

Positive Antinuclear Antibody in Atopic Dermatitis

Y. TANIGUCHI, A. YAMAKAMI, T. SAKAMOTO, Y. NAKAMURA, H. OKADA, H. TANAKA, H. MIZUTANI and M. SHIMIZU

Department of Dermatology, Mie University School of Medicine, Tsu, Japan

Serum samples from atopic dermatitis (AD) patients were examined with two antinuclear antibody-detecting methods, using HEp-2 cells as substrate. 34.0% of 47 AD patients tested with FITC-conjugated polyvalent immunoglobulins (method 1) had positive antinuclear antibody (ANA). 26.3% of 57 AD patients examined with FITC-conjugated anti-IgG (method 2) had positive ANA. We found that AD patients who had facial lesions tended to have positive ANA, whereas severe AD patients tended to have high titres of ANA. Key words: Atopic dermatitis; Facial lesion; Antinuclear antibody.

Acta Derm Venereol (Stockh) 1992; Suppl 176: 62-64.

Yoshiki Taniguchi, M.D., Department of Dermatology, Mie University School of Medicine, 2-174 Edobashi, Tsu-shi, Mie-ken 514, Japan.

Antinuclear antibody (ANA) is found in the sera of patients with systemic lupus erythematosus (SLE) (1). Recently, ANA has become one of the most important diagnostic markers of collagen disease because of the disease-specific fluorescent pattern on the substrate. There are several non-collagen diseases, including of viral syndromes and chronic inflammatory diseases, that show positive ANA (2, 3). Since atopic dermatitis (AD) patients have marked exacerbation of the lesions following sun exposure (4) and facial lesions resembling the butterfly rash of SLE are often seen, ANA is examined in AD patients.

MATERIALS AND METHODS

Ninety AD patients (26 males, 64 females) who visited Yokkaichi city hospital and Mie university hospital between June 1990 and April 1991 and who fulfilled the criteria of AD as designated by Hanifin & Rajka (5) were recruited to this study. They ranged in age from 15 to 30 years (average; 20.0 years old). Severity of lesions and presence of facial lesions were also examined. Twelve control serum samples were taken from patients of similar ages to the AD patients, who visited both hospitals for operations, including nevus pigmentosus. Serum samples were collected at the time of examination and stored at -20°C until testing. Serum samples from Yokkaichi city hospital were tested by the following method 1 (n = 47) and partly with method 2 (n = 14). Serum samples from Mie university hospital were examined with method 2 (n = 43). Other examinations including blood cell counting, eosinophils and IgE determinations were performed simultaneously. Control serum samples were also tested with the two methods.

Antinuclear antibody determinations

Antinuclear antibodies were examined on a substrate of HEp-2 cells fixed in acetone, using serum diluted in phosphate-buffered saline and fluorescein isothiocyanate (FITC)-conjugated goat antihuman polyvalent immunoglobulins (Sigma, method 1) and FITC-conjugated goat antihuman IgG (Hoechst, method 2). The presence of immunofluo-

rescence at a serum dilution of greater than or equal to 1:40 was considered positive.

RESULTS

Positive presence of antinuclear antibody was seen in 34.0% of patients tested with method 1 (Fig. 1) and in 26.0% examined with method 2 (Fig. 2). The fluorescent patterns of positive ANA in method 1 were: 2 homogeneous type, 8 speckled type, and 6 homogeneous-speckled type. In method 2, they showed 11 homogeneous type, 1 speckled type, and 3 homogeneous-speckled type. A higher titre of ANA was only found in the sera of female patients, with both methods. There seemed to be no correlation between positive ANA and a high IgE level or eosinophilia. Facial lesions were seen in 81.2% of AD patients who had positive ANA, though facial lesions were also found in 40.6% of ANA-negative AD patients (Fig. 3). Eleven patients needed hospitalization for their severe dermatitis (Fig. 2, arrowheads). Among these, 4 patients had a higher titre of ANA whose fluorescent patterns were all of the homogeneous type.

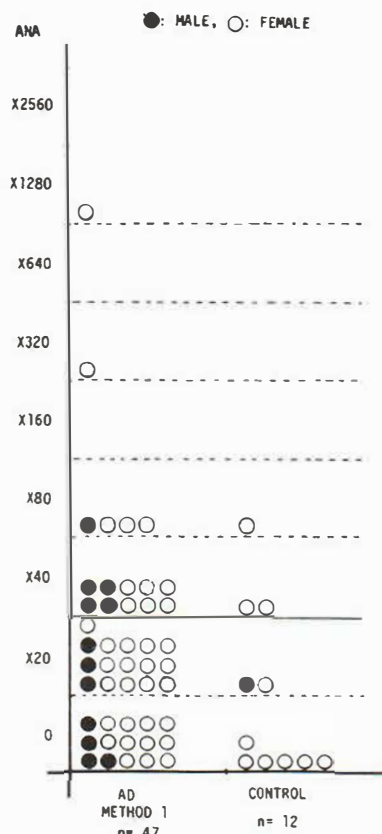


Fig. 1. ANA measured with method 1.

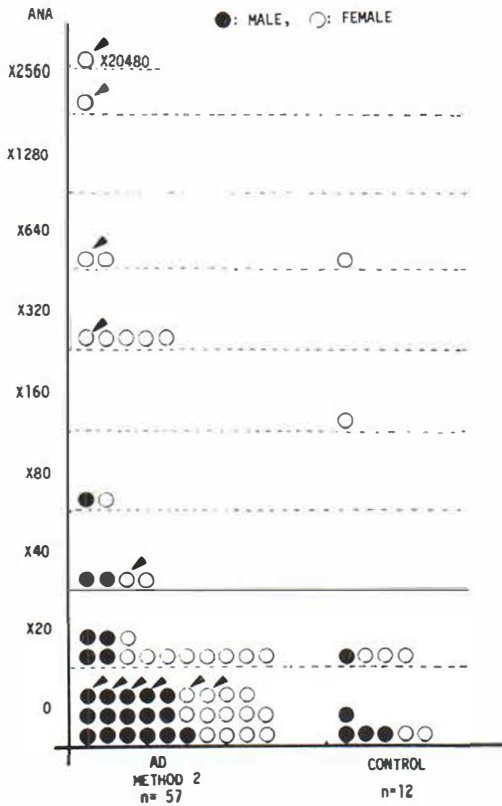


Fig. 2. ANA measured with method 2. Arrowheads: severe atopic dermatitis.

In the control study, positive ANA was found in 25.0% tested with method 1 and 16.7% examined with method 2 (Figs 1, 2). A high titre of ANA ($\times 640$, homogeneous and speckled type) was seen in a case examined by method 2 who had no other abnormal immunological data.

DISCUSSION

In our study, 34.0% of AD patients tested with method 1 and 26.0% of AD patients examined with method 2 had positive ANA. These values were obviously higher than control values. The frequency of positive ANA in healthy individuals younger than 60 years is said to be between 2% and 10% (6, 7, 8). Approximately 38% of individuals over 60 years of age have ANA in significant titres (2). Although the reason why our AD patients had higher ANA is not known, many of them had facial lesions resembling butterfly rash of SLE. We performed further investigations (including anti-DNA, serum complement level, gamma-globulin, and MED) in severe AD patients (shown in Fig. 2). However, the results all fell within the normal range. Recently, drug-induced antinuclear antibodies have been reported in epilepsy patients (9, 10). In addition, it is known that several inflammatory diseases have positive ANA; e.g., 32% of sarcoidosis patients had positive ANA (3). Chronic hepatitis patients tended to have a high frequency of positive ANA (2). Our patients had no other symptoms than skin eruption due to atopic dermatitis, nor did they receive medication with anti-epileptic agents.

Autoantibody formation in the sera of patients having ther-

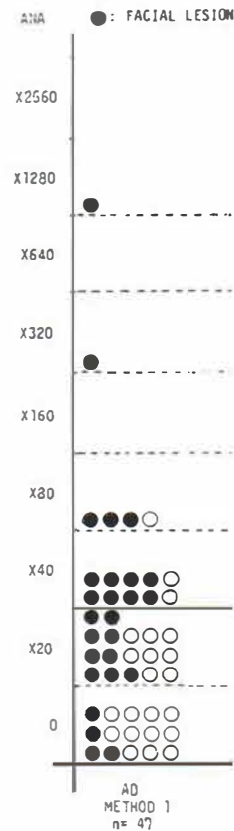


Fig. 3. Facial lesion (●) and ANA.

mal injury was reported recently and noticeably increased frequencies of ANA were found, ranging from 25% of pre-treatment serum samples to 78% of serum samples taken following treatment for burn injury in which polymyxin B was used (11). A small dose of polymyxin B in the treatment of burn injury has some ability with endotoxin to inhibit suppressor T cell activity (12). Although it is not clear whether thermal injury itself produces ANA, or whether polymyxin B with endotoxin induces ANA, AD patients usually have long-standing dermatitis causing considerable skin damage and have abnormalities of cell-mediated immunity, especially in suppressor T cell activity (13). Therefore, it is conceivable that ANA may be produced in AD patients when the clinical course is protracted. Further controlled study is needed.

ACKNOWLEDGEMENT

We would like to thank Mrs C. Kassai for her excellent technical assistance.

REFERENCES

- Davis JS. Antinuclear antibodies (ANA). In: Kelly WN, Harris ED, Ruddy S, Sledge CB, eds. Textbook of rheumatology. Philadelphia: WB Saunders Co, 1981: 691-709.
- Wilson MR. Antinuclear antibodies and anticytoplasmic antibodies in lupus erythematosus. In: Wallace DJ, Dubois EL, eds. Dubois' lupus erythematosus. Philadelphia: Lea & Febiger, 1987: 227-243.
- Veien NK, Hardt F, Bendixen G, Ringsted J, Brodthagen H, Farber V, Genner J, Heckscher T, Svejgaard A, Sørensen SF.

- Wanstrup J, Wiik A. Immunological studies in sarcoidosis: A comparison of disease activity and various immunological parameters. *Ann NY Acad Sci* 1976; 278: 47-51.
4. Frain-Bell W, Scatchard M. The association of photosensitivity and atopy in the child. *Br J Dermatol* 1971; 85: 105-110.
 5. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Dermatovener (Stockholm) suppl.* 1980; 92: 44-47.
 6. Rothfield NF. Detection of antibodies to nuclear antigens by immunofluorescence. In: *Manual of clinical immunology*. Washington, D.C.: American Society Microbiology, 1976; 647-651.
 7. Nakamura RM. Immunopathology. In: *Clinical laboratory concepts and methods*. Boston: Little, Brown, 1974.
 8. Xu L, Chang V, Murphy A, Rock JA, Damewood M, Schlaff W, Zacur HA. Antinuclear antibodies in sera of patients with recurrent pregnancy wastage. *Am J Obstet Gynecol* 1990; 163: 1493-1497.
 9. Alballa S, Fritzler M, Davis P. A case of drug induced lupus due to carbamazepine. *J Rheumatol* 1987; 14: 599-600.
 10. De Giorge CM, Rabinowicz AL, Olivas RD. Carbamazepine-induced antinuclear antibodies and systemic lupus erythematosus-like syndrome. *Epilepsia* 1991; 32: 128-129.
 11. Moran KT, Anholt GT, O'Reilly TJ, Thupari JN, Munster AM. Autoantibody formation in burn patients after inhibition of suppressor T cell activity with polymyxin B. *J Burn Care Rehabil* 1989; 10: 213-215.
 12. Munster AM. Immunologic alterations following injury. *Adv Orthop Surg* 1985; 1: 328-332.
 13. Valverde E, Vich JM, Huguet J, García-Calderón JV, García-Calderón PA. An *in vitro* study of lymphocytes in patients with atopic dermatitis. *Clin Allergy* 1983; 13: 81-88.