

Serum IgE concentrations, disease activity, and atopic disorders in systemic lupus erythematosus

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We investigated the relationship between disease activity and total IgE concentration in the sera of patients with active systemic lupus erythematosus (SLE). In addition, the prevalence of personal and family history of allergic rhinitis and asthma were examined with a questionnaire and immediate skin tests for common inhalant allergens in 24 patients in remission. In the 20 patients with active disease, we found that IgE concentration was significantly higher during the periods of active disease than the periods of remission. This elevation was not associated with an elevation in total serum IgG concentrations. The increase in IgE concentration during disease activity in patients with active nephritis was significantly higher than in patients without nephritis. Of the 24 patients in remission, only one reported allergic rhinitis, and two had positive skin tests for inhalant allergens. We concluded that, although patients with SLE do not have an increased rate of atopic disorders, serum IgE rises during disease activity and is associated with active nephritis. This phenomenon suggests that IgE may be involved in the pathogenesis of SLE, particularly in patients with nephritis.

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The mechanism whereby organ damage occurs in systemic lupus erythematosus (SLE) is believed to relate, in part, to the deposition of immune complexes within small blood vessels, which leads to complement activation and vascular impairment (2, 6). The role of IgE antibodies in immune complex diseases has not been extensively studied. Some authors have suggested that IgE, through the release of vasoactive mediators from basophils or mast cells, causes increased vasopermeability and may be important in the deposition of circulating complexes in experimental serum sickness in rabbits and in immune-mediated glomerulonephritis (3, 8, 10).

This study investigated the relationship of serum IgE concentration with SLE activity, and assessed the incidence of atopic diseases in patients with SLE.

Material and methods

Patients

To investigate the role of IgE and immediate hypersensitivity in SLE, we studied two different groups of patients with SLE who attended the Clinical Im-

munology and the Rheumatology Clinics and fulfilled the diagnostic clinical criteria of the American Rheumatic Association (12).

Group 1. Twenty patients with SLE were investigated for IgE concentration. Two serum samples were drawn from each, one during a period of disease exacerbation with elevated anti-DNA antibody titer, and one during remission with normal anti-DNA titer. Samples were stored at -20°C until tested. Clinical disease activity was assessed by chart analysis and serum anti-DNA level determination. Disease flare-up was defined when one of the typical symptoms of rash, arthritis, serositis, oral ulcers, renal disease, photosensitivity, and cerebral symptoms, in addition to elevated anti-DNA levels, was present. Remission was defined as absence of the above-mentioned clinical presentation and normal anti-DNA levels. None of the patients had a history of atopy or parasitic infection, except for one who had chronic parasitic infestation.

Group 2. Twenty-four consecutive SLE patients (23 women and one man) in remission, of mean age 46

years (range 22–60 years) and with mean A-DNA of 16% (normal 0–20%) and no clinical signs of disease, were asked to complete a questionnaire on their allergic history and were skin-tested for immediate hypersensitivity to common environmental allergens. All patients signed an informed consent form.

Immediate skin tests

Tests were done with six extract mixtures that included the most common environmental allergens in Israel: 1) house-dust mite; 2) grass mix (ryegrass, orchard grass, Bermuda grass); 3) weed mix (mugwort, pigweed, lamb's-quarters); 4) tree mix (olive, cypress, oak); 5) animal dander mix (cat and dog); and 6) mold mix (*Alternaria*, *Penicillium*, *Aspergillus*, *Fusarium*). Prick tests were done with glycerinated extracts 1:20 w/v (Hollister Stier, Spokane, WA, USA). Skin test response was measured after 20 min. A wheal size greater than the diluent control by 4 mm or more was considered to be positive. Results were considered to be positive when the subject had at least one positive skin test.

Laboratory data

Antinuclear antibodies were determined with immunofluorescent polyvalent antiglobulin and human epithelial cells. Anti-DNA was determined by the Farr method (normal anti-DNA level <20%). IgE was measured by the ELISA method (MELISA, Walker Diagnostics, UK). IgG levels were determined by nephelometry.

Data were analyzed by calculating geometric mean (± 1 standard error deviation) and range, and significance was determined by Student's *t*-test ($P < 0.05$ was considered to be significant).

Results

SLE activity and IgE levels

Group 1. The IgE levels in the sera of the 20 patients with active disease ranged from 5 to 4500 IU, with a mean of 696 ± 269 IU/ml (Fig. 1); levels in the same patients during remission ranged from 5 to 750 IU/ml, with a mean of 172 ± 53 IU/ml. Analysis of the data revealed that the difference between these mean values was statistically significant ($P = 0.02$).

Clinical nephritis was defined as the presence of red cell casts in urine, or proteinuria, or a decrease in renal function when other causes of renal failure were ruled out. Patients with active SLE and nephritis had a higher IgE level (mean: 1474 ± 511 IU/ml) than patients with active disease without this manifestation (157 ± 102 IU/ml) ($P < 0.05$) (Fig. 2).

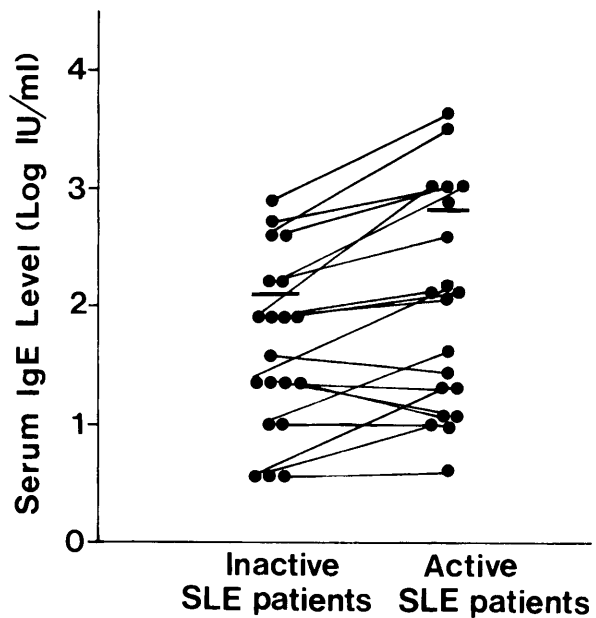


Fig. 1. Serum IgE concentration in SLE patients is significantly lower during remission than during disease activity ($P = 0.02$).

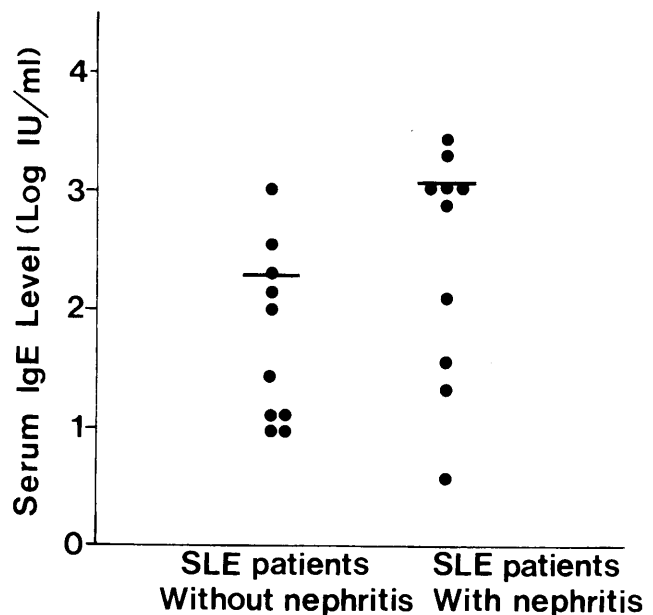


Fig. 2. Mean IgE concentration during disease activity in sera of patients with nephritis is significantly higher than in patients without nephritis ($P < 0.05$).

Serum IgG levels. To determine whether IgE elevation is part of a nonspecific polyclonal immunoglobulin elevation that commonly occurs in active SLE, we compared total serum IgG levels in two subgroups of patients with active SLE: those with elevated and those with normal IgE. Serum IgG levels were 1230 ± 643 and 1283 ± 773 IU/ml, respectively. This difference was not statistically significant, suggesting that IgE elevation is not related to IgG levels.

Group 2: allergy questionnaire. Only one patient reported a history of seasonal allergic rhinitis, and his serum IgE concentration was 60 IU/dl. The other patients denied having a history of allergic rhinitis, asthma, urticaria, or food allergy. Five patients reported a family history of allergy.

Skin tests. Skin tests were positive for at least one environmental allergen in two patients.

Serum IgE levels. Mean IgE concentration in serum was 88 IU/ml (range: 1–250 IU/ml).

Discussion

Organ damage in SLE may be related to the deposition of immune complexes within small blood vessels. A role for IgE in immune complex deposition has previously been suggested (3, 8, 10). We found that serum IgE concentration was significantly higher during a period of disease activity than during remission in the same group of patients (Fig. 1). These findings are consistent with those of Rehbun et al. (9), who reported higher mean serum concentrations of IgE in active SLE patients than in patients in remission. Five of their patients, in whom IgE concentrations were elevated during a period of active disease, showed a decrease in total IgE level during remission. We found similar results in 12/20 patients, suggesting that an increase in serum IgE concentration may accompany disease activity in certain cases. Although such elevation could reflect nonspecific B-cell stimulation unrelated to the disease process, this conclusion is unlikely, because, during disease activity, there was no significant difference in IgG levels between the subgroups with elevated and normal IgE levels. Analysis revealed a significant correlation between serum IgE concentration and active nephritis. This is not surprising, because the kidney is the most common site of immune complex deposition in SLE.

The significant correlation between disease activity and serum IgE may reflect the presence of an anti-DNA-specific IgE in these patients. This has been suggested by Egido et al. (4), who showed an increase in the number of surface IgE molecules on basophils of SLE patients and a positive basophil degranulation test with native DNA. Laurent et al. (7) reported increased serum IgE concentration in patients with lupus nephritis. IgE renal deposits in lupus nephritis have also been reported, and their presence linked to poor prognosis (13).

In view of a possible role of IgE in SLE activity and the well-recognized role of IgE in allergic disorders, we assessed 24 patients in remission for atopy. Although we did not use a control group, it

was apparent that the incidence of atopic disorders and positive immediate skin tests was not elevated.

Becker (1) found that there was no significant difference in the incidence of allergic rhinitis and asthma between patients with SLE and controls. Goldman et al. (5) found that SLE patients had more allergic diseases than a control group, but this increase was not statistically significant. In a recent study of 132 patients and their family members, Sequeira et al. (11) found an increased incidence of allergic rhinitis and asthma in family members of SLE patients, but not in the patients themselves, although they had a significantly increased prevalence of drug, skin, and insect allergies.

The present study shows that IgE levels correlate with the degree of activity of SLE in certain patients, especially in those with nephritis. Further studies are necessary to clarify the specificity of the IgE present in these patients and its part in the pathogenesis of SLE, particularly SLE nephritis.

References

1. BECKER LC. Allergy in systemic lupus erythematosus. *Hopkins Med J* 1973; 133: 38–44.
2. CHRISTIAN CL. Immune complex disease. *N Engl J Med* 1969; 280: 878–84.
3. COCHRANE CG, KOFFLER D. Immune complex disease in experimental animals and man. *Anv Immunol* 1973; 16: 185–264.
4. EGIDO J, CRESPO S, LAHOZ C, GARCIA R, LOPEZ-TRASCADA M, HERNANDO L. Evidence of an immediate hypersensitivity mechanism in systemic lupus erythematosus. *Ann Rheum Dis* 1980; 39: 312–17.
5. GOLDMAN JA, KLIMEK GA, ALI R. Allergy in systemic lupus erythematosus. IgE levels and reaginic phenomenon. *Arthritis Rheum* 1976; 4: 669–76.
6. KOFFLER D, AGNELLO V, KUNKEL HG. Polynucleotide immune complexes in serum and glomeruli of patients with systemic lupus erythematosus. *Am J Pathol* 1982; 74: 109–15.
7. LAURENT J, LAGRUE G, SOBEL A. Increased serum IgE levels in patients with lupus nephritis. *Am J Nephrol* 1986; 6: 413–14.
8. MCPAUL JJ, NEWCOMB RM, MULLINS JD, THOMPSON AL Jr, ROGERS PW. Participation of immunoglobulin E (IgE) in immune mediated glomerulonephritis. *Kidney Int* 1974; 5: 292–9.
9. REHBUN J, QUISMORO F, DUBOIS E, HEINER DC. Systemic lupus erythematosus activity and IgE. *Ann Allergy* 1983; 50: 34–6.
10. ROBERTSON MR, POTTER EV, ROBERTS ML, PATTERSON R. Immunoglobulin E in renal disease. *Nephron* 1976; 16: 256–71.
11. SEQUEIRA JF, CESIC D, KESSER G, et al. Allergic disorders in systemic lupus erythematosus. *Lupus* 1991; 2: 189–91.
12. TAN EM, COHEN AS, FRIES JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271–7.
13. TUMA SN, LLACH F, SOSTRIN S, DUBOIS EL, MASSRY SG. Glomerular IgE deposits in patients with lupus nephritis. *Am J Nephrol* 1981; 1: 31–6.