A Rare Case of Cardiac Sarcoidosis in a Patient with Progressive Systemic Sclerosis, Sjögren’s Syndrome, and Polymyositis

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A 56-year-old woman with overlap syndrome of progressive systemic sclerosis (PSS), Sjögren’s syndrome, and polymyositis is reported. She developed complete atrioventricular (AV) block and progressive bilateral hilar adenopathy, and was diagnosed as having sarcoidosis by histological examination of the hilar lymph nodes biopsied thoracoscopically. Although coexistence of one or two autoimmune diseases with sarcoidosis is not uncommon, coexistence of three or more autoimmune diseases with sarcoidosis is rare. To our knowledge, the described case is the first case in which the three above-mentioned autoimmune diseases were accompanied by myocardial sarcoidosis.

Key words: overlap syndrome, autoimmune disease, noncaseating granuloma

Introduction

Sarcoidosis is a chronic multisystem disease of unknown etiology characterized by noncaseating granulomatous inflammation. Sarcoidosis sometimes accompanies autoimmune diseases, although it is not clear whether they are related in terms of pathogenesis. Here, we report the first known case in which myocardial sarcoidosis coexisted with progressive systemic sclerosis (PSS), Sjögren’s syndrome, and polymyositis.

Case Report

A 56-year-old Japanese woman was admitted to our department in April 1994 for the evaluation of bilateral swelling and stiffness of her fingers, Raynaud’s phenomenon of the hands, dry eyes and dry mouth, which had begun two years earlier, and dyspnea on exertion, which had begun two months earlier.

Physical examination revealed microstomia, skin thickening of the bilateral fingers, and left parotid gland enlargement. On auscultation, systolic murmur (Levine 2/6) was audible at the apex and coarse inspiratory crackles were heard at the bilateral lung bases. Muscle weakness of the neck and arms was prominent, and more marked proximally.

Laboratory findings on admission revealed mild normochromic, normocytic anemia and an elevated white blood cell count of 12,400/μl (stab cell 12%, segmented leucocyte 82%, lymphocyte 5%, monocyte 1%, eosinophil 0%, basophil 0%). The serum protein electrophoresis showed a total protein level of 9.5 g/dl with an increased polyclonal gamma globulin fraction. The immunoglobulin levels were as follows: IgG 4,225 mg/dl, IgA 497 mg/dl, IgM 593 mg/dl. The serum creatinine phosphokinase (CPK) was elevated at 1,391 U/l, and the lactate dehydrogenase (LDH) level was elevated at 336 U/l. Serum angiotensin-converting enzyme (ACE) was within normal limits (15 U/l), and the serum lysozyme level was slightly elevated at 11.4 mg/dl. The albumin level was 2.8 g/dl, and aspartate aminotransferase (AST) was slightly elevated at 52 U/l. Thyroid function was normal. C-reactive protein (CRP) level was elevated at 7.2 mg/dl, and the erythrocyte sedimentation rate (ESR) was elevated at 121 mm/h. Serological test for syphilis was negative. Antinuclear antibody (ANA) was ×40 (speckled). Rheumatoid arthritis particle agglutination (RAPA) was ×640. Both the anti-Sjögren’s syndrome-A (ss-A) antibody and the anti-Sjögren’s syndrome-B (ss-B) antibody were positive. The anti-Smith (sm) antibody, anti-nuclear-ribonucleoprotein (RNP) antibody, anti-scleroderma 70 (scl-70) antibody, and anti-DNA antibody were all negative. The complement levels and urinalysis were normal. The tuberculin test was negative. The culture tests was negative for bacteria, fungi, and acid-fast bacilli.

The chest roentgenogram showed a reticulonodular interstitial pattern at the bilateral lung bases, and bilateral hilar adenoma.
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The chest roentgenogram on admission showing a reticulonodular interstitial pattern at the bilateral lung bases, and bilateral hilar adenopathy.

Figure 1. The chest roentgenogram on admission showing a reticulonodular interstitial pattern at the bilateral lung bases, and bilateral hilar adenopathy.

The electrocardiogram on admission showed first-degree atrioventricular (AV) block, and complete right bundle branch block (RBBB) with left anterior hemiblock (LAH) (Fig. 2). An electrocardiogram of 8 years prior to admission did not show similar findings. Gallium scan was positive; there are accumulation in the bilateral hilum pulmonis. Ultrasound and computed tomographic (CT) scan of abdomen confirmed mild hepatomegaly and splenomegaly. Echocardiography on admission showed no abnormal findings except moderate pulmonary hypertension. Spirometry demonstrated a mild restrictive pattern, compatible with interstitial pneumonia. Skin biopsy of the finger showed extension of collagen fibers from the dermis into the subcutaneous tissue (Fig. 3). The pathological diagnosis of PSS was established.

Shirmer and Rose Bengal tests were positive. Sialography showed an abnormal pooling with an apple tree-like pattern in the right parotid gland (Fig. 4). Biopsy of the left parotid gland demonstrated a lymphocytic infiltration. No granulomatous lesions were found. The pathological diagnosis of Sjögren’s syndrome was established.

An electromyogram of the deltoid and biceps muscles revealed a myopathic pattern with fibrillations and positive sharp waves in spontaneous activity and short-duration, low-ampli-

Figure 2. The electrocardiogram on admission showing first-degree AV block, and complete RBBB with LAH.

Figure 3. Microscopic examination of the skin of the finger showing extension of collagen fibers from the dermis into the subcutaneous tissue (HE stain, ×40).

Figure 4. Sialography showed an abnormal pooling with an apple tree-like pattern in the right parotid gland.
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tude, and polyphasic motor unit action potentials in the volitonal activity. Biopsy of the left deltoid muscle showed marked infiltration of macrophages and lymphocytes. No granulomatous lesions were found. The pathological diagnosis of polymyositis was established.

During the first month after her admission, there were remarkable changes both in the electrocardiogram and in the chest roentgenogram. In May 1994, the electrocardiogram showed complete AV block (Fig. 5) and she was treated by permanent pacemaker implantation. The chest roentgenogram revealed progression of the bilateral hilar adenopathy (Fig. 6).

Biopsy of the right hilar lymph nodes was conducted thoracoscopically to establish the definite diagnosis. Noncaseating granulomas were found (Fig. 7). Staining for fungi and acid-fast organisms were negative, and there was no evidence of tuberculosis. The definite diagnosis of sarcoidosis was established.

In view of the complications of PSS and sarcoidosis in this patient, the cardiac abnormalities could either be considered to be due to PSS or sarcoidosis. Biopsy of the myocardium was also performed. Although no granulomatous lesion was found in the biopsy specimens, the simultaneous progression of the AV block and the bilateral hilar adenopathy strongly suggested the existence of myocardial sarcoidosis.

Prednisolone therapy, 60 mg daily, was begun, resulting in slow improvement of the hilar lymph node enlargement, decrease of CPK values from 1,391 U/l to 58 U/l, decrease of ACE values from 15 U/l to 6.3 U/l and decrease of CRP values from 7.2 mg/dl to 0.3 mg/dl (Fig. 8). The dose of prednisolone was slowly tapered.
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Discussion

Here, we reported a case with overlap syndrome of PSS, Sjögren's syndrome, and polymyositis accompanied by myocardial sarcoidosis. This is the first case in which these four diseases coexisted in one patient.

PSS is shown to occur in association with other connective tissue diseases, as seen in this case. The term “overlap syndrome” is used to describe such patients. There is a similar syndrome called “mixed connective tissue disease (MCTD)”, which is characterized by a combination of typical overlapping clinical findings similar to PSS, polymyositis, systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA) and high titers of the anti-nuclear-RNP antibody. The present patient, in whom the anti-nuclear-RNP antibody was negative, did not fulfill the diagnostic criteria for MCTD.

There is an increasing number of reported cases of sarcoidosis coexisting with various autoimmune diseases in the literature (1-17). Enzenauer and West reported that 6 of 569 patients (1%) with connective tissue diseases developed sarcoidosis over a 10-year study period (1). Three of the cases had RA, one each had primary Sjögren’s syndrome, SLE, and PSS. Sarcoidosis has also been reported as a complication of a variety of other autoimmune diseases, including hemolytic anemia (2-4), thyroiditis (5-7), glomerulonephritis (8), or autoimmune thrombocytopenia (9). Sarcoidosis is also reported to complicate more than two diseases in a few cases (10-12), consistent with our case. Although the coexistence of sarcoidosis and autoimmune diseases might represent a simple coincidence, these disorders may have common immunopathogenic mechanisms. Sarcoidosis has been reported to show multiple common immunological abnormalities including defective cell-mediated immune function, hypergammaglobulinemia, loss of tolerance to self-antigens, depression of antibody-dependent cell-mediated cytotoxicity, and an increased number of monocytes, which are also seen in autoimmune diseases (17-19). Still not completely clarified, it is implicated that a similar pathogenic mechanism exists for both sarcoidosis and autoimmune diseases.

The coexistence of sarcoidosis with autoimmune diseases may be more widespread than the literature has suggested. Sarcoidosis and autoimmune diseases are both multisystem diseases; they may both involve the lungs, lymph nodes, heart, skin, muscles, eyes, parotid glands, or bone marrow. Furthermore, many signs and symptoms are common to both diseases. The diagnosis of sarcoidosis, which requires pathological confirmation of noncaseating granulomatous inflammation, may be difficult if the differential diagnosis of autoimmune diseases does not include sarcoidosis. In the present case, bilateral hilar adenopathy in this patient with the primary diagnosis of Sjögren’s syndrome would have been suspected just as the result of the primary diagnosis of Sjögren’s syndrome, if biopsy of the hilar lymph nodes had not been performed. Generally bilateral hilar adenopathy could either be due to the primary diagnosis of Sjögren’s syndrome, sarcoidosis, the metastasis of malignant tumors, tuberculosis, or malignant lymphoma which has been reported to develop in Sjögren’s syndrome with high frequency. Therapy would differ for each of these diseases. Further investigation of bilateral hilar adenopathy was critical in our case.

Acknowledgements: We are very grateful to Dr. Teruaki Oka of the Department of Pathology, Dr. Kanako Kikuchi of the Department of Dermatology, and Dr. Jun Shimizu of the Department of Neurology of the University of Tokyo for their excellent assistance. This material has not been previously reported elsewhere and is not under consideration for publication elsewhere.

References