Aplastic Anemia Complicating Sjögren's Syndrome

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A 47-year-old woman was referred to our hospital because of severe anemia and polyclonal gammopathy. She developed sicca syndrome after admission. Laboratory data revealed pancytopenia (white blood cells, 2,800/ μ l; hemoglobin, 6.4 g/dl; platelets, 6.1×10^4 / μ l) and hyper γ globulinemia (5.2 g/dl), and bone marrow was hypoplastic. Histology of the salivary gland showed infiltration of lymphocytes. We report a good response to immunosuppressive therapy in a rare case of aplastic anemia complicating Sjögren's syndrome.

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Introduction

Sjögren's syndrome (SjS) is an autoimmune disorder characterized by lymphocytic infiltration of the salivary and lacrimal glands (1). It has been suggested that immunological abnormalities in this syndrome may cause various hematological disorders. However, the association of aplastic anemia with SjS has only rarely been reported (2–4), and the pathogenesis of such anemia is obscure. This report describes a patient with aplastic anemia complicating SjS.

Case Report

A 47-year-old woman developed gingival bleeding in January 1995. After 4 months, she consulted her local doctor because of fatigue and exertional dyspnea. In June 1995, she was referred to our hospital because of severe anemia and polyclonal gammopathy. On admission, she was pale and had gingival bleeding, purpura in both legs, and erosions and vesicles in the mouth. However, there was no organomegaly, lymphadenopathy, or joint deformity. She developed sicca symptoms after admission. The initial laboratory findings are shown in Table 1. Pancytopenia, polyclonal gammopathy with elevated serum levels of IgG, IgA and IgM were found. Antibodies to nuclear antigen and SS-A were positive and rheumatoid factor was positive with a high titer, but other antibodies were negative. Bone marrow aspiration and biopsy showed a hypoplastic marrow with a nucleated cell count of 15,000/ μ l and no proliferation of blasts or plasma cells. There were no dysplastic changes in myeloid, erythroid, or megakaryocytic

lineages (Fig. 1).

A diagnosis of aplastic anemia was made on the basis of pancytopenia with hypoplastic marrow. Ophthalmological examination revealed diminished tear secretion by Schirmer's test (right, 4 mm; left, 4 mm). Salivary gland histology revealed interlobular and intralobular infiltration of mononuclear cells (Fig. 2). A diagnosis of SjS was made due to the absence of other collagen diseases. After admission, the platelet and neutrophil counts decreased gradually. On the 24th hospital day, prednisolone therapy (30 mg/day) was started. Her hematological status then improved gradually and her sicca symptoms also improved. On the 56th hospital day, she was given high dose methylprednisolone (1,000 mg/day $\times$ 3 days) because of the response to prednisolone. After this therapy, her hematological status further improved with a white blood cell count of 3,000/ μ l (49.0% neutrophils), a hemoglobin of 8.8 g/dl, and a platelet count of 11.1×10^4 / μ l. The dose of prednisolone was subsequently decreased with continued good hematological control and hyper γ globulinemia was improved (Fig. 3).

Discussion

The association of aplastic anemia with autoimmune diseases such as systemic lupus erythematosus (SLE) has been reported (5–7), but SjS is rarely associated with aplastic anemia (2–4). SjS is characterized by an increased risk of non-Hodgkin's lymphoma. The cause is unknown, but it is speculated that the chronic immunologic hyperactivity leads to proliferation of abnormal lymphocytes (8, 9). The hypothesis that aplastic anemia might be caused by autoimmune mechanisms is based

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Table 1. Laboratory Data on Admission

Hematology		Immunological examination	
Red blood cell	267×10 ⁴ /μl	IgA	2,959 mg/dl
Hemoglobin	6.4 g/dl	IgM	444 mg/dl
Hematocrit	22.8%	IgG	4,831 mg/dl
Platelet	6.1×10 ⁴ /μl	C3	108 mg/dl
White blood cell	2,800/μl	C4	81 mg/dl
Blast	0%	Rheumatoid factor	6,286 IU/ml
Promyelocyte	0%	LE test	(-)
Myelocyte	0%	Anti-nuclear antibody	(+)
Metamyelocyte	0%		diffuse type
Neutrophil	40.0%	Anti-DNA antibody	ds (-)
Basophil	0%		ss (-)
Eosinophil	0%	Anti-SS-A antibody	(+)
Lymphocyte	47.0%	Anti-SS-B antibody	(-)
Monocyte	12%	Anti-RNP antibody	(-)
Reticulocyte	0.86%	Anti-smooth muscle antibody	(-)
Blood chemistry		Anti-mitochondrial antibody	(-)
Aspartate aminotransferase	48 U/l	Bone marrow aspiration	
Alanine aminotransferase	38 U/l	NCC	15,000/μl
Lactate dehydrogenase	313 U/l	Megakaryocyte	0/μl
Alkaline phosphatase	170 U/l	Erythroid	1.6%
γ-glutamyl transpeptidase	30 U/l	Myeloid	
Total bilirubin	0.5 mg/dl	Myeloblast	2.0%
Cholinesterase	2,263 U/l	Promyelocyte	0.4%
Blood urea nitrogen	16 mg/dl	Myelocyte	3.6%
Creatinine	0.5 mg/dl	Metamyelocyte	3.2%
Creatine phosphokinase	23 U/l	Band neutrophil	25.6%
Total protein	9.8 g/dl	Segmented neutrophil	15.6%
Albumin	36.1%	Eosinophil	0.0%
α ₁ globulin	1.7%	Basophil	0.0%
α ₂ globulin	3.7%	Monocyte	6.8%
β globulin	5.1%	Lymphoid	
γ globulin	53.4%	Lymphocyte	39.6%
Fe	78 μg/dl	Plasma cell	0.0%
TIBC	229 μg/dl		
UIBC	151 μg/dl		
Ferritin	37.5 ng/ml		
C-reactive protein	0.30 mg/dl		
Erythrocyte sedimentation rate	160 mm/h		

on a numerous observations, including the response to immunosuppressive therapy (10–13). A patient who had aplastic anemia complicating SLE was reported to recover following treatment with steroids and plasmapheresis (6), while immunoglobulin obtained from the patient's serum suppressed the in vitro growth of granulocyte-macrophage progenitor cells (CFU-GM). Therefore, aplastic anemia associated with SLE is considered to develop because of circulating auto-antibodies (5, 7). In the case of aplastic anemia complicating SjS, Satoh et al reported that colony formation by mononuclear cells from the patient's bone marrow was decreased, but improved significantly when T cells were depleted from the culture system (3).

These findings suggest that one cause of pancytopenia in SjS is immune mechanisms, especially bone marrow-suppressive T cells. Among the four patients we were able to find with

concurrent SjS and aplastic anemia, both conditions were diagnosed simultaneously in one patient (4). In the remaining three patients, SjS occurred first, with sicca symptoms being observed from two to nine years before the onset of aplastic anemia (2, 3, 14). In the present patient, sicca symptoms appeared after hyper γ globulinemia and pancytopenia. There is no doubt that the autoimmune disorder causing SjS was related to the onset of aplastic anemia. The seriousness of aplastic anemia in the four patients ranged from severe to mild and it was categorized as mild in the present case. Thus, these does not seem to be a consistent trend with regard to the severity of aplastic anemia complicating SjS. With regard to the prognosis of concurrent SjS and aplastic anemia, a good hematological recovery was observed in the three patients with severe anemia when they received immunosuppressive therapy

Figure 1. Microscopic appearance of the bone marrow (HE stain, ×400). There is mild hypocellularity without proliferation of blasts or dysplastic change.

Figure 2. Microscopic appearance of the salivary gland (HE stain, ×100). Lymphocytes show interlobular and intralobular infiltration of the small salivary glands, which feature periductal fibrosis and ductal ectasia. These findings indicate moderate chronic sialoadenitis and are compatible with Sjögren's syndrome.

Figure 3. Clinical course.

using prednisolone. In the present patient, prednisolone and high-dose methylprednisolone improved both her sicca symptoms and her hematological status. Since the etiology of aplastic anemia is still unclear, further studies are needed to clarify the true incidence and its association with autoimmune disease.

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