Resazurin Disc test (Showa, Japan) was used to evaluate the bacterial and caries activity at the Department Conservative Dentistry. This test is a disc test used to determine the number of intraoral bacteria by a color change of the indicator, Resazurin, after 15 minutes. The results showed an orange-red color, indicating high risk. The patient was instructed in the use of artificial saliva and the consumption of anticariogenic foods, such as vegetables and large volumes of water. The patient's symptom of sensitivity was resolved (Figure 4). After six months of treatment at the Department of Hematology, the laboratory results related to anemia had returned to normal. However, the results were similar to the baseline when the salivary flow test was performed again at the Department of Conservative Dentistry, even though the patient had reported that her xerostomia symptoms had improved.

Therefore, it was concluded that xerostomia was not caused by iron deficiency anemia. It was decided that Sjögren's syndrome, the diagnosis that was discarded previously because the patient did not show the major characteristics, should be considered in the differential diagnosis (Tables 1 and 2).

The immune serum test carried out to differentially diagnose Sjögren's syndrome showed high levels of autoantibodies, such as anti-SS-A/Ro, rheumatoid factor IgM and rheumatoid factor IgA (Table 4). A lip biopsy was performed for a definitive diagnosis of Sjögren's syndrome. Infiltration

Table 2: *List of Tests Needed for Patients Suspected of Xerostomia*

Test	Purpose
Prior medical history	(Rule out) medication, radiation therapy, bone marrow transplantation, graft vs host disease
Saliva flow test	(Rule out) Objective indicator of xerostomia (non-stimulated 0.3-0.5ml/minute; xerostomia)
Measurement of intraoral bacterial activity	(Example) Resazurin Disc test, Scheider's test
Fungus smear test	The test for proliferation, such as candida, on the dorsal surface of tongue
Complete blood count	Tests for systemic disease (Rule out) primary biliary cirrhosis, chronic active hepatitis, anemia
Immune serum test	Diagnosis of autoimmune disease (Rule out) Sjögren's syndrome (female 90%)
Routine chemistry	T3, T4, glucose, ferritin, iron, Vitamin B12, folate (Rule out) DM, hypothyoidism, megaloblastic anemia
Urinalysis	Tests for systemic disease
Salivary scan	Salivary gland fuction test
Sialograpy	X-ray picture of the salivary ducts and the related glandular structures

Table 3: *Complete Blood Count (2002.08.26)*

	Result	**Reference**	**Interpretation**
Hemoglobin	9.7	12-16g/dl	Iron deficiency anemia
Hct	30.2	36-46%	
Neutrophil(%)	59	40-74%	Normal
Lymphocyte(%)	29.6	19-48%	
PLT count	287	150-450x1000/ul	
MCV	66.7	81-99fl	Iron deficiency anemia
MCH	21.4	27-33pg	
MCHC	32.0	33-37g/dL	

Table 4: *Immune Serum Test (2003.05.10)*

	Result	Reference	Interpretation
Anti-SS-A/Ro	Positive (143.0)	<20 units AU	H
Anti-SS-B/La	Negative	<20 units AU	
Reumatoid factor IgM	575	<20 U/ml	H
Reumatoid factor IgA	602.57	<20 U/ml	H
Reumatoid factor IgG	28.51	<70 U/ml	

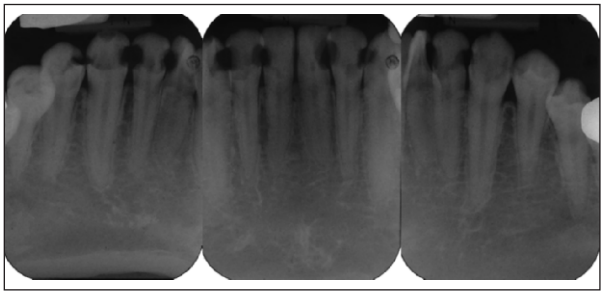

Figure 3. *Periapical view of the mandibular anterior region.*

of lymphocytes in the minor salivary glands was observed under low magnification (Figure 5). Under high magnification, there were three foci (a cluster of at least 50 lymphocytes) per 5.7 mm^2. The focus score 2.1 and grade 4 led to a diagnosis of Sjögren's syndrome, since the threshold of significance is a focus score of greater than one focus/4 mm^2 of gland area (Figure 6). A sialographic examination was performed to observe the duct of the parotid gland, which showed globular sialectasia, typically demonstrating a "fruit-laden, branchless tree" pattern[7] (Figure 7).

DISCUSSION

In the current case, it was significant that the xerostomia and multiple dental caries presented within a relatively short time.[8-10] Since the patient's last dental checkup was three years earlier and no treatment was considered necessary at that time, it is likely that the disease had initiated within the last two years. In addition, the patient was a healthy female in her twenties with a relatively high dental IQ (intelligence quotient) and sound dental hygiene, with no systemic diseases. Therefore, a cautious diagnostic approach was taken to her illness.

For this reason, the complaint of mouth dryness was not ignored and xerostomia was diagnosed objectively from a saliva flow rate examination. The severe decrease in saliva flow to the extent of 1/10 of normal flow influences the stimulation capacity, flow rate, composition, buffering capacity and pH of the saliva, as well as the acquired pellicle. This was considered a major contributory factor to the multiple dental caries.[8-11]

However, the cause of such severe xerostomia was unclear, and the above mentioned tests were deemed

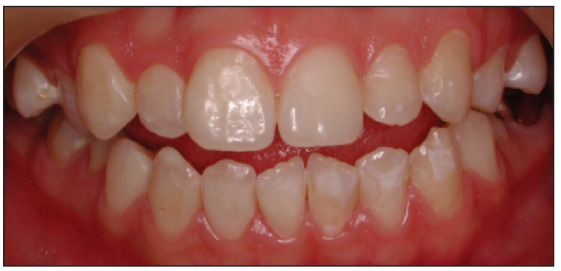

Figure 4. *Clinical photo after the resin restoration.*

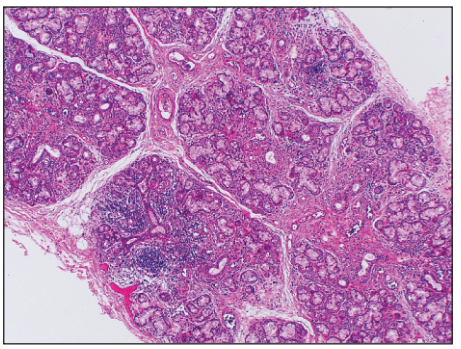

Figure 5. *Low magnification view of the lip biopsy (60x).*

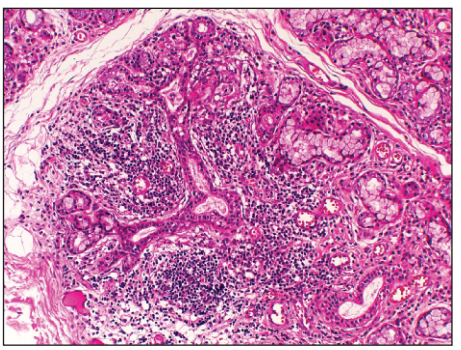

Figure 6. *A high magnification view of the lower lip biopsy showing multiple clusters of at least 50 lymphocytes (100x).*

necessary to determine the etiology of the rapid onset of the disease in an otherwise healthy individual. The common causes of xerostomia include specific drug use, diabetes, radiation therapy or Sjögren's syndrome.[8-10,12] However, she had no history of specific medication or radiation therapy. Sjögren's syndrome occurs most commonly in middle-aged women older than 50 years of age. It is accompanied by keratoconjunctivitis sicca, parotid gland enlargement, angular cheilitis and oral mucosal erythema with dorsal tongue fissuring and papillary atrophy. In secondary Sjögren's syndrome, it is accompanied by autoimmune diseases of other connective tissues. In this patient, there were no signs to suspect this disease.

Therefore, diabetes or other systemic conditions were suspected, and a CBC test, urinalysis and routine chemistry test were performed to determine the cause of xerostomia. The laboratory test results were within the normal range with the exception of iron deficiency anemia, which was presumed to be the cause of the xerostomia.[13-15] Iron deficiency anemia is prevalent in approximately 20% of women in their twenties.[16-18] Although anemia did not appear to be the sole cause of the xerostomia, because there were no other contributory results in the laboratory tests, she was only treated for iron deficiency anemia. Iron supplements were prescribed at the Department of Hematology, and resin composite fillings were placed to restore the multiple dental caries. However, despite the literature stating that anemia causes a decrease in saliva flow and that iron deficiency anemia particularly influences the iron related cell metabolism and oral mucosa, resulting in xerostomia,[13-15] the xerostomia did not subside even after the iron deficiency anemia had been resolved.

Therefore, the differential diagnosis had to be re-considered from the very beginning in order to determine the cause of xerostomia. Sjögren's syndrome, which had been dismissed without any tests during the initial differential diagnosis because the patient lacked any signs and symptoms, was reconsidered.

Since Sjögren's syndrome presents with various manifestations, there have been several attempts to diagnose it. Among these, the detection of abnormal auto-antibodies through immuno serum tests is useful.[2,5,19-20] A lip biopsy or parotid gland biopsy is most beneficial for making a definitive diagnosis.[4,19] In this patient, a high level of auto-antibody for anti-SS-A/Ro, rheumatoid factor IgM and rheumatoid factor IgA was detected in the immuno serum test. Among these factors, SS of anti-SS-A denotes Sjögren's syndrome, which is an auto-antibody unique to this disease.[19-20] For a definitive diagnosis, a lip biopsy with high accuracy and relatively fewer complications was performed. With the lip biopsy, the grade was determined by the number of foci (a cluster of at least 50 lymphocytes) per 4 mm^2. Since three foci were observed in a 5.7 mm^2 area, a focus score of 2.1 per 4 mm^2 and Grade 4 were determined. According to previous histology studies, Grade 4 is a clear diagnostic criterion for Sjögren's syndrome, leading to a definitive diagnosis.[4]

Sjögren's syndrome is a chronic auto-immune disease characterized by gland infiltration. The patient usually shows oral symptoms, such as chronic xerostaomia, recurrent dental caries, oral mucosal erythema, papillary atrophy of the tongue, candidiasis and xerostomia, along with kerotoconjuctivitis sicca. In addition, there is parotid gland enlargement in 50% of the patients. The condition may also be accompanied by other auto-

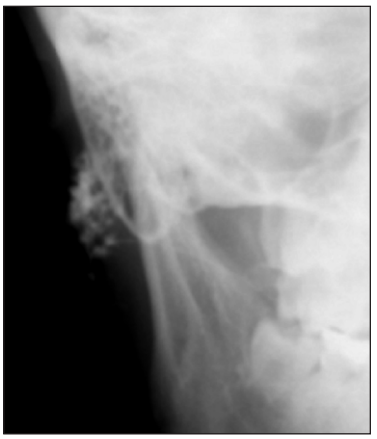

Figure 7. *Sialography of the right parotid gland demonstrating the typical "fruit-laden, branchless tree" appearance.*

immune diseases, such as rheumatoid arthritis. Supportive therapy is generally used to treat Sjögren's syndrome. However, medications, such as immuno-suppressants and steroid, are prescribed if the disease takes a severe course.[5,12-13] In terms of the prognosis, the disease can be fatal if malignant lymphoma or other autoimmune disease develops.[1-3,5] Therefore, early diagnosis and referral for treatment and follow-up is important.

Xerostomia is usually the chief complaint of Sjögren's syndrome patients.[8,19,21] The way to treat xerostomia in the simplest manner is by the use of water, followed by saline solution, tea and water with sodium bicarbonate. However, since excessive consumption may remove a small amount of mucous saliva from the oral tissue and worsen the dryness, care must be taken to avoid overuse.[19] In severe cases, there are two types of treatment, depending on the response to saliva stimulation. In patients who respond to saliva stimulation, gustatory and mechanical stimulation, such as sugarless chewing gum and dry fruit slices, can help.[8,19,21] In addition, patients may be treated by systemic stimulation using cholinergic drugs, such as pilocarpine and cevimeline.[8,19,21] But, in these cases, caution must be taken, since parasympathomimetic stimulating agents have side effects.[8,19,21] In non-respondent patients, saliva substitutes are the only option.[8,19,21]

In xerostomia patients, the buffering capacity of saliva and ion for remineralization is reduced, leading to an increase in cariogenic microorganisms and a high risk of dental caries. For these reasons, multiple dental caries often occur, especially in the cervical area.[8] However, there is controversy over the choice of restorative material. Conventional glass ionomers may be recommended in areas without strong occlusal forces, because of their high fluoride release rate and less susceptibility to desiccation.[22-24] However, some recommend resin-modified glass ionomers, due to the conventional glass ionomer's susceptibility to degradation and inferior mechanical properties.[24-25] On the other hand, although conventional glass ionomers or resin-modified glass ionomers are acceptable in patients with high-caries risk, in low-risk patients, resin composite with better mechanical properties is recommended in consideration of durability and esthetics.[23,25] In addition, resin composite provides a smooth surface, which resists plaque accumulation and an acid resistant hybrid layer, thus reducing the risk of secondary caries.[19] In the current case, the patient had a high dental IQ and good oral hygiene. In addition, this female patient, who was in her twenties, showed a deep concern for esthetics. Therefore, a resin composite restoration was recommended. In these patients, in order to increase tooth resistance, fluoride therapy using oral fluoride rinses or gels may be implemented.[19,22] An increase in fluoride concentration and exposure would increase caries reduction and, in order to avoid mucosa irritation, a neutral gel instead of acid fluoride gels should be recommended.[19,22]

A reduction in salivary flow predisposes the proliferation of C albicans. In such cases, topical or systemic treatment of antifungal drugs, such as nystatin, chlortrimazole and myconazole, are recommended.[8,21] In addition, the prevalence of such opportunistic infections may be reduced by increasing oral moisture.[8,19]

As mentioned above, the role of the dentist is significant in the treatment of Sjögren's syndrome. At the same time, consultation and cooperation with other specialists, such as internists, rheumatologists and oral medicine specialists, is necessary.[19]

In cases of a rapidly progressing xerostomia patient, as in the current case, a comprehensive and systemic approach to determine the etiology is essential, and systemic diseases should be considered.[15,19] In addition, the oral environment may show early symptoms, which can make it relatively easy for a dentist to detect. Therefore, oral presentations may be very important clues. In conclusion, dentists must be reminded of their role in the early diagnosis and treatment of some systemic diseases.

Acknowledgement

This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korean government (MEST) (No (R13-2003-013-05002-0).

(Received 26 May 2008)

References

1. Neville BW (1995) *Oral & Maxillofacial Pathology* Saunders, Philadelphia, Pa.
2. Lee SW (1998) *Oral Medicine 5th ed* Shinhung, Seoul.
3. Braunwald E & Harrison TR (2001) *Harrison's Principles of Internal Medicine 15th ed* McGraw-Hill, Medical Pub Division, London.
4. Greenspan JS, Daniels TE, Talal N & Sylvester RA (1974) The histopathology of Sjögren's syndrome in labial salivary gland biopsies *Oral Surgery Oral Medicine Oral Pathology* **37(2)** 217-229.

5. Ellis GL, Aucler P & Gnepp DR (1991) *Surgical Pathology of the Salivary Glands* WB Saunders.
6. Dafni UG, Tzioufas AG, Staikos P, Skopouli FN & Moutsopoulos HM (1997) Prevalence of Sjögren's syndrome in a closed rural community *Annals of the Rheumatic Diseases* **56(9)** 521-525.
7. Yu DS (1996) *Oral Maxillofacial Radiology 2nd ed* Ewoo Pub, Seoul.
8. Guggenheimer J & Moore PA (2003) Xerostomia: Etiology, recognition and treatment *Journal of the American Dental Association* **134(1)** 61-69.
9. Edgar WM (1990) Saliva and dental health. Clinical implications of saliva: Report of a consensus meeting *British Dental Journal* **169(3-4)** 96-98.
10. Cassolato SF & Turnbull RS (2003) Xerostomia: Clinical aspects and treatment *Gerodontology* **20(2)** 64-77.
11. Diaz-Arnold AM & Marek CA (2002) The impact of saliva on patient care: A literature review *The Journal of Prosthetic Dentistry* **88(3)** 337-343.
12. Brennan MT, Shariff G, Lockhart PB & Fox PC (2002) Treatment of xerostomia: A systematic review of therapeutic trials *Dental Clinics of North America* **46(4)** 847-856.
13. Mishra OP, Agarwal KN & Agarwal RM (1992) Salivary iron status in children with iron deficiency and iron overload *Journal of Tropical Pediatrics* **38(2)** 64-67.
14. Mukherji S, Naik SR, Srivastava PN, Choudhuri SN & Chuttani HK (1982) Salivary secretions in iron deficiency anemia *Journal of Oral Medicine* **37(4)** 130-132.
15. Johansson I & Fagernas C (1994) Effect of iron-deficiency anemia on saliva secretion rate and composition in the rat *Archives of Oral Biology* **39(1)** 51-56.
16. Boccio JR & Iyengar V (2003) Iron deficiency: Causes, consequences, and strategies to overcome this nutritional problem *Biological Trace Element Research* **94(1)** 1-32.
17. Zimmermann MB & Hurrell RF (2007) Nutritional iron deficiency *Lancet* **370(9586)** 511-520.
18. Little JW, Miller C, Rhodus NL & Falace D (1997) *Dental Management of the Medically Compromised Patient 5th ed* Mosby, St Louis, Mo, London.
19. Soto-Rojas AE & Kraus A (2002) The oral side of Sjögren syndrome. Diagnosis and treatment. A review *Archives of Medical Research* **33(2)** 95-106.
20. Mariette X (2002) Current and potential treatments for primary Sjögren's syndrome *Joint Bone Spine* **69(4)** 363-366.
21. Mathews SA, Kurien BT & Scofield RH (2008) Oral manifestations of Sjögren's syndrome *Journal of Dental Research* **87(4)** 308-318.
22. Gibson G (1998) Identifying and treating xerostomia in restorative patients *Journal of Esthetic Dentistry* **10(5)** 253-264.
23. Haveman CW, Summitt JB, Burgess JO & Carlson K (2003) Three restorative materials and topical fluoride gel used in xerostomic patients: A clinical comparison *Journal of the American Dental Association* **134(2)** 177-184.
24. McComb D, Erickson RL, Maxymiw WG & Wood RE (2002) A clinical comparison of glass ionomer, resin-modified glass ionomer and resin composite restorations in the treatment of cervical caries in xerostomic head and neck radiation patients *Operative Dentistry* **27(5)** 430-437.
25. Walter R (2007) Critical appraisal. Root caries *Journal of Esthetic and Restorative Dentistry* **19(2)** 120-124.