Sjögren's Syndrome Complicated by Scleroderma and Polymyositis

Report of a Case

Toshinori HARADA, Yohei FUKUMOTO, Minoru MIZUTA and Teruo FUJITA

The First Division, Department of Internal Medicine, Yamaguchi University School of Medicine, Ube, Japan

(Received November 12, 1974)

Since Henrik Sjögren,[1] an ophthalmologist, reported in 1934 the possibility of keratoconjunctivitis sicca being accompanied by xerosis of the oral mucosa, parotid swelling and chronic rheumatoid arthritis, this group of symptoms has been designated sicca syndrome or Sjögren's syndrome. It has been pointed out in recent years that the syndrome is frequently complicated not only by chronic rheumatoid arthritis, but also by various diseases in which autoimmunity is implicated.[2)-12)]

Described below is a patient who was initially attacked by Sjögren's syndrome, followed by complicating scleroderma and polymyositis, and finally suspected of having systemic lupus erythematosus.

CASE REPORT

The patient was a 50-year-old housewife who was admitted to our hospital on March 20, 1974, because of arthralgia and fever. Being healthy except for a hysterectomy in 1964 due to resecting myoma uteri, she began to note painful swelling of the joints in both hands and fingers toward November, 1972. This was complicated by dryness in both eyes and mouth, and an increase in dental caries. In january, 1974, she had a fever (38° to 39°C) and intensive arthralgia, and underwent therapy for rheumatoid arthritis at the office of a local physician. Early in February there was general edema and erythema, especially in the face, and desquamation and pigmentation of the skin. Early in March, a tightness of skin was noted in the forehead and arms, with the manifestation of Raynaud's phenomenon. There was also remarkable emaciation and weakened systemic muscular force and myalgia. At the time of admission her nutritive condition was poor and the emaciation was remarkable. The skin showed desquamation and pigmentation (Fig. 1) and both eye-lids were edematous with the tightness of the skin in the forehead and both arms, (Fig. 2) and

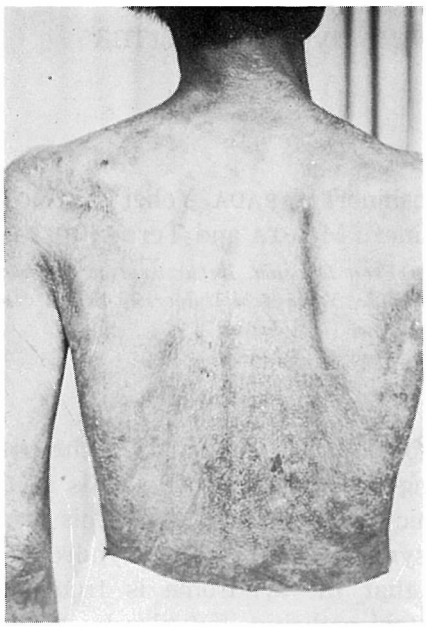

Fig. 1. Desquamation and pigmentation of the skin over the back and the waist.

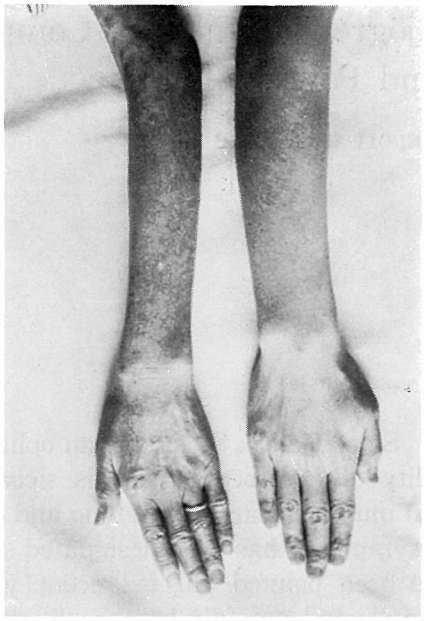

Fig. 2. Tightness of the skin and muscle atorophy over the left forearm. Left, patient. Right, healthy woman.

erythema on the palm. There was dryness in the mouth and dental caries in all of the teeth. The extremities and body muscles were atrophied and muscular weakness was remarkable. The lymphnodes were swollen as large as little fingers in both supraclavicular fossas, infraaxillary regions and inguinal regions. Cardiac dullness was enlarged to the left side, with a systolic murmur at the apex. The abdomen was flat, and the liver was palpable two finger breadths in the right mid-clavicular line. The right kidney was palpable. No abnormality was found in the neurological examinations. Her body temperature was 38°C. Examinations at the time of admission revealed: no abnormality in urinalysis, except for urine protein, 30 mg/dl; erythrocyte sedimentation rate, 138 mm (1 hour); red blood cells, 3,260,000 per cu. mm; white blood cells, 3,100 per cu. mm, with normal differential count; platelet count, normal; serum protein, 8.5 g/dl; serum albumin, 2.4 g/dl; serum gammaglobulin, 4.8 g/dl; SGPT, 163 units (normal, 40 units); SGOT, 78 units; serum lactic dehydrogenase, 640 units (normal, 220 units); serum creatine phosphokinase, 330 units (normal, 30 units); serum aldolase, 103 units (normal, 20 units); serum creatinine, 1.2 mg/dl; urine creatinine, 540 mg/day; urine creatine, 140 mg/day; indocyanine green retention test, 19.7% (15 minutes); rheumatoid factor,

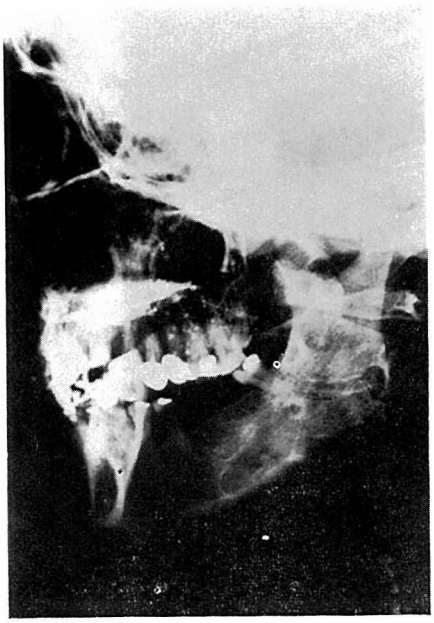

Fig. 3. Parotid sialogram, showing globular sialoectasia.

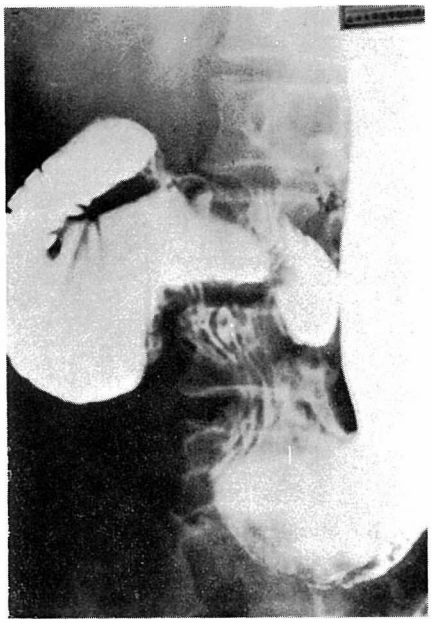

Fig. 4. Film from gastro-duodenal fluoroscopic examination, showing diminished peristalsis of the stomach and the duodenum, and remarkable dilatation of the infraduodenal horizontal leg.

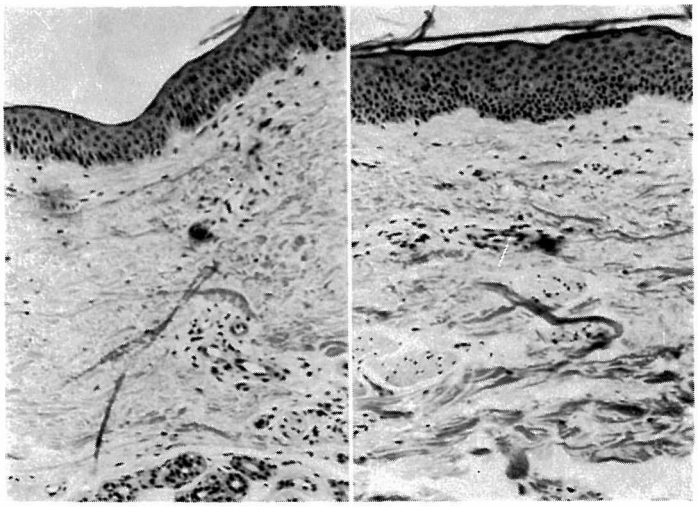

Fig. 5. Skin biopsy, showing atrophy and pigmentation in the epidermis and thickened collagen fibers in the dermis. Hematoxlin and eosin stain. ×360.

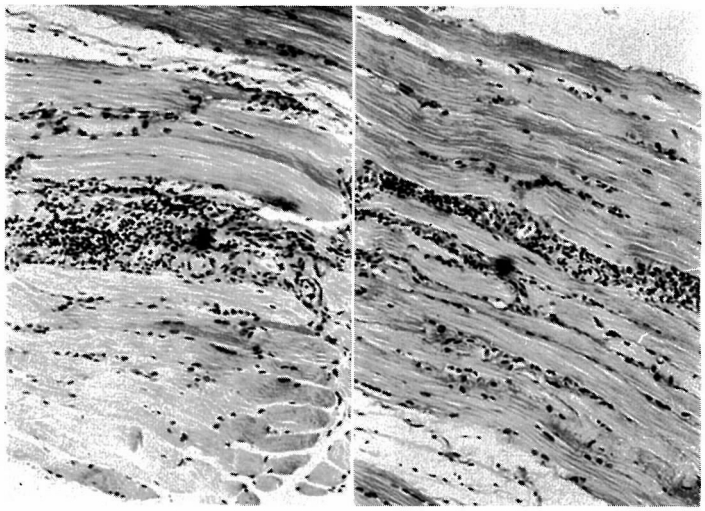

Fig. 6. Muscle biopsy, showing necrotic lesions with infiltration of small round cells in the muscle. Hematoxylin and eosin stain; ×360.

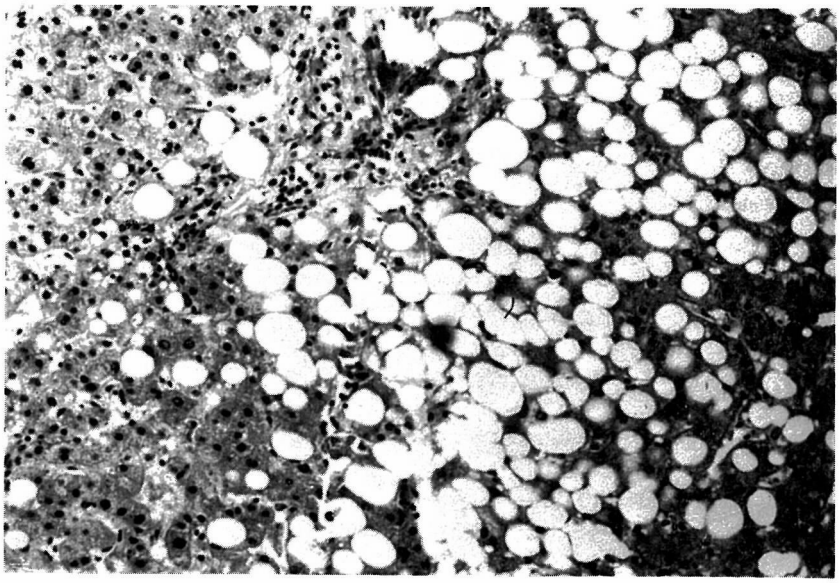

Fig. 7. Liver biopsy, showing moderate to severe fatty changes of liver cells. Hematoxylin and eosin stain; ×360.

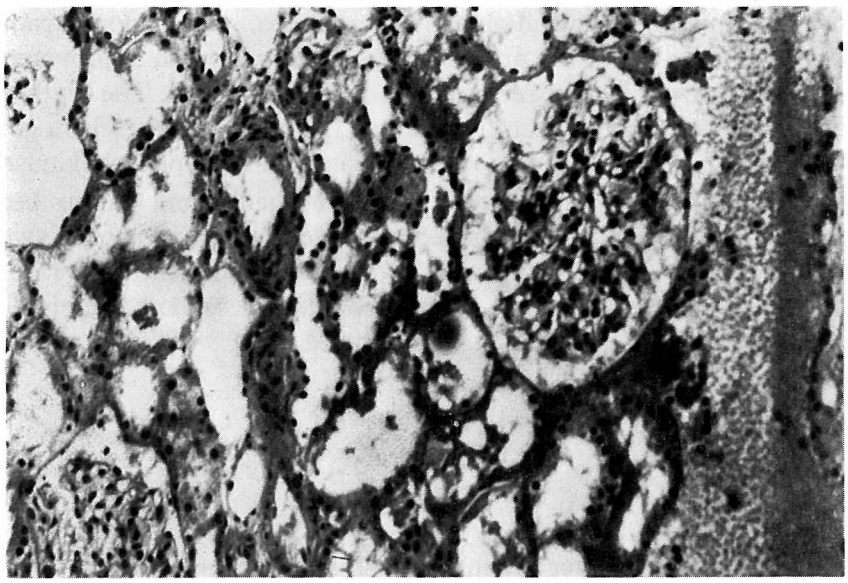

Fig. 8. Renal biopsy, showing no remarkable alterations. Hematoxylin and eosin stain; ×360.

positive; lupus erythematous cells, 2%; serum complement (CH50), 0; antinuclear factor, positive; thyroid antibody, negative; Coombs test, negative; and thyroid function, normal. Adrenocortical function was slightly disturbed, whereas renal function was normal. Schirmer's test revealed deficient lacrimation, and the Rose-Bengal test indicated the presence of keratoconjunctivitis sicca. Salivery secretion could barely be seen in the salivation test, and sialoectasia was detected sialographically. (Fig. 3) A gastro-duodenal fluoroscopic series disclosed diminished peristalsis of the gastrointestinal tract and remarkable dilatation of the infraduodenal horizontal leg. (Fig. 4) X-rays of the knee joints showed destructed bone typical of chronic rheumatoid arthritis. The gastric juice acidity was of low order, and electromyograms taken were of low amplitude. Skin and muscle biopsies revealed atrophy and pigmentation in the epidermis, remarkable deposition of collagen fibers in the dermis, and necrotic lesions accompanied by infiltration of small round cells in the muscle. (Figs. 5 and 6) The liver biopsy was not remarkable except for moderate to severe fatty changes of liver cells, (Fig. 7) and the renal biopsy did not disclose any remarkable alterations. (Fig. 8)

Hospital course: Therapy was started with prednisolone, 40 mg/day,

and the body temperature returned to normal in about 30 days, followed by improvement in subjective and objective symptoms, and various examination results. In July, 1974, the arthralgia disappeared, with improvement in the tightness of the skin and recovery of musular strength. The erythrocyte sedimentation rate was recovered at 37 mm (1 hour), with a serum gamma globulin level of 1.6 g/dl. Serum transaminase, creatine phosphokinase and complement titer were normalized, and the rheumatoid factor became negative. In August, 1974, the patient again noted fever and painful swelling of the knee joints, with increased erythrocyte sedimentation rate and elevated urine protein level (100 mg/dl). While she is now under clinical observation, no improvement is being observed even with increased doses of corticosteroid hormon.

DISCUSSION

This case developed as the typical Sjögren's syndrome, and was then complicated by scleroderma and polymyositis. Furthermore, the presence of systemic lupus erythematosus was suspected from such findings as fever, palmar erythema, arthralgia, Raynaud's phenomenon, highly elevated erythrocyte sedimentation rate, remarkably increased serum gamma globulin value, albuminuria, high titer of antinuclear factor, and a remarkable decrease in the serum complement titer at the acute stage. It was of particular interest that the co-existence of various clinical and pathological characteristics of autoimmune diseases were observed almost simmultaneously.

While it has long been known that chronic rheumatoid arthritis has a high incidence of concomitance with Sjögren's syndrome,[1),13),14)] there have been recent reports of occasional complications by other autoimmune diseases such as scleroderma,[3),4),5)] polymyositis,[6),7)] Hashimoto's disease,[8),9)] systemic lupus erythematosus,[9),10),11)] periarteritis nodosa[5)] and primary biliary cirrhosis[12)]. While most of these cases reported were complicated by a single autoimmune disease, a case report such as ours complicating two or three types of autoimmune diseases seems to be extremely rare.

In Sjögren's syndrome, various auto-antibodies have been demonstrated,[15),16)17)] and pathological lacrimal and salivary structures have been found to be similar to those of the thyroid gland in Hashimoto's thyroiditis,[16)] and various autoimmune diseases have occurred concomitantly in occasional instances. Therefore, it may be hypothesized that the autoimmune mechanism takes part in the etiology of the syndrome. There are various opinions[5),8),18)] as to whether the syndrome is an independent disease entity,

a variant type of chronic rheumatoid arthritis or systemic lupus erythematosus, or a complication of these diseases. While nothing was obtained in this respect from our present case, which exhibited the various clinical and sero-immunological findings stated above, it may be postulated that an abnormal mechanism of immunity may be present not only quantitatively but qualitatively in our case.

Honma et al.[19] pointed out the possible co-existence of clinical pictures characteristic of two different connective tissue diseases in the same patient, and designated such cases as "overlap syndrome". Our present case may belong to this category.

Another disease which needs to be enumerated is a mixed connective tissue disease, named by Sharp et al.,[20] because it is similar to our case and needs to be differentiated. This disease is characterized by a mixture of symptoms observed in systemic lupus erythematosus, polymyositis and scleroderma, and the presence of the antibody to the extractable nuclear antigen which is demonstrated in both active and clinically alleviated stages of the disease, and complete remission by corticosteroid therapy in many instanses, and normal or elevated levels of serum complement at the acute stage of the disease. While the antibody to the extractable nuclear antigen has not been studied in our present case, and no definite conclusion can be drawn, it is considered that our present case is different from the mixed connective tissue disease in view of the remarkable decrease of the serum complement titer at the acute stage and the present symptomatic aggravation of the patient by antagonizing to steroid therapy.

SUMMARY

This report deals with a 50-year-old woman who was initially attacked by Sjögren's syndrome, followed by complicating scleroderma and polymyositis, and finally suspected of having systemic lupus erythematosus. It has been pointed out that Sjögren's syndrome is often complicated by autoimmune diseases other than chronic rheumatoid arthritis. However, Sjögren's syndrome complicated by two or three different types of autoimmune diseases, as observed in our present case, seems to be extremely rare. The co-existence of Sjögren's syndrome and other autoimmune diseases and their possible interrelationship are discussed.

REFERENCES

1) Sjögren, H.: Zur Kenntnis der Keratoconjunctivitis sicca. *Acta Ophth., Suppl.* 2 : 1, 1933.
2) Sheum, M.A.: Sjögren's syndrome in association with scleroderma. *Ann. Intern. Med.*, 52 :

1352, 1960.
3) Alacón-Segovia, D., Ibanez, G., Hernández-Ortiz, J., Velázquez-Foreno, F. and González-Jiménez, Y.: Sjögren's syndrome in progressive systemic sclerosis. *Amer. J. Med.*, 57 : 78, 1974.
4) Harrington, A.B. and Dewar, H.A.: Case of Sjögren's disease with scleroderma. *Br. Med. J.*, 1 : 1302, 1951.
5) Ramage, J.H. and Kinnear, W.F.: Keratoconjunctivitis sicca and the collagen diseases. *Brit. J. Ophthal.*, 40 : 416, 1956.
6) Silberberg, D.H. and Drachman, P.A.: Late life myopathy occuring in Sjögren's syndrome. *Arch. Neurol.*, 6 : 428, 1962.
7) Bunium, J.J.: A broader spectrum of Sjögren's syndrome and it's pathologic implications. *Ann. Rheum. Dis.*, 20 : 1, 1961.
8) Vanselow, N.A. Angel, D.C. and Duff, I.F.: A clinical study of Sjögren's syndrome. *Ann. Intern. Med.*, 58 : 124, 1963.
9) Stoltze, C.A., Haulon, D.G., Pease, G.L. and Henoerson, J. W.: Kerato-conjunctivitis sicca and Sjögren's syndrome. *Arch. Intern. Med.*, 106 : 513, 1960.
10) Steinberg, A.D. and Talal, N.: Coexistence of Sjögren's syndrome and systemic lupus erythematosus. *Ann. Intern. Med.*, 74 : 55, 1971.
11) Bain, G.O.: The pathology of Mikulicz-Sjögren's disease in relation to disseminated lupus erythematosus. *Canad. Med. Ass. J.*, 82 : 143, 1960.
12) Alarcón-Segovia, D., Diáz-Jouanen, E. and Fishbein, E.: Features of Sjögren's syndrome in primary biliary cirrhosis. *Ann. Intern. Med.*, 79 : 31, 1973.
13) Block, K.J., Buchanan, W.W., Wohl, M.J. and Bunium, J.J.: Sjögren's syndrome: a clinical, pathological and serological study of 62 cases. *Medicine*, 44 : 187, 1965.
14) Stenstam, T: On the occurrence of keratoconjunctivitis sicca in case of rheumatoid arthritis. *Acta. Med. Scandinav.*, 127 : 130, 1947.
15) Whaley, K. et al.: Salivary duct autoantibody in Sjögren's syndrome. *Clin. Exp. Immunol.*, 4 : 273, 1969.
16) Jones, B.R.: Lacrimal and salivary precipitating antibodies in Sjögren's syndrome. *Lancet*, 2 : 773, 1958.
17) Anderson, J.R., Gray, K., Beck, J.S. and Kinnear, W.F.: Precipitating autoantibodies in Sjögren's disease. *Lancet*, 2 : 456, 1961.
18) Heaton, J.M.: Sjögren's syndrome and systemic lupus erythematosus. *Brit. Med. J.*, 1 : 466, 1959.
19) Honma, M. and Abe, T.: *Clin. Immunol*, 1 : 621, 1969. (in Japanese)
20) Sharp, G.C., Irvin, W.S., Tan, E.M., et al.: Mixed connective tissue disease-An apparently distinct rheumatic disease syndrome associated with a specific antibody to a extractable nuclear antigen. *Amer. J. Med.*, 52 : 148, 1972.