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CASE REPORT

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Primary Sjögren's syndrome complicated by sarcoidosis and psoriasis vulgaris

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Abstract Primary Sjögren's syndrome (SS), sarcoidosis (SA), and psoriasis vulgaris (PV) are all chronic diseases of unknown etiology. Recent studies suggest that activated T cells play a central role in their pathogenesis. We describe a case of a Japanese woman with primary SS complicated by SA and PV. To our knowledge, this is the first case in which these three diseases coexist. Although these three disorders may have a common immunopathogenic mechanism, the extreme rarity of their coexistence suggests that distinct etiological mechanisms are also involved and appear to play an important role in triggering and developing each disease.

Key words Psoriasis · Sarcoidosis (SA) · Sjögren's syndrome (SS) · T lymphocytes

Introduction

Primary Sjögren's syndrome (SS), sarcoidosis (SA), and psoriasis vulgaris (PV) are chronic diseases of uncertain etiology. Recent studies have revealed that similar immunological abnormalities may exist. Among those, activated T cells and the cytokines that they produce are considered to play an important role in triggering and perpetuating SS, SA, and PV.[1–5] We report the first known case of primary SS with SA and PV.

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Case report

A 61-year-old Japanese woman was admitted to our department on July 6, 1998, for an evaluation of bilateral hilar adenopathy. She had had PV and polyarthritis for about 30 years. In 1993, she underwent a right total hip replacement. A physical examination showed xerostomia and hyperkeratotic erythematous plaques on her face, chest, and upper extremities. Lung auscultation showed bibasilar inspiratory crackles. Muscle weakness in the left lower extremity, most probably due to the lesion in the left hip joint, was also observed.

The laboratory findings on admission revealed mild normochromic, macrocytic anemia (red blood cell count 294 × 10^4/μl, hemoglobin 9.0 g/dl), leukocytopenia (2550/μl), and polyclonal hypergammaglobulinemia: IgG 3475 mg/dl (normal 1125–1738 mg/dl); IgA 359 mg/dl (normal 179–349 mg/dl); IgM 204 mg/dl (normal, 26–252 mg/dl). The C-reactive protein level was slightly elevated at 0.75 mg/dl (normal ≤0.27 mg/dl), and the erythrocyte sedimentation rate (ESR) was elevated at 62 mm/h. Rheumatoid factor was 25 IU/ml (normal ≤25 IU/ml), and the complement levels (C_3, C_4) were normal. The titer of the antinuclear antibody was ×640 (speckled pattern). The titer of antibody to SS-A antigen was ×16. The antibody to SS-B antigen was negative. The serum angiotensin-converting enzyme level was elevated at 30.9 IU/l (normal 8.3–21.4 IU/l). Schirmer's test revealed a decrease in tear production.

A chest roentgenogram showed bilateral hilar adenopathy (Fig. 1). Chest computed tomography showed a swelling of the mediastinal, bilateral hilar, and left axillary lymph nodes, and reticular shadows in the right lung (Fig. 2). An X-ray of the left hip joint revealed a narrowing of the joint space. A gallium scan was positive; there were accumulations in the bilateral hilum and left axillary region. Sialography showed an abnormal pooling with an apple tree-like pattern in the right parotid gland (Fig. 3). Slit-lamp microscopy revealed a nodule on the right iris and bilateral peripheral anterior synechiae consistent with sarcoidosis. A skin biopsy from the right upper arm lesion

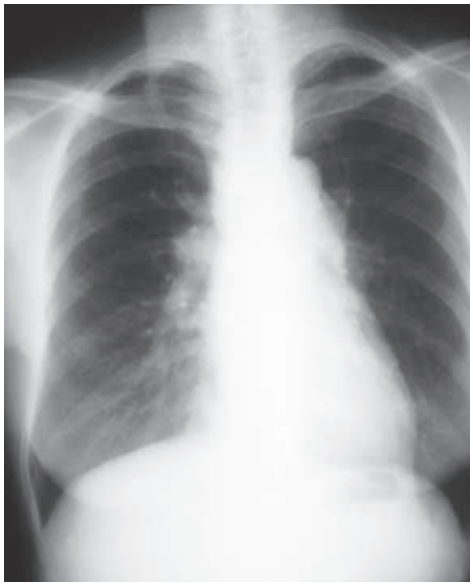

Fig. 1. Chest roentgenogram showing bilateral hilar adenopathy

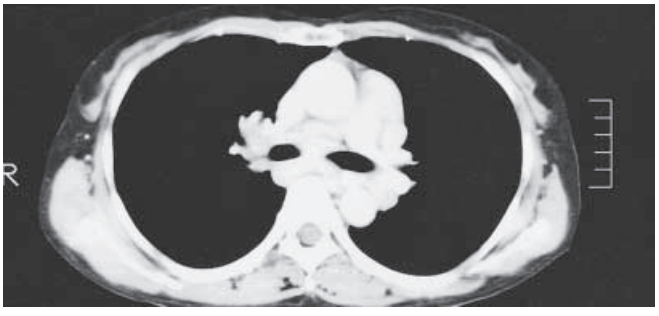

Fig. 2. Chest computed tomography scan showing a swelling of the mediastinal and bilateral hilar lymph nodes

showed superficial perivascular dermatitis with a psoriasiform proliferation. The epidermis showed a mild elongation of the rete ridges, mild papillomatosis, and moderate parakeratosis. In addition, hypogranulosis and mild thinning of the suprapapillary plate were observed. The capillaries in the upper dermis were dilated with perivascular edema and mild lymphocytic infiltration (Fig. 4). A biopsy of the left axillary lymph node showed noncaseating granuloma formation compatible with sarcoidosis (Fig. 5). A transbronchial lung biopsy and bronchoalveolar lavage revealed focal lymphocytic infiltration and an increased ratio of $CD4^+/CD8^+$ lymphocytes at 6.49 in the lavage fluid.

After the patient was discharged, the pain in her left hip joint later worsened. On October 25, 1999, she underwent a left total hip replacement at another hospital. A synovium specimen from the left hip joint showed marked hypertrophy covered by hyperplastic synovial cells with little inflammatory cell infiltration. These findings did not indicate any specific joint disorders.

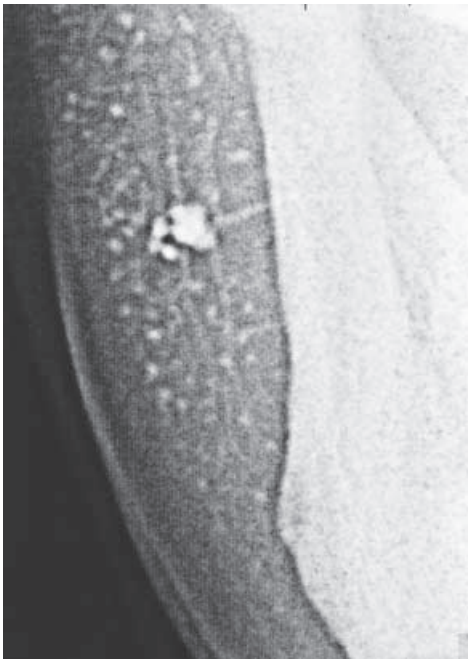

Fig. 3. Sialography showing an abnormal pooling with an apple tree-like pattern in the right parotid gland

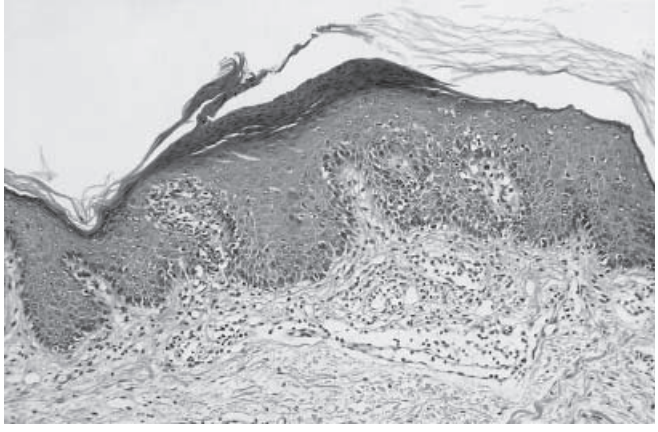

Fig. 4. Histology of a skin biopsy specimen from the right upper arm lesion (HE stain, ×125). The epidermis shows mild elongation of the rete ridges, mild papillomatosis, and moderate parakeratosis. There is hypogranulosis and a mild thinning of the suprapapillary plate. The capillaries in the upper dermis are dilated with perivascular edema and mild lymphocytic infiltration

Discussion

We have reported a case of primary SS with SA and PV. The coexistence of SS and SA,[6,7] SS and PV,[8] and SA and PV[9] have all been reported previously. To the best of our knowledge, this is the first report of the coexistence of SS, SA, and PV.

SA is a chronic multisystem disease of unknown etiology characterized by noncaseating granulomatous inflamma-

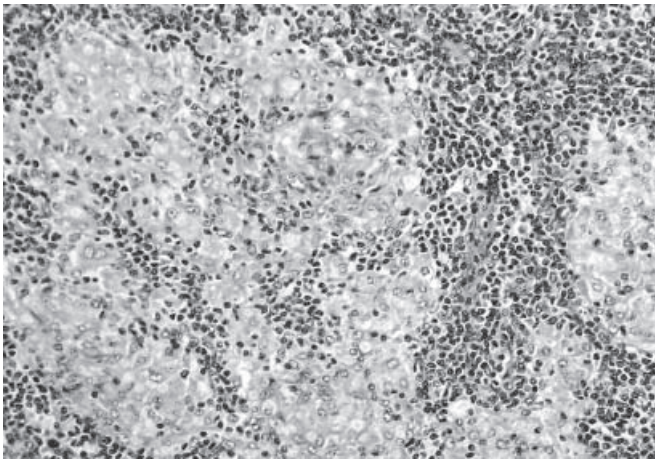

Fig. 5. Histology of the left axillary lymph node showing noncaseating granuloma formation (HE stain, ×250)

tion. This can occasionally affect the exocrine glands, causing parotid gland enlargement with dry eyes and mouth, which is similar to the symptoms of primary SS. The early involvement of labial salivary glands by SA, before the development of classical epithelioid granuloma, may result in lymphocytic infiltrates that are very similar to those seen in SS.[10] In addition, the pulmonary manifestations of SS may resemble those of SA.[11] Nonspecific infiltrations by mononuclear cells and fibrosis in the liver, lymph node, and pancreas have often been reported in primary SS and give it the features of multisystem diseases.[12] Therefore, the coexistence of SS and SA should be carefully distinguished from SA presenting with the clinical and histological features of SS, and SS showing similar clinical features to SA.

In our case, the clinical diagnosis of primary SS was supported by the typical salivary symptoms, the biochemical indices, including elevated ESR and gamma globulin values, and the positive anti-SS-A antibody test. A positive Schirmer's test and the apple-tree-like pattern seen on sialography further strengthened the diagnosis of SS. The diagnosis of SA was made based on the observation of bilateral hilar lymph node enlargement, noncaseating granulomas in an axillary lymph node biopsy, and an increased ratio of $CD4^+/CD8^+$ lymphocytes of 6.49 in the bronchoalveolar lavage fluid. This diagnosis was also supported by the increased angiotensin-converting enzyme concentration. In addition, the diagnosis of PV was made from the presence of hyperkeratotic erythema plaque on the face, chest, and upper extremities, and the findings of a skin biopsy from an upper arm lesion.

SS, SA, and PV are chronic diseases of unknown etiology. Recent studies suggest that activated T cells and the cytokines that they produce play a central role in their pathogenesis.[1–5] Immunohistochemical studies have demonstrated that the majority of infiltrating lymphocytes in the lesions of SS, SA, and PV are $CD4^+$ T cells,[1,3,5] and a clonotype analysis of infiltrating T cells suggested that some proliferate by an antigen-driven mechanism.[2,13,14] SS, SA, and PV are reported to exhibit a Th1-like cytokine secretion profile.[15–17] One can reasonably assume that disease entities with similar immunologic disturbances might coexist more frequently than would be expected by chance alone. However, the reported coexistence of these three diseases is extremely rare.

Although activated T cells might play an important role in the development and persistence of lesions in SS, SA, and PV, all have their own organ specificities and also show unique histological features. B cell activation is the most consistent immunoregulatory abnormality in SS. B lymphocytes in the salivary glands produce increased amounts of immunoglobulins with autoantibody activity, including RF,[18] anti-Ro/SS-A, and anti-La/SS-B.[19] An expansion of one or more B cell clones within the salivary gland specimens of SS patients has been demonstrated by both Southern blot and PCR methods.[20,21] SA is histologically characterized by the presence of noncaseating granulomas that are composed of tightly packed cells derived from the mononuclear phagocyte system. PV is characterized by a keratinocyte hyperproliferation with hyper- and parakeratotic differentiation. Although SS, SA, and PV may all have similar immunopathogenic mechanisms, in which T cells play a central role, the extremely rare coexistence of SS, SA, and PV prompts us to consider that distinct etiological mechanisms are also involved in triggering and developing each disease. It is also possible that the aberrant natures of cells other than T cells are involved in the pathogenesis of these diseases, and such cells include salivary epithelial cells in SS, macrophages in SA, and keratinocytes in PV.

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