

Brief communications

Elevated serum immunoglobulin E levels in patients with juvenile dermatomyositis

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Dermatomyositis (DMS), recognized as a multi-system disorder mediated through autoimmune mechanisms, affects both children and adults. A juvenile type of this disorder, called juvenile dermatomyositis (JDMS), is now considered to be somewhat different from the adult type, or adult dermatomyositis (ADMS), especially from a histopathologic point of view. Among many children with JDMS, deposition of immunoglobulin complexes can be observed, particularly within the walls of intramuscular arteries and veins.¹ However, the etiology and pathogenesis of JDMS has remained elusive. Cochrane and Koffler² suggested that IgE may play an important role in autoimmune diseases by mediating the release of chemical mediators and by facilitating the local deposition of immune complexes. Among patients with systemic lupus erythematosus (SLE), higher serum IgE levels can be seen during the active state of the disease when compared with the inactive state.³ A deficiency of suppressor T cells in the active SLE state may also contribute to elevations in the serum IgE levels.

In a previous study we demonstrated a significantly higher frequency of pruritus in patients with JDMS when compared with patients with ADMS in Japan.⁴ Most of the patients with JDMS in the present study who complained of severe itch showed elevated serum IgE levels accompanied by atopic disease clinically diagnosed before the onset of JDMS. Our findings suggest a correlation between elevated serum IgE levels in patients with JDMS and atopic disease or a

Abbreviations used

DMS:	Dermatomyositis
JDMS:	Juvenile dermatomyositis
ADMS:	Adult dermatomyositis
SLE:	Systemic lupus erythematosus
AD:	Atopic dermatitis

peculiarly defective immunosuppressive mechanism, as seen in cases of SLE. This study was designed to clarify this issue, and to determine whether atopic disease affects the occurrence of JDMS.

SUBJECTS AND METHODS

All patients with DMS in this study were those observed at Nagoya University Hospital over a period of 11 years, from 1980 through 1990. No specific method was used for selecting patients to participate in this study; patients who came to the hospital for treatment over the years were considered. All patients met at least three of the diagnostic criteria for DMS as proposed by Bohan and Peter.⁵ All patients with "active" disease who clearly demonstrated elevated muscle enzymes and muscular weakness at the time of examination were studied after diagnosis had been established and before treatment was begun. Patients with "inactive" disease who were in clinical and biochemical remission at the time of examination were studied during periodic visits for routine medical checkups.

Eighteen patients with JDMS (11 males and 7 females), ranging from 4 to 15 years of age, with a mean age of 11.0 years participated. Nine patients were in an active state, and the other nine were in an inactive state at the time serum samples were obtained. Two sets of control sera were used. The first set of juvenile controls consisted of sera from 36 normal children living in Nagoya City who matched the JDMS patients by age (± 1 year), sex, and residential area. The second set consisted of sera from 39 patients with ADMS (10 men and 29 women), ranging from 26 to 76 years of age, with a mean age of 52.3 years. Twenty-one patients were in an active state, and 18 were in an inactive state.

Total serum IgE levels were determined by use of a double antibody radioimmunoassay (Pharmacia Diagnostics AB,

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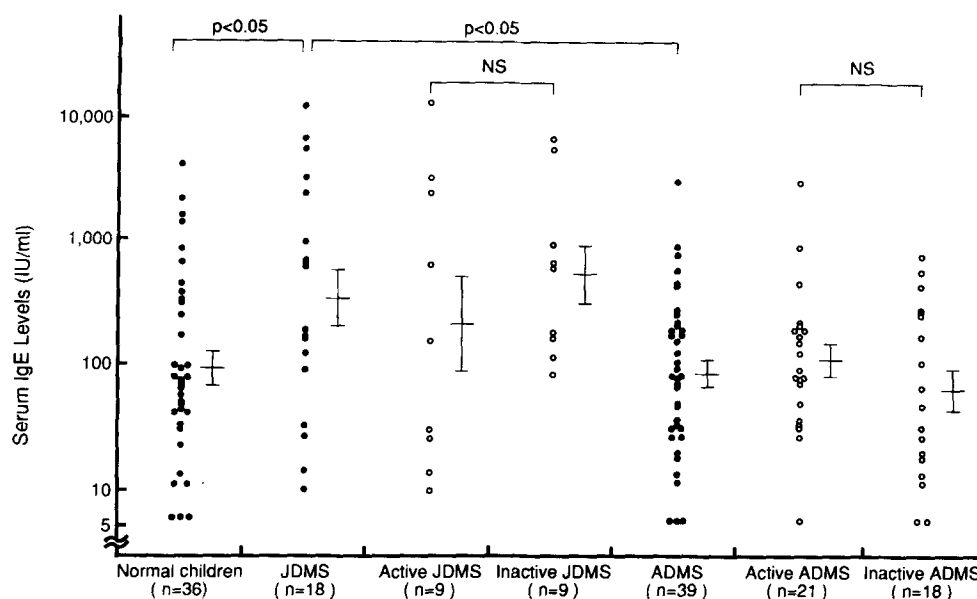


FIG. 1. Comparison of serum IgE levels among healthy children, patients with JDMS and patients with ADMS, and serum IgE levels in relation to disease activity. Bars represent geometric mean $\pm$ SE. NS, Not significant.

Uppsala, Sweden). Specific IgE antibodies determined with the RAST technique (Pharmacia Diagnostics AB) were defined as "positive" when the Pharmacia allergy class was at 2 or more. For intergroup comparisons of the means, we used the *t* test with Welch's correction or Student's unpaired *t* test. Values for serum IgE were analyzed after logarithmic ($\log_{10}$) translation. A *p* value of 0.05 or less was regarded as significant.

RESULTS

Serum IgE levels recorded for the 18 patients with JDMS, 36 normal children, and 39 patients with ADMS are shown in Fig. 1. A wide range was observed in serum IgE levels, especially among the patients with JDMS where values ranged from 10 to 13,000 IU/ml, with a geometric mean of 349.9 ($\log$ IgE $\pm$ SE: 2.544 ± 0.223). Among the 36 normal children, values ranged from 6 to 4,100 IU/ml, with a geometric mean of 92.7 (1.967 ± 0.123). Differences in the mean serum IgE levels were statistically significant between patients with JDMS and normal children ($p < 0.05$). Among the 39 patients with ADMS, values ranged from 6 to 3,100 IU/ml, with a geometric mean of 89.7 (1.953 ± 0.102). The patients with JDMS had a significantly higher ($p < 0.05$) mean than the patients with ADMS. Serum IgE levels were also compared between the active and inactive DMS states, but no significant differences could be seen for either the patients with JDMS or those with ADMS.

For the 18 patients with JDMS, atopic backgrounds taken from a questionnaire on their personal and family history of atopy were studied. At an early stage

of JDMS, children may have symptoms limited to only a rash either with or without mild muscle weakness.⁴ In such cases the rash is often misdiagnosed as atopic dermatitis (AD). In this study, therefore, investigation was limited to the typical morphology and distribution of AD and its diagnosis, with atypical cases excluded from the study.

Of the nine (50%) out of 18 patients with JDMS who had elevated serum IgE levels (>200 IU/ml), five (28%) cases in particular showed marked elevation (>1000 IU/ml). All nine patients with elevated serum IgE levels had a personal history of atopy (five of AD, two of allergic rhinitis, and two with both), whereas five also had a family history of atopic respiratory disease. By contrast, none of the nine patients with normal serum IgE levels had any personal episodes of atopy, even though two cases had a family history of atopic respiratory disease. All but three patients were subjected to RAST. Among the 15 patients with JDMS, nine with elevated serum IgE levels reacted to two or more common antigens, although the remainder (six patients) had negative RAST findings.

DISCUSSION

In our study all JDMS patients with elevated serum IgE levels had a prior history of atopic disease as well as positive RAST findings. Unlike SLE, however, no significant changes were observed in serum IgE levels during the disease state. We think, therefore, the elevation in serum IgE in patients with JDMS is attributable to a coexistence with atopic disease. However,

alterations in cell-mediated immunity in the already existing atopic disease derived from the onset of JDMS may result in abnormally high levels of serum IgE. Plans are being made to explore this matter further once enough patient data can be gathered for analysis.

The occurrence of atopy in the general population is estimated at 30%. The prevalence of AD has also been increasing with estimates at 6.6%.⁶ In our study coexistent atopic disease was found in nine (50%) of the 18 patients with JDMS, and coexistent AD was found in seven (39%). These figures are extremely high when compared with those mentioned above, especially for AD. AD is associated with impaired cell-mediated immunity.⁷ On the other hand, a viral etiology, such as the Coxsackie B virus,⁸ has been strongly postulated for JDMS. For these reasons, we deem that children with impaired cell-mediated immunity with such symptoms as AD may be more susceptible to JDMS than normal children, at least in Nagoya. Such susceptibility is believed to be unrelated to high dosages of steroids, because no prior systemic steroid medication for AD was prescribed for any of the patients with JDMS and AD in our series. Since AD states may vary from area to area because of such factors as changes in environment,⁹ a question remains as to whether our findings would hold true for AD in other localities. However, as speculative as this idea may be, it will no doubt be significant in elucidating the susceptibility to JDMS.

From our findings we conclude that, in general, children with impaired cell-mediated immunity with such symptoms as AD may have a higher tendency for developing DMS.

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Prophylaxis against fluorescein-induced anaphylactoid reactions

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Reactions to intravenous fluorescein are well described in the ophthalmology literature and include nausea and vomiting, flushing and urticaria, and anaphylactic shock.^{1,2} A 48.6% incidence of repeat reactions has been found in subjects with a history of a previous reaction to fluorescein.¹ Although most of these reactions consist of nausea and vomiting, approximately 15% of these repeat reactions represent anaphylactoid reactions. We report a patient who experienced nausea and urticaria immediately after fluorescein injections on three occasions in the past, de-

spite premedication with diphenhydramine and prednisone before the last two studies and who required another fluorescein angiographic study.

CASE REPORT

A 64-year-old man was referred in October of 1987 because of previous reactions to intravenous fluorescein. In 1983, because of a fluid leak in his left retina caused by presumed ocular histoplasmosis syndrome, the patient received intravenous fluorescein (5 ml bolus of 10% Fluorescein), and within 15 minutes he had nausea and urticaria of his entire face. He was treated with diphenhydramine, and in 1 hour the hives resolved. Two months later he required another fluorescein study. Two days before this study he was started on diphenhydramine, 50 mg four times a day, and 60 mg prednisone daily. He was then given the intravenous fluorescein, and again within 15 minutes he had

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