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Correlation Between Blood System Impairment and Immune Index in Patients with Primary Sjögren's Syndrome

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Abstract: Objective: To analyze the relationship between blood system impairment and immune indexes, including autoantibody, immunoglobulin and lip gland biopsy in patients with primary Sjogren's syndrome (pSS). Methods: The serological data of patients with Sjogren's syndrome in hospital were collected and divided into hematological system impairment group and normal group. The incidence of hematological system damage in patients with pSS and its correlation with immune indexes were analyzed. Results: 123 patients with pSS were included in this study. There were 57 patients in the blood system involvement group (46%), in which the proportions of leucopenia, anemia and thrombocytopenia were in turn; 17. 89%; 33. 3%; 4. 88%. The antibodies in the blood system affected group were abundant, and the positive rates of anti SSA and Ro-52 antibodies were significantly higher than those in the normal group. The increase of serum IgG in pSS patients accounted for nearly 50%; The levels of serum IgG and complement C3 were significantly different from those in the control group. The positive rate of lip gland biopsy in pSS patients was more than 90%, and there was no significant difference between the two groups.

Conclusion: Hematological system involvement was common in PSS patients. The positive rates of anti SSA and Ro-52 antibodies increased significantly, the level of IgG increased and the level of complement C3 decreased; However, there was no significant difference in blood system involvement between high IgG and low IgG groups; The positive rate of lip gland biopsy in PSS patients was more than 90%.

Keywords: Sjogren's Syndrome; Hematological System; Immunoglobulin; Labial Gland Biopsy

Introduction

Primary Sjogren's syndrome (pSS) is a chronic autoimmune disease invading exocrine glands, mainly involving salivary glands and lacrimal glands, with focal lymphocyte infiltration as pathological characteristics, clinical manifestations of dry keratoconjunctivitis, oral dryness, can also involve many other organs, such as skin, skeletal muscle, kidney, lung, nervous system and blood system, etc. Epidemiology suggests an increasing prevalence of 0. 33% -0. 77%, and the prevalence of the disease is about 1:9-1:20[1], the age of onset is 40-50 years at most. Hematological manifestations in pSS patients include hemopenia, hypergammaglobulinemia, monoclonal gammaglobulinopathy, cryoglobulinemia and lymphoma, with hemocytopenia most common and can present as leukopenia, anemia, thrombocytopenia, primary or multilineage injury. At present, the pathogenesis of this disease is unknown, and hyperglobulinemia is very prominent in the disease of Sjogren's syndrome, especially the elevated IgG is mainly[2]. In this paper, the serological characteristics of pSS patients are further investigated for the correlation of hematological involvement and immune indicators.

1. Data and methods

1.1 Object

The selected cases were primary Sjogren's syndrome patients admitted to our hospital at 2018. 1-2021. 12, who all met

the 2002 International Classification of Sjogren's syndrome (diagnosis) standard[3], with a total of 123 cases. Patients with other connective tissue diseases, iron deficiency anemia, and tumors were excluded. Abnormal hematology criteria: ① leukocyte count <3. 5 * 10 ^ 9 / L; ② anaemia: male Hb <130g / L, female Hb <115g / L; ③ thrombocytopenia: Platelet count <125 * 10 ^ 9 / L.

1.2 Method

Clinical data of pSS patients, including sex, age, disease duration, laboratory indicators (including blood routine, humoral immunity, autoantibodies: anti-SSA, anti-SSB, anti-RO-52, anti-CENP-B antibody), and labial gland biopsy; selected cases were grouped according to hematological involvement.

2. Statistical treatment

Statistical analysis was performed using the SPSS 23. 0 software. Relevant data were tested for normality test, with mean ± standard deviation, t-test, mean comparison; non-normal measurement data (quartile P25-P75), Mann-Whitney U test, count data, 2 test, correlation with P <0. 05.

General: Among the pSS patients, 15 men, 108 women, 21-83 years, average age (49.85 ± 15.72). Blood system damage: 57 patients occurred in this study, accounting for 46. 34%; leukopenia, anemia, and thrombocytopenia; 17.89%; 33.3%; 4.88%. ① single blood system: 12 leukopenia, 9.76%; 33 anemia, 26.83%; 3 thrombocytopenia, 2.44%; ② 2 blood system: 7 leukopenia + anemia, 5.69%; 2 leukopenia + thrombocytopenia, 1.63%; 1 ③ blood triad, 0.81%.

Table 1 of Autoantibodies and Humoral Immunity between the two groups based on the hematological involvement

Observational indicators	Hematological normal group（n=66）	Hematological impairment group（n=57）	P value
anti-SSA	39（59.1%）	46（80.7%）	0.01＊
anti-Ro-52	38（57.6%）	44（77.2%）	0.021＊
anti-SSB	19（28.8%）	20（35.1%）	0.454
anti-CENP-B	5（7.6%）	6（10.5%）	0.567
IgG	16. 2（13.63; 19.65）	17. 7（15.4; 22.95）	0.02＊
IgA	3. 31（2.41; 3.9）	3. 4（2.42; 4.52）	0.436
IgM	1. 19（0.77; 1.72）	1. 1（0. 72; 1.67）	0.587
Complement C3	1. 04（0.93; 1.17）	0. 96（0.84; 1.11）	0.017＊
Complement C4	0. 2（0.18; 0.24）	0. 2（0.15; 0.27）	0.58

2. 1 Correlation analysis

Through statistical analysis, the correlation coefficient of blood system involvement and autoantibody SSA was 0.213, and the P-value was 0.018;

The correlation coefficient of anti-Ro-52 antibody was 0.208, P value 0.021, IgG correlation coefficient 0.224, and P value 0.013;

Complement C3 correlation coefficient was 0. 217; the P-value was 0.016.

In conclusion, the autoantibodies SSA, Ro-52 antibody, IgG and complement C3 were correlated.

2. 2 Lip gland biopsy results

A total of 45 lip biopsy in the group, including 41 or 91.1%, 59 in the normal group, 57 with 1 or more lymphocyte lesions, accounting for 96.6%; the positive rate was more than 90%, no significant difference between the two groups.

3. Discussion

Primary Sjogren's syndrome is a common autoimmune disease whose pathogenesis is currently believed to be the result

of multiple factors, including heredity, viral infection, and sex hormones. In addition to the damaging symptoms of exocrine glands such as dry mouth and dry eyes, pSS patients can also show extramandular damage of the blood system and nervous system. Blood system damage to blood triad decline is the most common, Nishishinya research found that repeated parotid gland enlargement, lymph node enlargement, lymphopenia, low complement C4 and hyperglobulinemia is an important predictor of lymphoma [4], the study mainly for analysis, identify system damage in patients with Sjogren's syndrome, early interventional therapy.

Blood system damage in Sjogren's syndrome can involve white blood cells, red blood cells, and platelets, and show a single or multilineage decline. The pathogenesis of blood system damage may be related to the destruction of blood cells by multiple autoantibodies or immune complexes produced by B cells in peripheral blood. Multiple autoantibodies can be detected in the serum of pSS patients, and studies have shown that SSA antibodies on the surface of blood cells can induce autoantibody formation against this cell, causing cytolytic[6] through an antibody-mediated complement-dependent pathway. This study also found that the positive rate of anti-SSA and Ro-52 antibodies was higher in the blood involvement group, which was consistent with previous studies;

The complement system can exert its biological effects through the classical pathway, bypass pathway and lectin pathway, and the damage of the target organs can occur when the complement inappropriately recognizes and attacks its own tissues. Complement plays an important role in autoimmune diseases. Previous studies have found that some gene variants encoding complement are related to the occurrence of systemic lupus erythematosus, leading to the deposition of circulating immune complexes, and clinically found decreased complement levels in SLE patients. In the study of Sjogren's syndrome, the complement C3 levels in the affected patients were lower than those in the normal group, considering the involvement of complement-mediated cytotoxic effects in the destruction of blood cells.

Through research, Zhang Youli et al found that pSS patients can be combined with various hematological abnormalities, including anemia 51%, leukopenia 25%, thrombocytopenia 23% and pancytopenia 7.7% [7]. This study suggests that anemia was the most common in the incidence of haematological abnormalities, consistent with previous studies. The mechanism of anemia in pSS patients is currently unknown, the most common are immune-mediated chronic anemia, and secondary anemia, including hemolytic anemia, iron deficiency anemia, mostly mild anemia.

In this study, leukocyte decline accounted for 17. 89%, and some patients took leukopenia as the first symptom, leading to misdiagnosis. Some scholars have shown that the bone marrow hematopoiesis of pSS patients is basically normal, and the reduction of leukocytes may be related to the destruction of autoantibodies and the reduced transfer to the peripheral pool in [8]. Anti-M3R autoantibodies were found to induce downregulation of plasma membrane-resident M3R and M H C class I molecules in leukocytes, and NK cells mediate leukocyte apoptosis of [9]. Combined with previous studies on the association of leukopenia and the occurrence of lymphoma, some attention should be paid.

Studies have found that the prevalence of thrombocytopenia in pSS patients is 5% -13%, which can occur at any period during the course of the disease, either alone, or combined with leukopenia, anemia and other conditions[10]. Severe thrombocytopenia is less common in pSS patients, where antiplatelet antibodies are important antibodies causing platelet destruction, which can directly bind to bone marrow megakaryocytes, and affect their growth and maturation, leading to megakaryocyte maturation and platelet production disorders [11]. This study found that the incidence of thrombocytopenia was low, and the sample size was considered small, with some experimental error.

Lipial gland biopsy is a means of examination for the diagnosis of Sjogren's syndrome, mainly for lymphocyte infiltration of labial gland tissue. In this study, most patients completed labial gland biopsy, and the positive rate accounted for more than 90%, which is more consistent with clinical cognition.

Through a retrospective study of SS patients with hyperglobulin, Sun Yu found that the hyperglobulin group was more prone to blood systemic involvement, accounting for 41. 7%, among which anemia was more common in [12] than leukocytopenia and thrombocytopenia. Among the people included in this study, 61 cases had high IgG, accounting for 49. 6%, indicating that hyperglobulinemia is very common in clinical work. The EULAR Sjogren's syndrome activity index, widely used in the clinic, has scoring criteria for only one laboratory class containing hyperimmunoglobulinemia, monoclonal components and hypocomplemenemia, and another 11 classes related to [13] with organ involvement.

In conclusion, it is not uncommon in patients with pSS, associated with anti-SSA, RO-52 antibodies in autoantibodies, and associated with IgG and complement C3.

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