J Korean Med Sci 2000; 15: 115-8
ISSN 1011-8934

Primary Sjögren's Syndrome Manifested as Multiple Sclerosis and Cutaneous Erythematous Lesions
: A Case Report

Sjögren's syndrome is a chronic autoimmune disorder characterized by lymphocytic infiltration of the lacrimal and salivary glands, leading to dryness of eyes (kerato-conjunctivitis sicca) and mouth (xerostomia). The skin lesions in Sjögren's syndrome are usually manifested as xeroderma, but sometimes appear as annular erythema or vasculitis. Central nervous system symptoms may be presented as one of extraglandular manifestations, though rare in incidence, and need differential diagnosis from multiple sclerosis. We report a case of a 45-year-old woman diagnosed as multiple sclerosis at first but later as neurologic manifestation of primary Sjögren's syndrome, showing signs of multiple sclerosis and cutaneous erythematous lesions.

Key Words: *Sjögren's Syndrome; Multiple Sclerosis; Erythema*

Sung-Moon Jung, Byung-Gun Lee, Gwang-Yeol Joh, Jae-Kwan Cha*, Won-Tae Chung†, Ki-Ho Kim

Departments of Dermatology, Neurology*, and Internal Medicine†, College of Medicine, Dong-A University, Pusan, Korea

Received: 1 April 1999
Accepted: 22 June 1999

Address for correspondence
Ki-Ho Kim, M.D.
Department of Dermatology, College of Medicine, Dong-A University, #1, 3 ga, Dongdaeshin-dong, Seo-gu, Pusan 602-714, Korea
Tel: +82.51-240-2942, Fax: +82.51-241-6726

INTRODUCTION

Sjögren's syndrome (SS), a chronic autoimmune exocrinopathy, occurs mainly in middle-aged women. SS can manifest as a primary or secondary disorder in association with other connective tissue diseases, including rheumatoid arthritis, systemic lupus erythematosus or polymyositis/dermatomyositis and so on. In addition to two characteristic manifestations, dry eyes and dry mouth, there may be extraglandular manifestations in various organs such as lung, heart, genitourinary, vascular, and nervous systems in primary Sjögren's syndrome. The neurologic manifestations in primary Sjögren's syndrome can mimic multiple sclerosis (MS) in physical findings and cerebrospinal fluid profiles. Primary SS can also manifests as skin lesions, though rarely such as xerodermia, vasculitis, and so on.

Due to a complex array of symptoms, physicians should pay attention to atypical extraglandular symptoms in addition to classic clinical triad: 1) xerophthalmia 2) xerostomia 3) laboratory evidence suggesting a systemic autoimmune disease, and also need diagnostic criteria to recognize the real natures of individual symptoms and signs.

CASE REPORT

A 45-year-old woman had suffered from dry eyes and dry mouth intermittently since 1992 without any detailed evaluation for them. In October 1996, she had weakness in both lower extremities, voiding difficulty, and sensory change below the T10 dermatome after the compression fracture of L1 spine due to fall down one month previously. She visited a neurology clinic and was treated under the impression of transverse myelitis. One month later, she recognized decreased visual acuity and headache with intermittent fever. She then visited the neurology department of Dong-A University Hospital. On neurologic examinations at that time, she showed decreased visual acuity, spasticity of both lower extremities, more decreased muscle power in lower extremities than in upper extremities, hyperesthesia on both lower extremities, and hyperreflexia on both upper and lower extremities. She also suffered from general weakness, arthralgia, and soarness of oral cavity. The MRI findings showed multifocally increased opacity in T2-enhanced sagittal and axial views (Fig. 1). The cerebrospinal fluid profiles revealed pleocytosis composed predominantly of lymphoid cells and increased protein level as 84 mg/dL

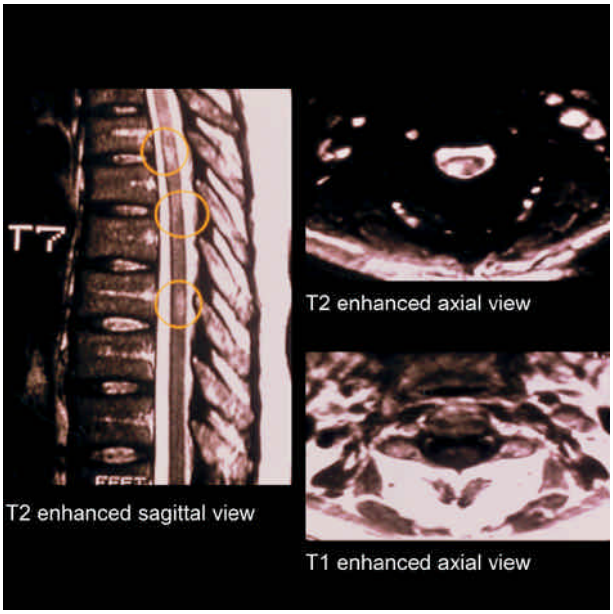

Fig. 1. MRI findings showed multifocally increased opacity in T2-enhanced sagittal and axial views.

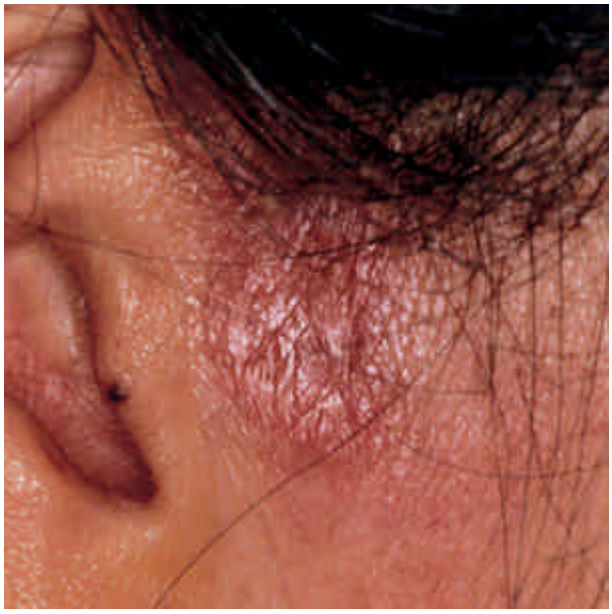

Fig. 2. Erythematous swollen plaques on the right periauricular area.

(normal; <45 mg/dL). The cerebrospinal fluid IgG/albumin index was increased to 1.157 (normal; <0.70). Myelin basic protein level was abnormal at 4.26 mg/mL (normal; <1.0 mg/mL). She was treated with systemic corticosteroid 20 mg/day for one month under the impression of multiple sclerosis. In November 1997, skin lesions developed after tapering the dose of corticosteroid to 5 mg/day as ocular and neurologic symptoms were improved. Initially erythematous swollen plaques appeared on both periauricular area (Fig. 2) and one month later, erythematous skin lesions cropped out on both lower extremities (Fig. 3).

Ophthalmological examination revealed shortened tear film break-up time 3/2 (Rt./Lt.) seconds (normal; <15 second) and decreased lacrimation 0/2 (Rt./Lt.) mm/5 min (normal; >8 mm/5 min) in Schirmer test. A biopsy specimen taken from minor salivary gland within lower lip showed that small lymphocytes were densely infiltrated throughout most of the salivary gland lobules (Fig. 4). CBC profiles revealed a finding of pancytopenia,

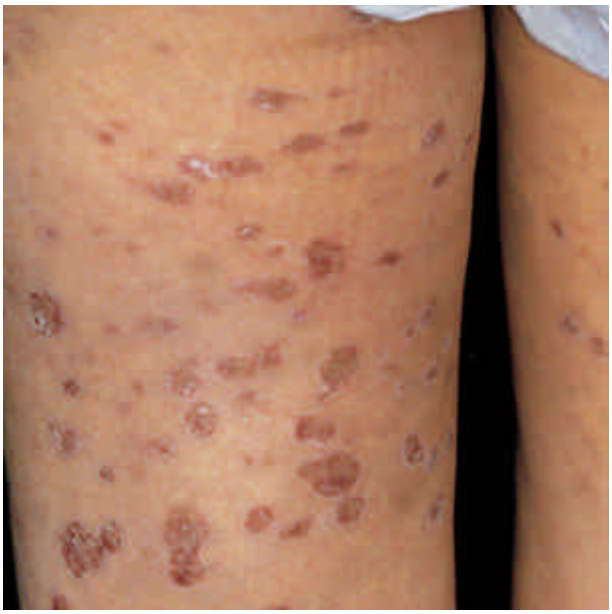

Fig. 3. Erythematous skin lesions on the left thigh.

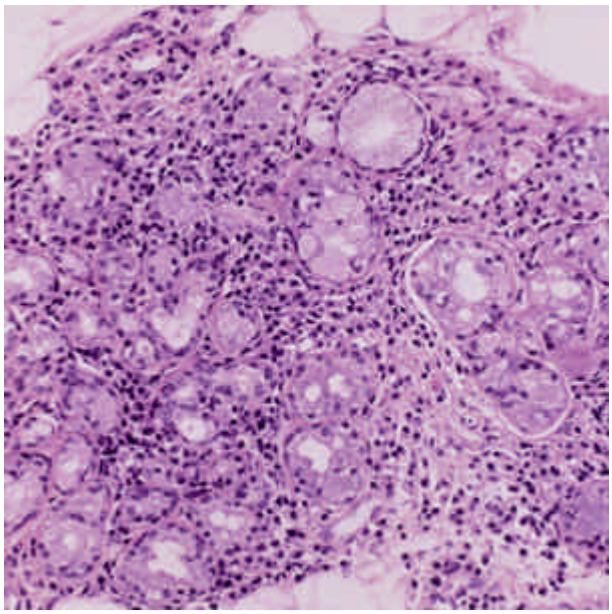

Fig. 4. Most of salivary gland lobules were densely infiltrated with small lymphocytes (H&E, ×100).

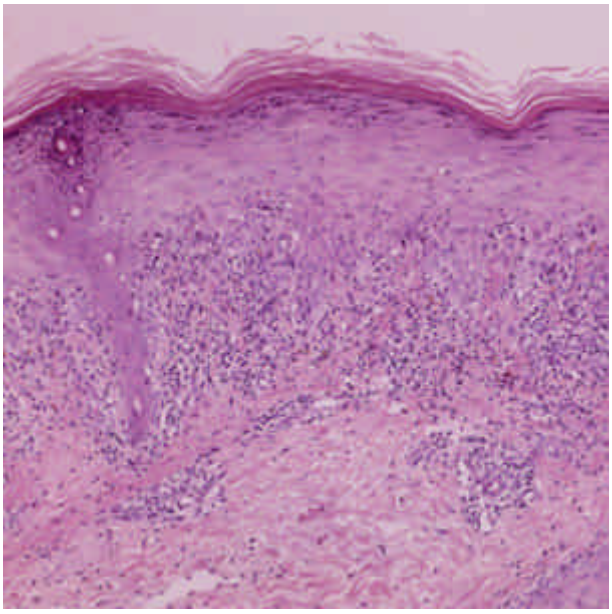

Fig. 5. Perivascular lymphocytic infiltration in the upper and mid dermis and hydropic degeneration in basal layer of the biopsy specimen from facial lesion (H&E, ×100).

including anemia (RBC: $3.46\times10^6/\mu L$, Hb: 10.10 g/dL), leukopenia (WBC: $3.14\times10^3/\mu L$) and thrombocytopenia (Plt: $104.00\times10^3/\mu L$) at that time. There was no history of drug intake which can induce pancytopenia. Erythrocyte sedimentation rate (ESR) increased at 40.00 mm/hr (normal; 3.00-9.00 mm/hr) and CRP was detected at a subnormal level. Immunologic studies showed the presence of antinuclear antibody (speckled type) at a titer of 1:320 as well as Ro/SS-A and La/SS-B antibodies. But dsDNA Ab, nRNP Ab, rheumatoid factor and anti-Smith Ab were not detected. A series of immunoglobulins and complement components were normal. The HLA typing showed DR 9 and DR 14 phenotypes.

Skin biopsy specimens taken from the facial and thigh lesions showed a common finding of perivascular lymphocytic infiltration in the upper and mid dermis and hydropic degeneration in basal layer, especially in the facial lesion (Fig. 5). There were no remarkable immunoreactants at the dermoepidermal junction and the walls of blood vessels. She was treated with hydroxychloroquine 400 mg/day, resulting in improvement of skin lesions.

DISCUSSION

SS, a chronic autoimmune exocrinopathy that is found mainly in middle-aged women, is characterized by dry eyes and dry mouth clinically in association with lymphocytic infiltration of lacrimal and salivary gland pathologically (1). Many criteria have been tried to classify SS until now and they reflect the controversies surrounding this entity as a newly described disease and the difficult situations in establishing diagnostic criteria in both nosology and research fields (2-4). Though SS is probably the most common rheumatic disease, it is often underrecognized. The reasons for this are a lack of patient awareness and education about SS, physician recognition and appreciation of the range of SS. The symptoms of SS may be subtle, often insidious, and dismissed as secondary to normal aging process, depression, neurosis, etc. SS mimic other diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), chronic fatigue syndrome, MS and so on (4). Actually other connective tissue diseases such as RA, SLE, progressive systemic sclerosis, can be found in patients with SS (5). However, the external stigmata characteristic of other rheumatic diseases are usually subtle or absent in SS. Although most SS patients are antibody positive: anti-Ro (SS-A)/anti-La (SS-B), ANA, or rheumatoid factor, the absence of antibodies does not exclude diagnosis of SS (4). SS may exist as a primary condition or as a secondary condition in association with RA, SLE, or progressive systemic sclerosis (1, 5). In primary SS patients, there may be extraglandular manifestations in pulmonary, cardiac, genitourinary, vascular, and nervous systems. Futhermore, these patients have an increased risk of developing lymphoproliferative disease, including lymphadenopathy and non-Hodgkin's lymphoma compared to normal controls or with patients of most other autoimmune diseases (6). If a patient has unusual neurologic problems and a serologic profile of positive SS-A or SS-B autoantibodies, it often represents a difficult diagnostic problem (7). Central nervous system (CNS) signs were found in up to 20% of the patients with SS and were multifocal, either progressive or relapsing, and often mimicking multiple sclerosis in cerebrospinal fluid profiles (8). CNS signs can manifest as hyperesthesia, spasticity, hyperreflexia, monocular visual loss, hemiparesis and so on (8). The relationship between SS and MS is ambiguous since SS may mimic MS both clinically and neuroradiologically (8-10). In fact, many patients had been thought to have MS before the diagnosis of SS was made (8). The changes in CSF profiles, which are indistinguishable from those seen in MS (11), are thought to be secondary to CNS inflammatory infiltrates composed predominantly of reactive lymphoid cells and occasional plasma cells with intrathecal synthesis of IgG (12). But some differences are present in cerebrospinal fluid profiles. Typical oligoclonal banding patterns of immunoglobulin on electrophoresis can be found in more than 90% of MS patients (13). Whereas, MS patients most commonly have multiple bands, SS patients usually have only one or two bands (8). The IgG indices and oligoclonal bands improve in response to corticosteroid therapy in most SS patients, but in MS patients

the number of bands remains constant over time and does not change with therapy (14). The cutaneous symptoms of Sjögren's syndrome are rare. Among these, dry skin with pruritus and vasculitis are common findings. Annular erythema associated with anti-Ro/La antibody positive patients of Sjögren's syndrome has been described in Asians (15-17). These annular erythemas were distinguished clinically as well as histopathologically from annular lesions of subacute cutaneous LE (SCLE), occurring mostly in anti-Ro antibody positive Caucasian patients (18, 19). In our case, the cutaneous lesions developed as discoid erythematous plaques and patches showing perivascular lymphocytic infiltration in the upper and mid dermis and hydropic degeneration in basal layer with no remarkable immunoreactants at the dermoepidermal junction and the walls of blood vessels.

Several studies have been undertaken to clarify the roles of particular alleles of major histocompatibility complex (MHC)-linked genes in association with SS patients (20, 21). However, no single MHC allele has been associated with SS of different ethnic backgrounds (22). In each ethnic population, predisposition to SS is associated with a particular class II allele (23). The patient in this report also showed DR 9 and DR 14 phenotypes.

Because of the similarity in clinical manifestations and laboratory findings of patients with MS and SS, we suggest that SS should be considered as a differential diagnosis of a patient presenting with a syndrome that resembles MS.

REFERENCES

1. Fox RI, Chan EK, Kang HI. *Laboratory evaluation of patients with Sjögren's syndrome. Clin Biochem 1992; 25: 213-22.*
2. Fox RI. *Sjögren's syndrome. Curr Opin Rheumatol 1995; 7: 409-16.*
3. Fox RI, Howell FV, Bone RC, Michelson P. *Primary Sjögren's syndrome: clinical and immunopathologic features. Semin Arthritis Rheum 1984; 14: 77-105.*
4. Alexander E. *Why is Sjögren's syndrome under-recognized? The Moisture Seekers Newsletter, 1992; 9.*
5. Fox RI, Kang HI. *Current therapy in allergy, immunology, and rheumatology. 4th ed. St. Louis: Mosby-Year Book, Inc., 1992.*
6. Kassan SS, Thomas TL, Moutsopoulos HM, Hoover R, Kimberly RP, Budman DR, Costa J, Decker JL, Chused TM. *Increased risk of lymphoma in sicca syndrome. Ann Intern Med 1978; 89: 888-92.*
7. Alexander EL, Ransenbach M, Kumar AWK, Kozachuk WE, Rosenbaum AE, Patronas N, Harley JB, Reichlin M. *Anti-SSA autoantibodies in central nervous system disease associated with Sjögren's syndrome: clinical, neuroimaging, and angiographic correlates. Neurology 1994; 44: 899-908.*
8. Alexander EL, Manilow K, Lejewski JE, Jerdan MS, Provost TT, Alexander GE. *Primary Sjögren's syndrome with central nervous system disease mimicking multiple sclerosis. Ann Intern Med 1986; 104: 323-30.*
9. Alexander EL, Beall SS, Gordon B, Selnes OA, Yannakakis GD, Patronas N, Provost TT, McFarland HF. *Magnetic resonance imaging of cerebral lesions in patients with the Sjögren's syndrome. Ann Intern Med 1988; 108: 815-23.*
10. Sandberg-Wollheim M, Axell T, Hansen BU, Henricsson V, Ingesson E, Jacobsson L, Larsson A, Lieberkind K, Manthorpe R. *Primary Sjögren's syndrome in patients with multiple sclerosis. Neurology 1992; 42: 845-7.*
11. Poser CM. *Diseases of the myelin sheath. In: Baker AB, Baker LH, eds. Clinical Neurology. Vol. 2. Philadelphia: J.B. Lippincott Company, 1983.*
12. De La Monte SM, Hutchins GM, Gupta PK. *Polymorphous meningitits with atypical mononuclear cells in Sjögren's syndrome. Ann Neurol 1983; 14: 455-61.*
13. Greenspan JS, Daniels TE, Talal N, Sylvester RA. *The histopathology of Sjögren's syndrome in labial salivary gland biopsies. Oral Surg Oral Med Oral Pathol 1974; 37: 217-9.*
14. Olsson JE, Link H, Muller R. *Immunoglobulin abnormalities in multiple sclerosis: relation to clinical parameters: disability, duration and age of onset. J Neurol Sci 1976; 27: 233-45.*
15. Teramoto N, Karayama I, Arai H, Eto H, Kamimura K, Uetsuka M, Kondo S, Nishioka K, Nishiyama S. *Annular erythema: a possible association with primay Sjögren's syndrome, J Am Acad Dermatol 1989; 20: 596-601.*
16. Ruzicka T, Faes J, Bergner T, Peter RU, Braun-Falco O. *Annular erythema associated with Sjögren's syndrome: a variant of systemic lupus erythematosus. J Am Acad Dermatol 1991; 25: 557-60.*
17. Katayama I, Teramoto N, Arai H, Nishioka K, Nishiyama S. *Annular erythema: a comparative study of Sjögren's syndrome with subacute cutaneous lupus erythematosus. Int J Dermatol 1991; 30: 635-9.*
18. Sontheimer RD, Maddison PJ, Reichlin M, Jordon RE, Stastny P, Gilliam JN. *Serologic and HLA associations in subacute cutaneous lupus erythematosus, a clinical subset of lupus erythematosus. Ann Int Med 1982; 97: 664-71.*
19. Nishikawa T, Provost T. *Differences in clinical, serologic, and immunologic features of white versus Oriental anti-SSA/Ro-positive patients. J Am Acad Dermatol 1991; 25: 563-4.*
20. Harley JB, Sheldon P, Neas B, Murphy S, Wallace DJ, Scofield RH, Shaver TS, Moser KL. *Systemic lupus erythematosus: considerations for a genetic approach. J Invest Dermatol 1994; 103: S144-9.*
21. Ricchiuti V, Isenberg D, Muller S. *HLA association of anti-Ro60 and anti-Ro52 antibodies in Sjögren's syndrome. J Autoimmun 1994; 7: 611-21.*
22. Kang HI, Fei HM, Saito I, Sawada S, Che SI, Yi D Chan E, Peebles C, Bugawan TL, Erlich HA, Fox RI. *Comparison of HLA class II genes in Caucasoid, Chinese, and Japanese patients with primary Sjögren's syndrome. J Immunol 1993; 150: 3615-23.*
23. Fei HM, Kang HI, Scharf S, Erlich HA, Peebles C, Fox RI. *Specific HLA-DQA and HLA-DRB1 alleles confer susceptibility to Sjögren's syndrome and autoantibody production. J Clin Lab Anal 1991; 5: 382-91.*