

Short communication

Increased levels of serum IgE in children of mothers with systemic lupus erythematosus

Sasai K, Furukawa S, Hashimoto H, Yabuta K. Increased levels of serum IgE in children of mothers with systemic lupus erythematosus. Allergy 1995; 50: 370–373. © Munksgaard 1995.

Various allergic diseases have been described in patients with systemic lupus erythematosus (SLE). In the present study, we evaluated the prevalence of allergic disease and serum IgE levels in 36 children of 26 mothers with SLE. None of the subjects had any rheumatic symptoms. There was at least one type of allergic disease in 28 (78%) of the 36 children of mothers with SLE, as compared with 30% in Japanese control children ($P < 0.01$). The prevalence of atopic dermatitis and bronchial asthma was higher in children of mothers with SLE (64% and 28%) than in controls (19% and 9%) ($P < 0.01$, respectively). Fourteen of the 36 subjects (39%) had higher levels of serum IgE than those of normal range for age-matched healthy Japanese children with no atopic family disease in the immediate family history, and these children had atopic disease. Among the 14 children with high serum-IgE levels, seven had neither immediate nor remote family history of atopic disease, while the others had an immediate family history of atopic disease. We think that genetic factors may influence the presence of allergic disease in children of mothers with SLE, and that the increased serum IgE levels in children of SLE mothers with no allergic family history may be a part of subclinical immunologic abnormalities related to SLE.

K. Sasai¹, S. Furukawa², H. Hashimoto³, K. Yabuta¹

¹ Department of Pediatrics, Juntendo University School of Medicine, Tokyo; ² Department of Pediatrics, Yamaguchi University School of Medicine, Yamaguchi; ³ Department of Internal Medicine (Division of Rheumatology), Juntendo University School of Medicine, Tokyo, Japan

Key words: allergic disease; IgE; systemic lupus erythematosus.

Keiko Sasai, MD
Department of Pediatrics
Juntendo University School of Medicine
Hongo 2-1-1, Bunkyo-ku, Tokyo 113
Japan

Accepted for publication 4 November 1994

Introduction

Various allergic diseases have been described in patients with systemic lupus erythematosus (SLE), and a higher level of serum IgE has been reported in some patients at the active stage of the disease than in remission (3, 9, 10, 12). While the etiology of SLE is thought to be multifactorial, some papers focus on the hereditary factor in the pathogenesis of SLE. In familial studies on SLE, serologic abnormalities such as hyperglobulinemia, biologic false-positive tests for syphilis, and antinuclear antibodies have been observed in first-degree relatives of SLE patients (11). However, there has been no study on serum-IgE levels in children of mothers with SLE. In the present study, we evaluated serum-IgE levels, as well as the prevalence of allergic disease, in children of mothers with SLE.

Material and methods

Thirty-six children of 26 mothers with SLE, 18 boys and 17 girls, aged from 7 months to 11 years (me-

dian, 4.2 years) were enrolled in the study. Each mother fulfilled the American Rheumatism Association revised criteria for SLE (13), and gave informed consent before allowing participation in the study. The mothers were interviewed concerning allergic manifestations of the skin, respiratory tract, eyes, and gastrointestinal tract, and rheumatic symptoms such as arthralgia, Raynaud's phenomenon, and photosensitivity in their children.

Allergic diseases were defined as follows: *atopic dermatitis*: chronic or chronically relapsing, itchy dermatitis lasting 3 months with characteristic features (areas of scaly, erythematous, and pruritic lesions) and distribution (face, postauricular area, scalp, extensor surface of extremities, and flexural creases); *bronchial asthma*: three or more separate episodes of cough and wheezing; *allergic rhinitis*: recurrent nasal discharge or blockage with attacks of sneezing; *food allergy*: history of vomiting, diarrhea, colic, or rash within 4 h of ingestion of a particular food on at least two occasions; and *drug allergy*: urticaria, angioedema, or anaphylaxis attributed to ingestion of a drug.

Mothers were also questioned about the allergic history of the immediate family. A family history of allergic disease was considered to be positive when allergic disease was confirmed in parents or siblings. Examinations were performed in all children, and these children were measured for IgE levels in serum by enzyme immunoassay. SLE mothers were also measured for IgE levels when they were in remission.

Statistical analysis

The chi-square and Mann-Whitney U tests were used to detect difference between proportion.

Results

Allergic disease

Among the 26 parents, eight fathers (30%) and nine mothers (35%) had a history of at least one type of allergic disease. Five fathers and seven mothers had allergic rhinitis, three fathers and three mothers had bronchial asthma, one father and one mother had drug allergy, and two mothers had food allergy.

Table 1 shows the prevalence of each allergic disease in children of mothers with SLE and Japanese control children (6). There was at least one type of allergic disease in 28 (78%) of the 36 children of mothers with SLE, as compared with 30% in controls ($P < 0.01$, by chi-square test). With respect to the type of allergic disease, the prevalence of atopic dermatitis and bronchial asthma was significantly higher in children of mothers with SLE (64% and 28%) than in controls (19% and 9%) ($P < 0.01$, respectively, by chi-square test). There was no difference in the prevalence of allergic rhinitis between these two groups. Neither food allergy nor drug allergy was found in children of mothers with SLE.

None of the subjects had rheumatic symptoms, parasitic infections, or hematologic disorders.

IgE levels

Serum-IgE level in each child of a mother with SLE is shown in Fig. 1. In this analysis, serum-IgE levels were evaluated as high when the value was more

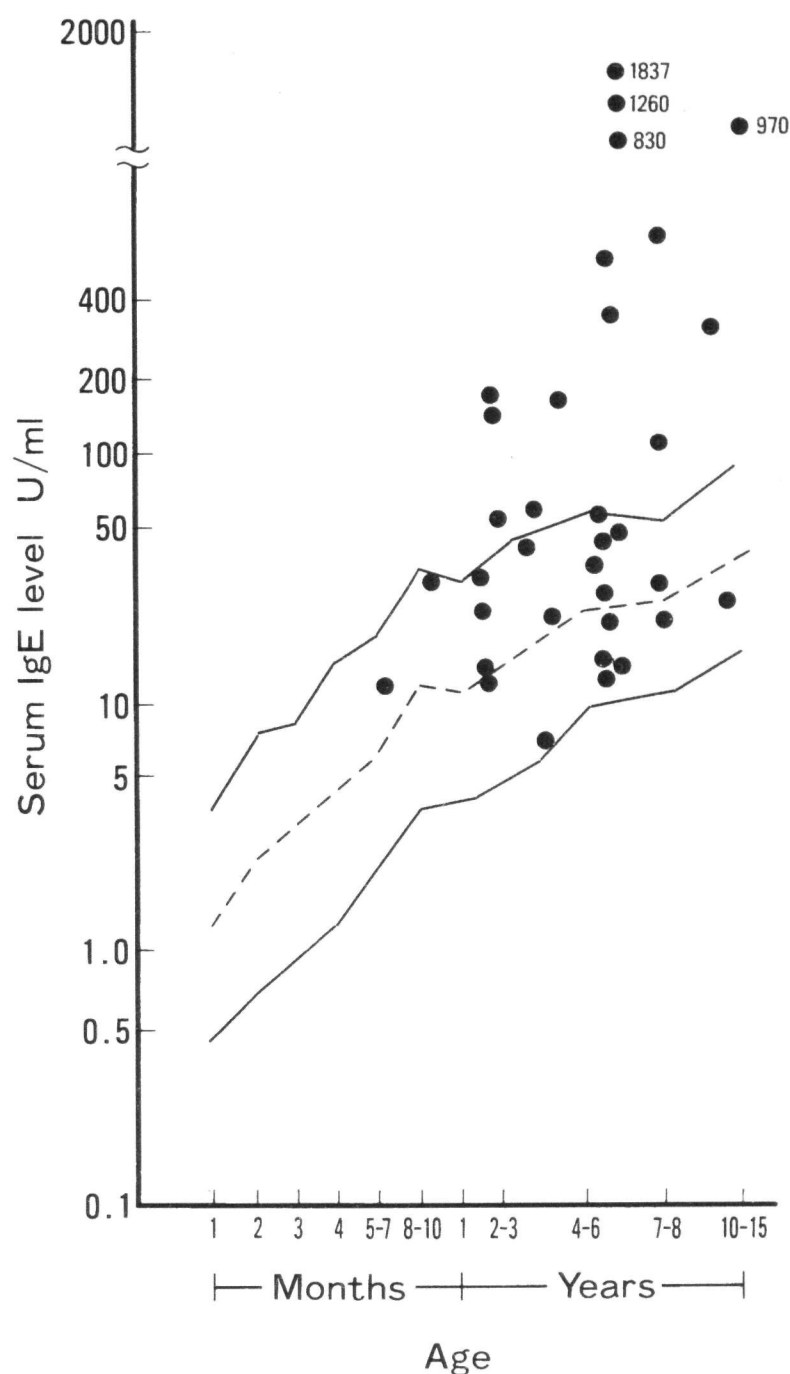


Fig. 1. Serum-IgE levels in children of mothers with SLE. Broken line shows geometric mean levels of serum IgE in age-matched healthy children; solid line shows mean value plus or minus 1 SD of age-matched healthy children.

than normal range for age-matched healthy Japanese children with no atopic family disease in the immediate family history, as we have previously described (1). This normal range is accepted by Japanese pediatricians. Fourteen of the 36 subjects (39%) had higher levels of serum IgE than those of age-matched healthy nonatopic children, and these children had atopic disease. Among the 14 children with high serum-IgE levels, seven children had neither immediate nor remote family history of atopic disease, while the others had an immediate family history of atopic disease.

To evaluate the genetic effect for the children's IgE levels, we classified the mothers into two groups, the 10 mothers who had borne at least one child with high serum-IgE levels (group A), and the other 16 mothers who had not borne children with high IgE

Table 1. Allergic disease in children of mothers with SLE and Japanese control children

n	Children of mothers with SLE 36	Japanese controls* 8016	P value
Allergic disease	28 (78%)	2376 (30%)	<0.01
Atopic dermatitis	23 (64%)	1498 (19%)	<0.01
Bronchial asthma	10 (28%)	748 (9%)	<0.01
Allergic rhinitis	5 (14%)	1128 (14%)	NS

NS: not significant.

* Japanese Health and Welfare Statistics Association (6).

levels (group B). Moreover, these mothers were classified into four subgroups, with or without allergic disease. In group A, four mothers had allergic diseases (group A-1), and the other five mothers had no allergic disease (group A-2). In group B, five mothers had allergic disease (group B-1), and the other 11 mothers had no allergic disease (group B-2). The median IgE level of each group was as follows: 320 U/ml (range: 153–1125, group A-1), 65 U/ml (range: 25–315, group A-2), 330 U/ml (range: 45–1988, group B-1), and 40 U/ml (range: 16–65, group B-2). There were no significant differences in IgE levels either between group A-1 and group B-1, or between group A-2 and group B-2 (by Mann-Whitney U test, respectively).

Discussion

In patients with SLE, various allergic diseases have been described (3, 9, 10, 12). Sequeira et al. (12) have reported an increased prevalence of allergic disease, particularly allergic rhinitis and drug allergy, in patients with SLE. It has also been reported that allergy to certain drugs, especially antibiotics, is common and occasionally acts as an exacerbating agent in SLE. We present here a higher prevalence of allergic disease in children of SLE mothers, as compared with Japanese control children, than has been reported previously (6). In our subjects, atopic dermatitis and bronchial asthma were particularly frequent, while there were no children with either drug allergy or food allergy. Our results suggest that some genetic factors in SLE patients may influence the presence of allergic disease in their children and that children with SLE mothers seem to be susceptible to atopic disease.

With respect to IgE levels, it was reported that patients with active SLE had higher serum levels of IgE than patients with SLE in remission (10). The IgE synthesis is tightly controlled by a complex network of T cells, B cells, and cytokines, and is known to increase markedly in allergic diseases, primary immune deficiencies, viral or parasitic infections, human immunodeficiency virus infection, and some autoimmune disorders (2, 5, 8). Recently, two different patterns of lymphokine secretion have been defined among mouse CD4⁺ T-cell clones, namely, TH1 cells that produce interleukin-2 (IL-2), interferon-gamma, and lymphotoxin, and TH2 cells that synthesize IL-4, IL-5, and IL-6 (7). TH1 cells and TH2 cells play different immunopathologic roles. TH1 cells are involved in delayed-type hypersensitivity, contact dermatitis, and allograft rejection. TH2 cells are known to be responsible for the IgE regulation and the initiation of the allergic cascade. Regarding the linkage of IgE regulation and autoimmunity, Goldman et al. demonstrated systemic

autoimmune disease in rodents experimentally induced by chemicals (4). This model had increased IgE levels, elevated IL-4 activity and impairment of IL-2 production, as well as production of antinuclear antibodies, immune glomerulonephritis, and MHC class II hyperexpression on B cells. This profile of lymphokines suggests a central role for TH2 cells in certain systemic autoimmunity as well as in IgE regulation.

In the present results, we have shown the increased level of serum IgE in 39% of children of mothers with SLE. In this analysis, IgE values of greater than each geometric mean plus 1 SD of age-matched Japanese healthy children were defined to be high (1). All of these children with high serum-IgE levels had allergic disease, but half of these 14 children had neither immediate nor remote family history of allergic disease. None of the subjects had parasitic infections or hematologic disorders, and there were no other abnormalities of immunologic parameters. To evaluate the genetic effect for children's IgE levels, we classified mothers into two groups, mothers who had borne at least one child with high serum-IgE levels, and mothers who had not borne children with high IgE levels. However, there were no significant differences in serum levels or titers of immunologic parameters, such as IgG, IgA, IgM, complement components (C3 and C4), antinuclear antibodies, and antibodies against native DNA, Sm, nuclear RNP, Ro/SS-A, and La/SS-B, between these two groups of mothers (data not presented). Moreover, no significant differences could be found in serum-IgE levels between these two groups either. Although the specific mechanism underlying the increase in IgE levels of children of SLE mothers remains to be clarified, we believe that the increased serum-IgE levels in these children with no allergic family history may be part of the abnormal IgE immune response to the hereditary factor in the pathogenesis of SLE.

Acknowledgment

This work was supported by a grant-in-aid for scientific research from the Japanese Ministry of Education, Science, and Culture (1993).

References

1. FURUKAWA S, TAKEUCHI T, TSUDA M, BABA M. Age-related serum IgE levels in healthy children [in Japanese]. *Saishin Igaku* 1981; 36: 1217–19.
2. GEHA RS. Regulation of IgE synthesis in humans. *J Allergy Clin Immunol* 1992; 90: 143–50.
3. GOLDMAN JA, KLIMEK GA, ALI R. Allergy in systemic lupus erythematosus. IgE levels and reaginic phenomenon. *Arthritis Rheum* 1976; 19: 669–74.
4. GOLDMAN M, DRUET P, GLEICHMANN E. TH2 cells in systemic autoimmunity: insights from allogenic diseases and

- chemically-induced autoimmunity. *Immunol Today* 1991; 12: 223-7.
5. ISRAEL-BIET D, LABROUSSE F, TOURANI JM, SORS H, ANDRIEU JM, EVEN P. Elevation of IgE in HIV-infected subjects: a marker of poor prognosis. *J Allergy Clin Immunol* 1992; 89: 68-74.
6. JAPANESE HEALTH AND WELFARE STATISTICS ASSOCIATION. The prevalence of allergic diseases in Japan [in Japanese]. *J Health Welfare Stat* 1992; 39: 39-52.
7. MOSMANN TR, COFFMAN RL. Heterogeneity of cytokine secretion patterns and functions of helper T cells. *Adv Immunol* 1989; 46: 1111-47.
8. OWNBY DR. Clinical significance of IgE. In: MIDDLETON E Jr, REED CE, ELLIS EF, eds. *Allergy; principles and practice*. 4th ed. St Louis, MO: Mosby Year Book, Inc, 1993: 1059-76.
9. PETRI M, ALLBRITTON J. Antibiotic allergy in systemic lupus erythematosus: a case-control study. *J Rheum* 1992; 19: 265-9.
10. REBHUN J, QUISMORIO F Jr, DUBOIS E, HEINER DC. Systemic lupus erythematosus activity and IgE. *Ann Allergy* 1983; 50: 34-6.
11. SATO EI, ATRA E, GABRIEL A Jr, MASI AT. Systemic lupus erythematosus. A family study of 25 probands. *Clin Exp Rheum* 1991; 9: 455-61.
12. SEQUERIA JF, CESIC D, LESER G, et al. Allergic disorders in systemic lupus erythematosus. *Lupus* 1993; 2: 187-91.
13. TAN EM, COHEN AS, FRIES JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 5: 1271-7.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.