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SHORT PAPER

Antigen-Specific Antibody Response in Juvenile-Onset SLE Patients Following Routine Immunization with Tetanus Toxoid

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ABSTRACT

Background: Infection is now the most common cause of morbidity in Systemic Lupus Erythematosus (SLE). There is lack of information regarding the specific antibody formation in response to vaccines in young SLE patients. **Objective:** To determine the efficacy of anti-tetanus antibody response in young patients with SLE. **Methods:** Forty SLE patients with mean age of 14.1 years (range: 7-21) and 60 age and sex matched normal controls were enrolled in this study over a period of one year. Diagnosis was made according to the ACR criteria and disease activity was determined based on SLE Disease Activity Index (SLEDAI). All patients and controls had received the complete schedule of tetanus vaccinations consisting of three primary doses and two boosters by the age of six. Serum immunoglobulins and anti-tetanus antibody titers were determined by Nephelometry and ELISA. Anti-tetanus antibody levels greater than 0.1 IU/ml have been suggested as protective. **Results:** In all of the patients and controls anti-tetanus antibody titer was > 0.1 IU/ml. IgG, IgA, and IgM levels were in the normal range for their age. Mean disease activity score was 4.9 (range: 0-16). There was no association between SLEDAI score and anti-tetanus antibody response. **Conclusion:** School age onset and immunosuppressive therapy does not seem to interfere with development of consistent immunity to tetanus vaccine in young SLE patients.

Keywords: SLE, SLEDAI, Anti-tetanus antibody

INTRODUCTION

Patients with Systemic Lupus Erythematosus (SLE) are predisposed to a variety of infections as a result of their disease as well as treatment with immunosuppressive

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agents. Infections and organ damage are common co-morbidities in juvenile-onset SLE. Recurrent infections could predict poor disease outcome and associated organ damage in SLE (1). Infections in SLE patients are caused by common bacterial and by opportunistic organisms (2).

It is expected that immunization in SLE patients would decrease morbidity and mortality upon decreasing the incidence of infection; however, a decreased incidence of infection after immunization has not been determined. The response to immunization in adult SLE patients remains controversial, with serum antibody level reported as normal, subnormal or supernormal (3-5).

There is lack of information regarding specific antibody formation in response to vaccines in younger patients with SLE. The present study was undertaken to evaluate the specific antibody response of young SLE patients to tetanus vaccine and the possible effect of disease activity in attenuating the antibody response.

MATERIALS AND METHODS

Forty patients with SLE fulfilling the 1997 revised criteria of the American College of Rheumatology (6) were enrolled in the current study. They were followed in immunology and nephrology out-patient clinics affiliated with Shiraz University of Medical Sciences over a period of one year (2006-2007). Informed consent was obtained from all patients and their families.

Disease activity was assessed by SLE Disease Activity Index (SLEDAI) (7). Complete blood cell count (CBC), urinalysis, and serum level of IgG, IgM, and IgA, complement components (C_3, C_4), anti-double stranded DNA antibody, anti-nuclear antibodies, and anti-cardiolipin antibodies were determined. IgG antibody titer was measured in patients and controls using enzyme linked immunoassay kit for tetanus vaccine (tetanus IgG ELISA RE56901).

Sixty age and sex matched healthy controls were recruited from children and young adults who attended out-patient clinics for routine check up. All patients and controls had received the complete schedule of tetanus vaccinations consisting of three primary doses and two boosters by the age of six.

RESULTS AND DISCUSSION

Thirty one percent of controls were males and 69% were females. The mean age of the controls was 14.4 years. There was no relation between post tetanus antibody titer and the age of the patients and the controls.

Thirty two patients (80%) were females and 8 were males, with mean age of 14.1 years (range: 7-21). The mean age of disease onset was 10.5 years (range: 4-16), mean disease duration was 7 years, and rate of hospitalization since the time of diagnosis was 60%.

Four patients had disseminated infection (fatal disseminated varicella infection, primary peritonitis, meningitis, and pneumonia) warranting hospital admission. Prevalence of major organ involvement in this group of patients was as follows: renal in 42% of patients, neurologic in 12.5%, and hematologic in 10% of the patients.

Thirteen patients were taking azathioprine, 10 cyclophosphamide, 5 combinations of cyclophosphamide and azathioprine, and 8 were taking mycophenolate. All of the

patients were taking prednisolone. The IgG, IgM, and IgA levels were in normal range. Mean IgG level was 11.38 g/l. Patients with low disease activity and a SLEDAI score of less than 8 (78% of patients) compared with those with active disease and a score of greater than 8 (22% of patients) revealed no difference. The mean disease activity score was 4.9 (range: 0-16).

None of the participants had their tetanus vaccination after 6 years of age. Anti-tetanus antibody titers were above 0.1 IU/ml (range: 0.6-4.5 IU/ml) with a mean of 1.90 ± 1.33 IU/ml for the patients (Table 1) and 2.00 ± 1.24 IU/ml for the controls. There was no significant difference in anti-tetanus titer between the two groups (P-value: 0.694).

Table 1. Characteristics of SLE patients

	Age	Sex	SLE-DAI	Anti-Tetanus (IU/ml)	IgG g/l	IgA g/l		Age	Sex	SLE DAI	Anti-Tetanus (IU/ml)	IgG g/l	IgA g/l
1	13	M	2	1.40	10.80	1.06	21	12	F	0	1.90	12.50	1.54
2	16	F	4	0.60	9	1.10	22	14	F	16	0.60	10	0.80
3	17	M	12	4.20	11.22	2.55	23	16	F	4	0.60	12	1.65
4	17	F	2	3	13	2.10	24	18	F	0	0.60	13	4.20
5	18	F	8	2.40	11	1.84	25	18	F	2	1.90	15	3.10
6	18	M	2	0.60	7.69	0.99	26	14	F	4	1.10	11.30	1.23
7	18	F	14	0.60	10	2.54	27	10	F	2	1.60	19.60	0.20
8	10	F	4	1.80	12.40	2.06	28	10	F	13	1.90	10.50	1.65
9	9	F	3	0.90	9.50	2.33	29	17	F	12	4.20	8.40	2.44
10	16	F	2	3.30	9	1.84	30	16	F	4	4.40	10.50	2.27
11	15	M	4	3	11	1.75	31	12	F	3	2.60	8.80	2.10
12	15	F	2	4.50	11.54	1.09	32	18	F	4	0.60	10	0.90
13	14	F	2	3.70	12.85	2.03	33	10	F	9	0.60	10.32	1.45
14	16	F	2	0.90	9.80	2.60	34	14	F	4	4.20	7.40	0.80
15	15	M	2	1	12	1.90	35	13	F	10	0.60	9.40	1.34
16	21	M	12	1.50	7	0.75	36	12	F	0	0.70	8.70	1.64
17	10	F	2	0.60	15	2.44	37	7	M	8	0.80	7.80	1.05
18	16	F	4	3.90	17.88	2.80	38	12	M	2	2.30	11	2.30
19	12	F	0	2.90	16	1.85	39	15	F	4	2.80	17.55	1.85
20	14	F	0	0.90	18	1.98	40	16	F	15	0.60	7	2.30

Infection is the leading cause of morbidity and mortality in patients with SLE (8, 9). The response to immunization in SLE patients and immunity against viral and bacterial infections remains controversial. In this study all of the patients and the controls demonstrated baseline immunity with protective antibody levels from immunization. In the study of Battafarano et al. (10), anti-tetanus antibody titer was determined in 73 SLE patients with a mean age of 45 years before and 2 weeks after tetanus vaccination. Anti-tetanus antibody titer was in the protective range in 50% of patients before and 90% after vaccination.

The current UK department of health guideline (11) of immunization recommends that the primary course of tetanus immunization should be given at 2, 3, and 4 months of age. This is followed by a pre-school booster and a school leaving booster. The primary tetanus vaccination (3 doses) will give protection up to 10 years (12).

Comparing the present study with that of Battafarano et al. (9) reveals that the difference in base line immunity may be related to age difference of patients in the two studies. The mean age of patients in the current study was 15 years compared to 45 years in their study.

Our results do not support previous findings (14) of low antibody response to immunization in SLE patients compared to controls. Reports indicate that antibody response to

immunization with pneumococci, influenza, hepatitis B, and tentanus vaccine in SLE is variable, with enhanced, normal, or diminished antibody production (3, 13, 14).
Our findings are comparable with previous reports of normal post tetanus antibody titers in older SLE patients (13, 15). The limitation of the present study is that the pre- vaccination titer of tetanus was not measured. Although in those patients with high SLEDAI score (> 8) the anti-tetanus antibody titer remained in the protective range, the number of patients with lower SLEDAI score (<8) was considerably larger. Further studies with larger samples are needed to determine the precise effect of disease activity on specific antibody formation.
The presence of a protective level of antibody to tetanus toxoid in all patients irrespective of the age of the disease onset implies that school age onset of SLE does not interfere with the development of consistent immunity. It could be assumed that revaccination of lupus patients without a protective level of antibody after 18 years of age can produce a protective immunity.

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