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ORIGINAL PAPER

Clinical and serological correlates of anti-Sm autoantibodies in Chinese patients with systemic lupus erythematosus: 1,584 cases

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Abstract To investigate the association of anti-Sm antibodies with clinical and serological features in systemic lupus erythematosus. A group of 1,584 patients with SLE was recruited. Clinical and laboratory data were compared between patients with and without anti-Sm antibodies. There were 1,424 females and 160 males, the mean age of the patients was 33.2 ± 12.3 years, and the mean duration of disease was 32.5 ± 59.4 months. A total of 469 (29.6%) were anti-Sm antibodies positive. The presence of anti-Sm antibodies was associated with arthritis, renal involvement, malar rash, vasculitis and low serum complement C3. The positive rate of anti-nuclear, anti-dsDNA, anti-La/SSB and anti-U1RNP antibodies were significant higher in anti-Sm positive group when compared with anti-Sm negative group. A trend towards a higher presence of anti-Sm antibodies related to an early disease onset was observed. In conclusion, Anti-Sm antibodies are associated with lupus related clinical and laboratory profiles and correlated significantly with disease activity.

Keywords Anti-Sm · Autoantibodies · China · Clinical feature · Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multisystemic involvement with a broad spectrum of clinical manifestations. The pathogenesis and etiology are unknown certainly, but the loss of tolerance to self chromatin and the presence of specific autoantibodies are recognized to be one of its prominent features, some good examples are the detection of antinuclear antibodies (ANA), anti-Sm, anti double-stranded DNA (dsDNA) and anti-cardiolipin (aCL) autoantibodies in SLE [1, 2]. Anti-Sm antibodies are well documented to be the most specific to patients with SLE and are considered one of the American College for Rheumatology (ACR) criteria for the classification of SLE [1, 2]. Previous data show a highly variable prevalence ranging from 15 to 55.5% [3–8]. Some studies have suggested an association between anti-Sm antibodies with some particular disease manifestations, such as lupus nephritis [9, 10]. However, other authors failed to find the correlations with disease manifestations [4, 11]. The possible association between anti-Sm antibodies and the disease activity of SLE has only been analyzed in a few work, the results are also controversial [4, 11]. The ethnic origin of the patients may partly explain these conflicting results, including the wide range of Anti-Sm frequencies among SLE patients from different population. In addition, in some investigations, the low number of enrolled patients did not permit reliable conclusion. Conflicting results have also been reported on the presence of anti-Sm antibodies in the sex variant of SLE [8, 10], as well as in early onset patients [12, 13].

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In the present study, 1,584 patients with SLE were recruited from the Departments of Rheumatology at Anhui Provincial Hospital and at the First Affiliated Hospital to Anhui Medical University. SLE was diagnosed by the presence of four or more ACR diagnostic criteria (1982), revised in 1997 [1, 2]. All patients were divided into two groups: anti-Sm positive group and anti-Sm negative group. Clinical and laboratory data were collected from hospital records or by questionnaire and were reviewed by experienced physicians. Individual disease activity was quantified using the SLE disease activity index (SLEDAI) score. More active lupus was defined as a SLEDAI score $\geq$10, those patients with SLEDAI <10 were classed as inactive.

Antibodies to Sm, U1-RNP, Ro/SSA, La/SSB cellular antigens and ANAs were tested by indirect immunofluorescence, dsDNA (by enzyme-linked immunosorbent assay; ELISA). Other laboratory abnormalities was also recorded, mainly including leukopenia (white blood cell count <4,000/mm^3) and thrombocytopenia (platelet count <100,000/mm^3); or the occurrence of proteinuria, elevated erythrocyte sedimentation rate (ESR) (Male: >15 mm/h; Female: >20 mm/h), or complement reduction (by immunoturbidimetry; ITM). The reliability of these tests was improved by duplicate determinations for each sample.

All data were analyzed using SPSS 10.01 software (SPSS Inc., 2000). For comparing the mean values between different groups, the Student's *t* test was used. The Chi-square test or Fisher's exact test was used to assess differences in clinical and serological data between different groups. For the correlation between anti-Sm antibodies with age and disease duration, univariate logistic analysis was performed. Probability level less than 0.05 in two-tailed test were used as a criterion of significance.

Among the 1,584 SLE patients, there were 1,424 (89.9%) females and 160 (10.1%) males; the female-to-male ratio was 8.9:1. The mean age of the patients was 33.2 $\pm$ 12.3 years, range 5–80 years. The mean duration of the disease was 32.5 $\pm$ 59.4 months, range 0–723.6 months. A total of 469 (29.6%) were anti-Sm antibodies positive, 1,115 (70.4%) were negative.

The positive rate of anti-Sm antibodies were slight higher in female than in male (30.1 vs. 25.0%), but the difference did not reach significant level ($P > 0.05$). The mean age at investigation of the patients with anti-Sm antibodies was 29.9 $\pm$ 9.9 years, which was significantly younger than the patients without anti-Sm antibodies 34.6 $\pm$ 12.9 years ($P < 0.001$). The mean age at onset was also significant difference between two groups (27.9 $\pm$ 9.5 vs. 31.8 $\pm$ 12.5, $P < 0.001$). The disease duration was shorter in positive anti-Sm patients than in negative patients (26.5 $\pm$ 48.4 vs. 35.0 $\pm$ 63.3 months, $P < 0.01$). Through univariate logistic analysis, both age and disease duration showed adverse correlation with anti-Sm antibodies positive rate (OR = 1.036, 95% CI: 1.025–1.046, $P < 0.001$; OR = 1.003, 95% CI: 1.001–1.005, $P < 0.05$).

The clinical features in patients positive and negative for anti-Sm antibodies are summarized in Table 1. The prevalence of arthritis (66.1%), renal involvement (63.1%), malar rash (57.6%) and vasculitis (13.7%) in SLE patient with positive anti-Sm antibodies was higher than those in SLE patients with negative anti-Sm antibodies (60.7, 54.62, 47.7 and 7.4%, respectively, $P < 0.05$). There was no significant difference between the two groups in other clinical features including fever, photosensitivity, discoid rash, alopecia, oral ulcers, serositis, pleuritis, pericarditis, myositis and central nervous system involvement ($P > 0.05$, Table 1).

Low serum complement C3 was significantly more frequent in the patients positive for anti-Sm antibodies than in those negative for the antibodies (67.9 vs. 58. 5%, $P < 0.05$). There was no significant difference in leukopenia, thrombocytopenia, proteinuria and ESR between the two groups ($P > 0.05$, Table 2).

The immunological profile differed between the groups. The frequency of anti-nuclear (91.3%), anti-dsDNA (46.0%), anti-La/SSB (18.7%) and anti- U1RNP (29.2%) antibodies were significant higher in anti-Sm positive SLE patients than in the negative anti-Sm antibodies patients (77.3, 38.2, 13.3 and 8.6%; $P < 0.05$). However, the positive rate of anti-Ro/SSA antibodies has no significant difference between the two groups (30.4 vs. 32.4%, $P > 0.05$; Table 2).

According to SLEDAI score, the mean score in patient with positive anti-Sm was higher than patients negative for

Table 1 SLE common clinical present in the patients subdivided according to the presence or absence of serum anti-Sm antibodies

Clinical features	Anti-Sm positive (%)	Anti-Sm negative (%)	χ^2	*P* value
Arthritis	66.1	60.7	4.07	0.044
Renal involvement	63.1	54.6	9.73	0.002
Fever	61.6	58.2	1.60	0.205
Malar rash	57.6	47.7	12.83	<0.001
Alopecia	25.1	20.6	3.68	0.055
Photosensitivity	16.8	14.1	1.97	0.161
Serositis	17.3	15.5	0.74	0.389
Oral ulcers	14.3	12.9	0.54	0.464
Pleuritis	9.4	10.3	0.32	0.573
Pericarditis	12.2	9.2	3.09	0.079
Vasculitis	13.7	7.4	15.28	<0.001
CNS involvement	3.9	3.2	0.57	0.452
Discoid rash	5.3	5.1	0.03	0.858
Myositis	6.1	5.1	0.72	0.398

Table 2 The correlation between anti-Sm antibodies and other laboratory parameters in SLE

Laboratory features	Anti-Sm positive (%)	Anti-Sm negative (%)	χ^2	*P* values
Thrombocytopenia	37.1	40.8	1.93	0.165
Leukopenia	37.5	40.1	0.93	0.334
Low C_3	67.9	58.5	10.47	0.001
Proteinuria	68. 5	64.0	2.90	0.088
Elevated ESR	83.6	82.5	0.24	0.624
ANA	91.3	77.3	53.38	<0.001
Anti-dsDNA	46.0	38.2	8.07	0.004
Anti-Ro/SSA	30.4	32.4	0.55	0.457
Anti-La/SSB	18.7	13.3	6.99	0.008
Anti-U1RNP	29.2	8.6	67.54	<0.001

anti-Sm antibodies (13.9 ± 8.2 vs. 11.7 ± 7.4, $P < 0.001$). Patients with anti-Sm antibodies were more likely to present active disease (64.5%) than patients without the antibodies (58.7%, $P < 0.05$).

Anti-Sm antibodies are specific to patients with SLE and are considered one of the diagnostic criteria for this disease according to ACR guidelines. The present study is an analysis of the prevalence of anti-Sm and their clinicoserologic relationship in Chinese patients with SLE. The prevalence of anti-Sm antibodies of 29.6% was detected in our study is in accordance with data from African American patients (27.2%) [3], Singaporean (26%) [4], Indians (25.3%) [5]. But considerably lower than those from black South Africans patients (44.2%) [6] and Tunisians (55.5%) [7], higher than that reported from Malaysian patients (15%) [8]. Racial differences in prevalence of anti-Sm antibodies may be related to genetic and environmental factors. Another possible reason for the discrepancies may be attributed to different laboratory methods [14].

Our data shows that the female to male ratio was 8.9:1, confirming the well-known fact of a female predominance of SLE. It is well documented that sex hormone play an important role in SLE development. However, whether and how the hormonal factors affected the production of autoantibodies were not certainly [13, 15]. Previous studies showed significant gender differences in the prevalence of anti-Sm antibodies [11]. We observed a slight higher positive rate of anti-Sm antibodies in females than males, but the difference did not reach statistical significant.

It has been shown that age was an influential factor for autoantibodies profiles in SLE patients. Similarly to previous study [12, 16], our study showed that anti-Sm antibodies more frequently presented in younger patients and at early stage of disease. In addition, anti-Sm antibodies were more likely coexist with other key autoantibodies in SLE, such as ANA, anti-dsDNA. It confirmed that anti-Sm antibody was an important serologic parameter in the diagnosis of SLE.

The association between the clinical and serological features with autoantibodies including anti-Sm has been widely studied in different population. However, the conclusions were not consistent [4, 6, 7, 9, 11]. Alba et al. [9] reported that anti-Sm antibodies were significantly related to renal involvement. Tikly et al. [6] revealed positive clinicoserological associations between anti-Sm antibodies with psychosis. Ghedira et al. [7] showed that anti-Sm antibody was associated with serositis. Boey et al. [4] reported that SLE patients with anti-Sm antibodies were more likely to have active disease, but there was no increased prevalence or specific type of autoantibody in those with renal manifestations. However, some report that anti-Sm antibodies were not related with disease activity [17]. In our patients, anti-Sm antibodies were significantly associated with disease activity and certain clinical and laboratory presentations, such as arthritis, renal involvement, malar rash and low C3, etc. These variations may be influenced by the following factors, such as genetic differences, the lack of standardization of laboratory methods and the low sample size.

Some clinical manifestations, such as arthritis, malar rash and renal involvement more likely presented as the initial symptoms in SLE [18, 19]. Anti-Sm antibodies were associated with those clinical features in our patients. Together with the relationship of anti-Sm antibodies with age or disease duration, we supposed that anti-Sm antibodies are more likely produced in younger patients with SLE and at early stage of disease. Further longitudinal studies are still needed to confirm this point.

In conclusion, anti-Sm antibodies are associated with lupus related clinical and laboratory profiles. In addition, the presence of Sm may serve as a useful marker for early onset lupus and assessment of the disease activity of SLE.

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