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CASE REPORT

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Dilated cardiomyopathy (DCM) associated with SSA antibody in primary Sjögren syndrome

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Abstract A 33-year-old Japanese woman was diagnosed with primary Sjögren syndrome (SS) in 1995. At this time, SSA antibody had not been detected by the Oucterlony or EIA methods. Two years later, the patient developed dyspnea. A chest X-ray showed cardiomegaly. An echocardiogram indicated severe diffuse hypokynesis of the cardiac wall with a left ventricular ejection fraction of 32%. Positive SSA antibody (over 500 u/ml) was noted in her serum as measured by the EIA method. We considered her cardiac manifestation to be dilated cardiomyopathy associated with primary SS.

Key words Dilated myopathy · Sjögren syndrome · SSA antibody · Cardiac manifestation · Elevation of IgG

Introduction

Primary Sjögren syndrome (SS) (sicca syndrome) presents various symptoms including arthritis, skin lesions, interstitial pneumonia, and thyroiditis. However, cardiac involvement in SS is rare. Neonates with positive anti-SSA antibodies (neonatal lupus erythematosus) showing a skin rash or congenital heart block have been reported. In this report, we describe a patient with SS showing dilated cardiomyopathy (DCM) that was similar to cardiac involvement. The patient did not show positive anti-SSA antibodies at the initial serum examination (December 1995). Two years later, severe heart failure occurred and positive anti-SSA antibodies became apparent. We discuss a possibile relationship between anti-SSA antibodies and cardiac involvement.

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Case report

A 33-year-old Japanese woman was admitted to our hospital because of arthralgia and general malaise in December 1995. Two years prior to admission, she had symptoms of sicca syndrome (dry eyes or dry mouth) and an episode of Raynaud's phenomenon. Her previous health record was good. She did not drink alcohol or smoke, and there was no family history of cardiac disorders.

On admission, she was febrile at 37.5°C, with a respiratory rate of 16/min, a pulse rate of 82/min, and a blood pressure of 104/76 mm/Hg. She had no lymphadenopathy or cardiac murmurs, and her chest findings were normal. An abdominal examination revealed no abnormalities. She had no skin lesions, scleroderma, or pitting edema on her limbs. She had limited motion of the right hand and the foot joint without swelling. Roentgenographic changes were not consistent with rheumatoid arthritis, joint space narrowing, or erosive changes.

Laboratory studies revealed a hemoglobin level of 9.5 g/dl, a leukocyte count of 3040/μl (lymphocytes 26%), and a platelet count of 29.1×10^4/μl. A urinalysis detected no protein. Blood chemistry, including total bilirubin, serum transaminase, lactate dehydrogenase (LDH), alkaline phosphatase (ALP), blood urea nitrogen (BUN), and creatinine levels, was normal. Total serum protein was 7.5 g/dl. Electrophoresis disclosed hypergammaglobulinemia (35.3%), IgG of 2030 mg/dl, IgA of 235 mg/dl, and IgM of 388 mg/dl. The rheumatoid factor was 44 IU/ml, and mild hypocomplementemia was observed (CH50, 29.8 U; C_3, 55 mg/dl; C_4, 13 mg/dl). Direct and indirect Coombs' test, flourescent antinuclear antibody (FANA), and double-strand anti-DNA antibody were negative. Single-strand anti-DNA antibody (IgG) was positive (152 U/ml). At this time, the anti-SSA antibody was not detected by the Oucterlony or EIA methods.

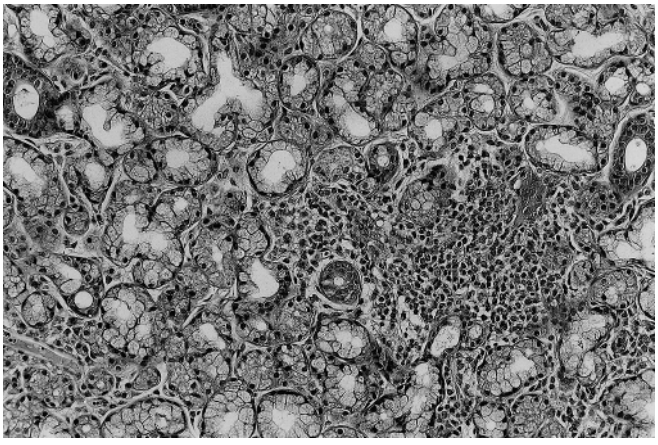

Fig. 1. Histological examination of a minor salivary gland in the oral mucosa, showing focal lymphocytic sialadenitis with degeneration of the ductular epithelium which is compatible with the histology of Sjögren syndrome (hematoxylin and eosin)

A Schirmer test resulted in 3 mm of wetting in 5 min. A histological analysis of a minor salivary gland from an oral mucosa biopsy revealed focal lymphocytic sialadenitis with degeneration of the ductular epithelium (Fig. 1). Based on these observations, primary SS was diagnosed. Her symptoms gradually improved, so treatment was not initiated.

In September 1997, she had a syncopal attack. She was admitted to our hospital in October 1997 with dyspnea, chest discomfort, and palpitation. Her pulse was irregular, at a rate of 110/min, and her blood pressure was 94/50 mm/Hg. A chest X-ray demonstrated cardiomegaly at a cardiothoracic ratio of 61% and bilateral pleural effusion. Electrocardiography (ECG) revealed a low voltage in all leads and a QS pattern in the V_1–V_3 leads with some premature ventricular contractions. An echocardiogram indicated severe diffuse hypokinesis of the cardiac wall with a left ventricular ejection fraction of 32% and mild pericardial effusion, which did not suggest a valvular disease. A mild left ventricular dilatation was also observed (Fig. 2). Thallium-201 scintigraphy showed severe defects except in the posterior wall. The diagnosis of DCM was based on these findings. Cardiac catheterization was not performed because of the patient's poor cardiac function. An elevation of the viral titer, including adenovirus, parainfluenza virus (1,2), echovirus, coxaxie virus (A,B), and cytomegalo virus, was not found. At this time, a positive anti-SSA antibody (over 500 U/ml measured by the EIA method) was noted in her serum, and a marked elevation of the serum IgG level (5841 mg/dl) was observed. FANA was negative, but the cytoplasm was stained. Anti-DNA, anti-RNP, anticentromere, antitopoisomerase I, and anti-SSB antibodies were all negative. Although massive doses of prednisolone (50 mg/day) were injected, her cardiac dysfunction gradually progressed. A ventricular tachycardia attack occurred sometime later, and the patient died 4 months after that (Fig. 3). An autopsy was not performed.

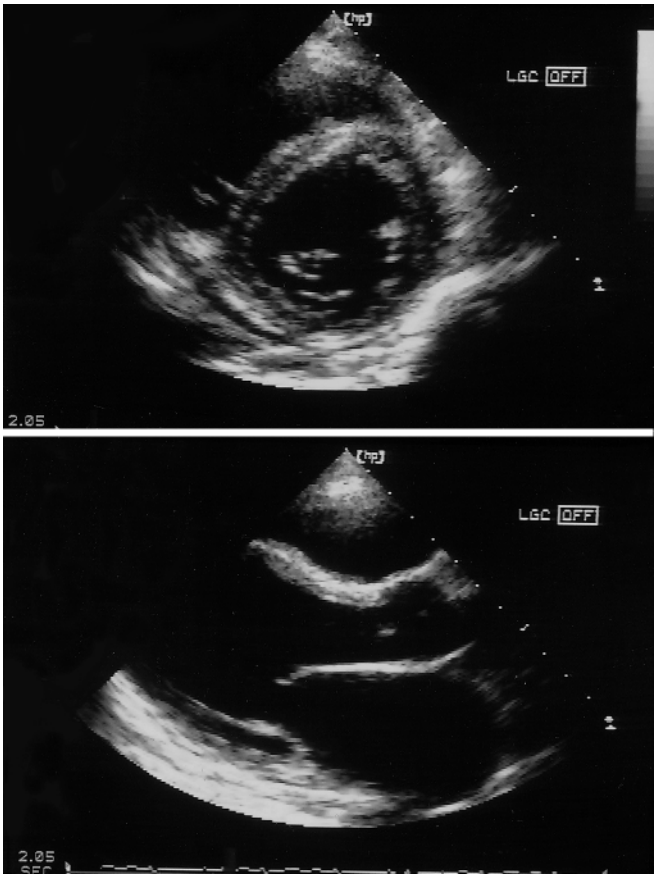

Fig. 2. Echocardiography indicated severe hypokynesis of the cardiac wall with a left ventricular ejection fraction of 32%. The left cardiac wall is very thin

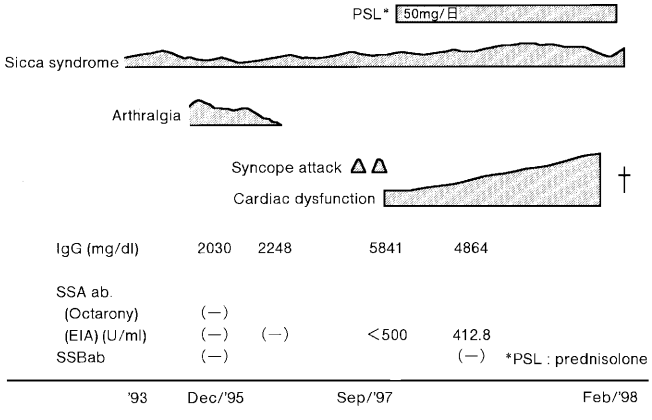

Fig. 3. Clinical course

Discussion

Based on the sicca symptoms, leukopenia, the positive Schirmer test, and the histological examination of a minor salivary gland, primary SS was diagnosed. Arthralgia and Raynaud's phenomena were compatible with SS. This patient had the characteristic cardiac manifestation of DCM.

Generally, genetic factors, infectious agents, chemical agents, or sarcoidosis have been suspected of being involved in the development of DCM.

The patient did not drink alcohol. The patient's family history was not contributory. Her clinical symptoms and laboratory findings were not suggestive of a viral infection or sarcoidosis. An elevation of the viral titer was not found, and she did not show any clinical symptoms which accompany a viral infection. The serum angiotensin-converting enzyme level was in the normal range, and she had no skin lesions, no lymphadenopathy (including bilateral hilus lymphadenopathy). Based on these findings, we negated the existence of sarcoidosis.

When her cardiac symptoms occurred, a marked elevation of the serum IgG level and a positive anti-SSA antibody became apparent. We then considered her cardiac manifestation as DCM associated with primary SS. Cardiomyopathy in collagen diseases is common in systemic lupus erythematosus (SLE), systemic sclerosis, or polymyositis. In autopsied cases of SLE, the reported prevalence of cardiomyopathy is about 40%.[1] Cardiac involvement in primary SS is relatively rare. Congenital heart block,[2,3] pulmonary hypertension,[4] and pericarditis[5] accompanied by primary SS have been reported. Takaoka et al.[6] reported a case that showed a reduced left ventricular systolic function in primary SS. In that case, myocarditis did not exist, and oral corticosteroid therapy was effective in alleviating the symptoms. The authors concluded that the reduced left ventricular systolic function was of concern in the autoimmune mechanism.

Only one case of myopathy with primary SS has been reported. Yoshida et al.[7] reported a case that showed myopathic involvement with primary SS and a positive anti-SSA antibody as in our patient. In their patient, a diffuse fibrotic proliferation and lymphocytic infiltration were also noted in the perivascular lesions of the intracardiac muscle during autopsy. In our patient, a positive anti-SSA antibody was not observed, and the elevation of serum IgG was mild in the initial serum. A positive anti-SSA antibody and a marked elevation of serum IgG appeared during the course of her illness. Therefore, we considered that the autoantibodies, including anti-SSA antibodies, were connected with her cardiac manifestion.

In primary SS, Alexander[8] found a relationship between various symptoms due to angitis and anti-SSA antibodies. It is also considered that some other gland manifestations in primary SS are involved with hypergammaglobulinemia or circulating autoantibodies (anti-SSA, anti-SSB antibody).[5] Therefore, we speculated that the DCM in this patient was induced by the an anti-SSA antibody. Unfortunately, we could not perform a pathological examination.

Furthermore, it is unclear why anti-SSA antibodies appeared in the late clinical course of our patient's illness despite being negative in the initial serum test. Generally, the production of autoantibodies, including rheumatoid factor, is strongly influenced by an exogenous infection or somatic mutation.[9] A point mutation occurring at the antigen binding site in immunoglobulin molecules sometimes alters its antigen specificity[10] or idiotypic expression.[11] However, there are no reports on the production of anti-SSA antibody.

This case suggests that anti-SSA antibody played an important role in DCM appearing as a cardiac manifestation in primary SS.

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