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Association of Anti-Smith Antibody with Clinical Manifestations in Patients with Disseminated Systemic Lupus Erythematosus

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Abstract

Introduction: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune rheumatic disease of unknown etiology interceded by auto antibodies and immune complexes that cause systemic cell and organ damages. This study aimed to evaluate the association between Anti-Smith Antibody (anti-SM ab) and clinical manifestations in patients with disseminated systemic lupus erythematosus.

Method: In this cross-sectional study, 72 females with SLE included. Activity disease in patients was assessed by using the University of Toronto SLE Disease Activity Index (SLE-DAI). Serum level of anti-SM ab was measured and clinical manifestations were extracted from patient`s medical records.

Results: Six out of 72 patients (8.3%) were anti-Sm positive. Among the patients with anti-Sm positive, the majority of clinical manifestations were observed in one or two patients, except for both mucocutaneous involvement and Lupus nephritis that these were positive in four patients (66.7%). There was no significant association between the anti-SM ab and any clinical manifestations.

Conclusion: Due to the lower sample size patients with positive anti-Smith, the relationship between anti-Smith and clinical manifestations was not found.

Keywords: Anti-smith antibody; Clinical manifestations; Systemic lupus erythematosus

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Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune rheumatic disease of unknown etiology interceded by auto antibodies and immune complexes that cause systemic cell and organ damages. Auto antibodies in SLE are produced against intracellular targets; mostly Anti Nuclear Antibodies (ANAs) but there are less frequent antibodies, such as anti-double-stranded DNA (dsDNA), anti-Smith (anti-Sm), anti-Ro, and anti-La antibodies [1-3]. The prevalence and incidence of SLE vary by the population and the methodology used for diagnosis but studies revealed the incidence rates of 1 to 25 per 100,000 worldwide [4-7]. Also, the reported prevalence of SLE in the United States is 20 to 150 cases per 100,000 [7-9].

In fact, SLE can affect any organ and dramatically can vary from patient to patient. Clinical manifestations mostly are a mixture of constitutional complaints with dermal, musculoskeletal, hematologic, serologic, renal, or central nervous system [10,11]. The etiology of SLE is still unknown but it is most probably multifactorial. Many studies indicated the role of genetic [12-14], hormonal [15-18], immunologic [19-22], and environmental factors [23] in the pathogenesis of the disease. Due to the role of immune complexes in the pathogenesis of the disease, some of these antibodies are being considered laboratory findings to complete clinical criteria of SLE [24].

Anti-Sm antibodies target proteins of B/B0, D1, D2, D3, E, F, and G that form the common core of U1, U2, U4, and U5 small nuclear ribonucleoprotein particles [25,26]. The anti-Sm autoimmune response is directed against the B/B0, D1, D3, and less frequently D2 proteins. Less recognized proteins are the E, F and G proteins [27,28].

Some studies reported an association between clinical manifestations and anti-Sm ab (Anti-Smith antibody) presence in serum of patients [24] but it's still controversial. Due to the importance of anti-Sm ab in the pathophysiology of SLE, and the limited number of studies with controversial

results in Iran, here we aimed to evaluate the serum levels of anti-Sm ab and its association with selected clinical manifestations and prognosis of SLE.

Materials and Methods

This cross-sectional study was conducted in 72 Systemic Lupus Erythematous (SLE) female patients. The patients who referred to the rheumatology clinic of the University hospital between October 2018 and February 2019 were included. This study approved by the ethics committee of the Urmia University of Medical Sciences (UMSU) and written consent was obtained from patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Activity disease in patients was assessed by using the University of Toronto SLE Disease Activity Index (SLE-DAI). Demographic characteristics, clinical manifestations and history of lupus nephritis (proteinuria, biopsy, RBC cast), vasculitis, organic brain syndrome (acute confusion state), psychological symptoms (headache, mood disorder, cognitive impairment), Blood involvements (anemia, leukopenia, thrombocytopenia), mucocutaneous manifestations (oral ulcer, alopecia, malar rash), thromboembolic events (DVT/PTE), and serosal involvements or serositis (pericarditis, pleuritis) were extracted from patients' medical records.

For measuring the Serum level of anti-SM ab, Venous blood samples were collected after overnight fasting, allowed to clot at 15°C to 24°C and serum was isolated by centrifugation. Serum samples were preceded to chemical analyses or kept frozen until the assessments. Level of serum anti-Sm antibody was measured by an ELISA method as described by the manufacturer. Other laboratory findings including the levels of other antibodies were extracted from the patients' medical records.

Statistical analysis

All the values were summarized as frequency (percent) for categorical variables. Based on the Serum levels of anti-SM ab, patients were stratified into two groups (negative and positive). Clinical factors were compared between patients with anti-SM ab positive and negative using Fisher's exact test. P-value <0.05 was considered statistically significant.

Results

The results were summarized in Table 1. Six out of 72 patients (8.3%) were anti-Sm positive, but other 66 patients were anti-Sm negative (91.7%). Fatigue was observed in one patient (16.67) with positive anti-Smab and in 17 patients (25.8%) with negative anti-Sm ab. History of fever was reported in one patient (16.67) with positive anti-Sm ab and in seven patients (10.6%) of subjects with negative anti-Sm ab. None of the patients with positive anti-Sm ab had a history of weight loss, but five (7.6%) cases with significant weight loss were found in patients with negative anti-Sm ab. No history of gastrointestinal involvement was found in patients with a positive anti-smith antibody. But, eight patients with a negative anti-smith antibody (12.1%) had a history of gastrointestinal involvements. Serositis was only detected in one (16.7%) anti-Sm ab positive patient but nine patients with a negative anti-smith antibody (13.6%) had a history of serositis. No significant relationship was found between serositis and serum level of anti-Sm ab (P-value =0.6).

Cardiac involvements were found in two (33.3%) anti-Sm ab positive patients and in five (7.6%) patients with a negative anti-smith antibody. Lymphadenopathy was not detected in any of patients with positive anti-Sm ab, but in one patient with a negative anti-smith antibody (1.5%) had lymphadenopathy.

Table 1: Distribution of complications and anti-Sm antibody in SLE patients.

Complication		Anti-Smith antibody		
		Positive (%)	Negative (%)	P-value
Fatigue	+	1 (16.67)	17 (25.8)	0.53
	-	5 (83.33)	49 (74.2)	
Fever	+	1 (16.67)	7 (10.6)	0.53
	-	5 (83.33)	59 (89.4)	
Weight loss	+	0 (0)	5 (7.6)	0.63
	-	6 (100)	61 (92.4)	
Gastrointestinal involvement	+	0 (0)	8 (12.1)	0.48
	-	6 (100)	58 (87.9)	
Serositis	+	1 (16.67)	9 (13.6)	0.6
	-	5 (83.33)	57 (86.4)	
Cardiac involvement	+	2 (33.3)	5 (7.6)	0.1
	-	4 (66.7)	61 (92.4)	
Lymphadenopathy	+	0 (0)	1 (1.5)	0.9
	-	6 (100)	65 (98.5)	
Mucocutaneous involvement	+	4 (66.7)	46 (69.7)	0.6
	-	2 (33.3)	20 (30.3)	
Vasculitis	+	1 (16.67)	6 (9.1)	0.47
	-	5 (83.33)	60 (90.9)	
Organic brain syndrome	+	2 (33.3)	8 (12.1)	0.19
	-	4 (66.7)	58 (87.9)	
Psychosis	+	0 (0)	6 (9.1)	0.55
	-	6 (100)	60 (90.9)	
Thromboembolic events	+	3 (50)	10 (15.2)	0.06
	-	3 (50)	56 (84.8)	
Arthritis & Arthralgia	+	2 (33.33)	32 (48.5)	0.39
	-	4 (66.66)	34 (51.5)	
Blood involvement	+	2 (33.33)	32 (48.5)	0.42
	-	4 (66.66)	34 (51.5)	
Lupus nephritis	+	4 (66.66)	29 (43.9)	0.26
	-	2 (33.33)	37 (53.1)	
Anti-Smith antibody		6 (8.33)	66 (91.67)	

Among patients with positive anti-smith four patients had Mucocutaneous involvements (66.7%) and 2 of them had a negative anti-smith antibody (33.3%). 46 patients with a negative anti-smith antibody (69.7%) had skin and mucosal involvement, but 20 (30.3%) had no skin and mucosal involvement. Vasculitis was observed in one (16.7%) patient with positive anti-Sm ab and in six patients with negative anti-Sm ab (9.1%). Five cases with positive anti-Sm ab (83.3%) and 60 cases (90.9%) with negative anti-Sm ab had no sign of clinical vasculitis.

Two patients with positive anti-Sm ab (33.3%) and eight patients with negative anti-Sm ab (12.1%) had organic brain syndrome. This syndrome was not found in four patients with positive anti-Sm ab (66.67%) and 58 patients with a negative anti-Sm antibody.

Psychosis was not reported in patients with positive anti-Sm ab,

but in patients with negative anti-Sm ab, six patients had psychosis (9.1%) and 60 patients had not any sign or symptom of clinical psychosis (90.9%).

Three patients with positive anti-Sm ab (50%) and 10 patients with negative anti-Sm ab (15.2%) had thromboembolic events. Thromboembolic events were not detected in three patients of positive (50%) and 56 patients of negative anti-Sm ab (84.8%).

Out of the six patients with positive anti-Sm ab, two (33.3%) had arthritis and arthralgia. And among the rest, 32 cases (48.5%) had positive arthritis and arthralgia. In patients with positive anti-Sm ab, three (50%) had blood involvements and among the patients with negative anti-Sm ab, 25 (37.9%) had blood involvements. In patients with positive anti-Sm ab, 4 (66.7%) and in patients with negative anti-Sm ab, 29 (43.9%) had Lupus nephritis. there was no significant association between the anti-SM ab and any clinical manifestations (P-value >0.05).

Discussion

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune rheumatic disease of unclarified etiology inducted by auto antibodies and immune complexes that cause systemic damages [1-3]. It's more prevalent in females [29] and all of 72 patients in the current study were female. The role of anti-Sm antibody in induction, pathogenesis, and severity of disease is still controversial and to the best of our knowledge, this is the first comprehensive report for serum level of anti-smith antibody in Iranian females with SLE. We also investigated the relationship of serum anti-Smith (anti-Sm) antibody with common clinical manifestations of systemic lupus erythematosus. The significant association was not found between serum anti-smith antibody and history or presence of vasculitis, organic brain syndrome, psychosis, thromboembolic events, arthritis and arthralgia, blood involvement, lupus nephritis, and other clinical symptoms. However, Alba et al. found a relationship between anti-Sm ab and lupus nephritis [3]. The other study with smaller sample size showed that in SLE patients, the presence of anti-Sm antibody is associated with a much higher incidence of some clinical complications such as vasculitis and poor response to therapy [30]. Since the sample size of the current study is larger than two others, such controversies should result from other factors such as race or geographical factors. A study conducted at the University of Texas in the United States indicated that anti-Sm ab in black people was more positive than whites, with 25% positive results in black people than 10% in whites [31]. So, a multi-racial study should be conducted to clearly investigate the impacts of race and geographical differences in serum levels of anti-Sm ab (Table 1).

The methodological difference in measurement of anti-Sm ab is the other possible factor that may cause some controversial results. Hirohata S et al. [32] has reported that anti-Sm antibody increases in serum and CSF fluid of systemic lupus erythematosus patients. Therefore, assessment of anti-Sm antibody in CSF samples may yield higher sensitivity than serum samples.

Conclusion

Due to the lower sample size patients with positive anti-Smith, the relationship between anti-Smith and clinical manifestations was not found. Studies with more sample sizes are suggested to investigate the relationship between anti-Smith and clinical manifestations.

References

1. Alspaugh MA, Talal N, Tan EM. Differentiation and characterization of autoantibodies and their antigens in Sjögren's syndrome. Arthritis Rheum. 1976;19(2):216-22.
2. Swaak AJ, Huysen V, Nossent JC, Smeenk RJ. Antinuclear antibody profiles in relation to specific disease manifestations of systemic lupus erythematosus. Clin Rheumatol. 1990;9(Suppl 1):82-94.
3. Alba P, Bento L, Cuadrado MJ, Karim Y, Tungekar MF, Abbs I, et al. Anti-dsDNA, anti-Sm antibodies, and the lupus anticoagulant: significant factors associated with lupus nephritis. Ann Rheum Dis. 2003;62(6):556-60.
4. Peschken CA, Esdaile JM. Rheumatic diseases in North America's indigenous peoples. Semin Arthritis Rheum. 1999;28(6):368-91.
5. Wallace D. The clinical presentation of systemic lupus erythematosus. Dubois' lupus erythematosus. 2002.
6. Danchenko N, Satia JA, Anthony MS. Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. Lupus. 2006;15(5):308-18.
7. Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum. 2010;39(4):257-68.
8. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum. 1998;41(5):778-99.
9. Chakravarty EF, Bush TM, Manzi S, Clarke AE, Ward MM. Prevalence of adult systemic lupus erythematosus in California and Pennsylvania in 2000: estimates obtained using hospitalization data. Arthritis Rheum. 2007;56(6):2092-4.
10. Von Feldt JM. Systemic lupus erythematosus: recognizing its various presentations. Postgrad Med. 1995;97(4):79.
11. Gladman DD. Overview of the clinical manifestations of systemic lupus erythematosus in adults. 2017.
12. Schur PH. Genetics of systemic lupus erythematosus. Lupus. 1995;4(6):425-37.
13. Harley JB, Kelly JA, Kaufman KM. Unraveling the genetics of systemic lupus erythematosus. Springer Semin Immunopathol. 2006;28(2):119-30.
14. Wong M, Tsao BP. Current topics in human SLE genetics. Springer Semin Immunopathol. 2006;28(2):97-107.
15. Lahita RG. The role of sex hormones in systemic lupus erythematosus. Curr Opin Rheumatol. 1999;11(5):352-6.
16. McMurray RW, May W. Sex hormones and systemic lupus erythematosus: review and meta-analysis. Arthritis Rheum. 2003;48(8):2100-10.
17. Li J, May W, McMurray RW. Pituitary hormones and systemic lupus erythematosus. Arthritis Rheum. 2005;52(12):3701-12.
18. Costenbader KH, Feskanich D, Stampfer MJ, Karlson EW. Reproductive and menopausal factors and risk of systemic lupus erythematosus in women. Arthritis Rheum. 2007;56(4):1251-62.
19. Theofilopoulos AN. The basis of autoimmunity: Part I. Mechanisms of aberrant self-recognition. Immunol Today. 1995;16(2):90-8.
20. Kotzin BL. Systemic lupus erythematosus. Cell. 1996;85(3):303-6.
21. Hahn BH, Ebling F, Singh RR, Singh RP, Karpouzas G, La Cava A. Cellular and molecular mechanisms of regulation of autoantibody production in lupus. Ann NY Acad Sci. 2005;1051:433-41.
22. Koh YT, Scatizzi JC, Gahan JD, Lawson BR, Baccala R, Pollard KM, et al. Role of nucleic acid-sensing TLRs in diverse autoantibody specificities and anti-nuclear antibody-producing B cells. J Immunol. 2013;190(10):4982-90.

23. Somers EC, Richardson BC. Environmental exposures, epigenetic changes and the risk of lupus. Lupus. 2014;23(6):568-76.

24. Arroyo-Avila M, Santiago-Casas Y, McGwin G, Cantor RS, Petri M, Ramsey-Goldman R, et al. Clinical associations of anti-Smith antibodies in PROFILE: a multi-ethnic lupus cohort. Clin Rheumatol. 2015;34(7):1217-23.

25. Will CL, Luhrmann R. Spliceosomal UsnRNP biogenesis, structure and function. Curr Opin Cell Biol. 2001;13(3):290-301.

26. Zieve GW, Khusial PR. The anti-Sm immune response in autoimmunity and cell biology. Autoimmun Rev. 2003;2(5):235-40.

27. Lehmeier T, Foulaki K, Luhrmann R. Evidence for three distinct D proteins, which react differentially with anti-Sm autoantibodies, in the cores of the major snRNPs U1, U2, U4/U6 and U5. Nucleic Acids Res. 1990;18(22):6475-84.

28. Brahms H, Raker VA, van Venrooij WJ, Luhrmann R. A major, novel systemic lupus erythematosus autoantibody class recognizes the E, F, and G Sm snRNP proteins as an E-F-G complex but not in their denatured states. Arthritis Rheum. 1997;40(4):672-82.

29. Yacoub Wasef SZ. Gender differences in systemic lupus erythematosus. Gend Med. 2004;1(1):12-7.

30. Beaufils M, Kouki F, Mignon F, Camus JP, Morel-Maroger L, Richet G. Clinical significance of anti-Sm antibodies in systemic lupus erythematosus. Am J Med. 1983;74(2):201-5.

31. Arnett FC, Hamilton RG, Roebber MG, Harley JB, Reichlin M. Increased frequencies of Sm and nRNP autoantibodies in American blacks compared to whites with systemic lupus erythematosus. J Rheumatol. 1988;15(12):1773-6.

32. Hirohata S, Sakuma Y, Yanagida T, Yoshio T. Association of cerebrospinal fluid anti-Sm antibodies with acute confusional state in systemic lupus erythematosus. Arthritis Res Ther. 2014;16(5):450.