Acta Dermatovenerol Croat 2006;14(3):149-152 ORIGINAL SCIENTIFIC ARTICLE

Serum Levels of Total Immunoglobulin E in Patients with Alopecia Areata: Relationship with Clinical Type of the Disease

Emina Kasumagić-Halilović, Asja Prohić

Department of Dermatovenereology, Sarajevo University Clinical Center, Sarajevo, Bosnia and Herzegovina

Corresponding author:
Emina Kasumagić-Halilović, MD, MS
Department of Dermatovenereology
Sarajevo University Clinical Center
Bolnička 28
71000 Sarajevo
Bosnia and Herzegovina
kasumagicemina@yahoo.com

Received: June 13, 2006
Accepted: July 12, 2006

SUMMARY Alopecia areata (AA) is a heterogeneous disease characterized by nonscarring hair loss on the scalp or any hair-bearing surface. A wide range of clinical presentations can occur, from a single patch of hair loss to complete loss of hair on the scalp (alopecia totalis, AT) or over the entire body (alopecia universalis, AU). The cause of AA is unknown although most evidence supports the hypothesis that AA is an immunologically mediated disease. The aim of the study was to compare serum levels of total immunoglobulin E (IgE) between patients with AA and healthy subjects, and to assess the difference between the localized form and extensive forms of the disease such as AT and AU. Sixty patients with AA and 50 healthy subjects were enrolled in the study. Fifty patients had localized AA (LAA), and ten patients had AT, AU or AT/AU. Serum levels of IgE were measured using fluoroenzyme immunoassay techniques. Serum levels of total IgE were significantly higher in AA patients than in controls ($p<0.05$). There was no significant difference in serum levels of total IgE between patients with LAA and those with extensive forms of the disease ($p>0.05$). The exact role of serum IgE in AA should be additionally investigated in future studies.

KEY WORDS: alopecia areata; total serum immunoglobulin E

INTRODUCTION

Alopecia areata (AA) is a heterogeneous disease characterized by nonscarring hair loss on the scalp or any hair-bearing surface. It occurs in either sex, and any age can be affected. Approximately 1.7% of the population will experience an episode of AA during their lifetime (1). A wide range of clinical presentations can occur, from a single patch of hair loss to complete loss of hair on the scalp (alopecia totalis, AT) or over the entire body (alopecia universalis, AU). The cause of AA is unknown although most evidence supports the hypothesis that it is an immunologically mediated disease (2,3). The loss of hair is related to alterations in the normal cycle of hair growth. A hereditary component has been identified in patients with AA, and according to current information it is most likely a polygenic disease (4). The factors that influence the course and extent of AA are not known, making it impossible to predict the disease outcome at the time of presentation (5).

The discovery of immunoglobulin E (IgE) and the development of radioimmunoassay techniques for IgE estimation were major stimuli to the investigation of allergic diseases (6). Although serum IgE concentrations are low in normal health condition, they are high in atopy, parasitosis (7),

Acta Dermatovenerol Croat
2006;14(3):149-152

human immunodeficiency virus (HIV) infection (8), and certain types of cancer. In some of these diseases, serum IgE concentration correlated with the activity and intensity of the disease, and may be used as a prognostic factor. Serum IgE levels in dermatologic condition other than atopic dermatitis usually have been reported as normal (9,10), although increased serum IgE concentrations have been documented in patients with contact allergic dermatitis, systemic lupus erythematosus (11), and psoriasis (12).

Literature data on serum IgE in patients with AA are very limited and results are controversial. Therefore, the aim of our study was to evaluate serum concentrations of total IgE in AA patients and control subjects, and also to assess the difference between the localized and extensive forms of the disease such as AT and AU.

PATIENTS AND METHODS

Patients

The study included 60 patients with AA (32 female and 28 male, median age 32.5 years). Family history and data on the duration and severity of the disease were collected. Fifty patients had LAA, and ten patients had AT, AU or AT/AU. The patients were characterized according to AA investigational assessment guidelines (13). None of the patients included in the study received systemic treatment for AA.

Control group consisted of 50 generally healthy subjects (38 female and 12 male, median age 36.9 years). They did not have any scalp lesions in their personal history or on clinical examination.

The total group of AA patients and the two patient subgroups divided according to scalp hair loss were compared to the control group. Group 1 (n=60) included all AA patients, group 2 (n=50) patients with localized AA, and group 3 (n=10) patients with AT, AU or AT/AU.

Methods

The levels of total IgE were determined by the CAP system fluoroenzyme immunoassay (Pharmacia CAP System FEIA Pharmacia Diagnostics AB) according to the manufacturer's instructions. Results were expressed in kU/L. The assay was calibrated against the World Health Organization standard for IgE, with 2-2000 kU/L for total IgE.

Statistical analysis

Statistical comparisons were performed using χ^2-test. Data were considered statistically significant at $p<0.05$.

RESULTS

A total of 60 patients (32 female and 28 male) were examined. Family history was positive for AA in 5 of 60 (8.3%) patients. The duration of AA ranged from 1 to 168 months. Twenty-two of 60 (36.6%) AA patients had elevated serum concentrations of total IgE. The range of individual IgE levels was wide. IgE values showed no significant sex difference. There was no correlation between the duration of AA and serum IgE concentration. Concerning two subgroups of AA patients with extensive forms, LAA group and AT, AU or AT/AU group, elevated IgE levels were recorded in 18 (36.0%) and 4 (40.0%) patients, respectively. In control group, 8 (16.0%) volunteers had elevated serum IgE levels. Serum levels of total IgE were significantly higher in AA patients than in control subjects ($p<0.05$). A significant difference was observed in serum levels of IgE between LAA patients and control group ($p<0.05$). In AT/AU patients, serum levels of IgE were not significantly higher than those measured in controls ($p>0.05$). There was no significant difference in IgE levels between LAA patients and extensive AA group ($p>0.05$) (Table 1).

Table 1. Serum levels of IgE in patients with AA, LAA, AT, UA and in control group

	Number of patients	Elevated IgE n (%)
AA	60	22 (37)
LAA	50	18 (36)
AT, AU or AT/AU	10	4 (40)
Control group	50	8 (16)

AA, alopecia areata; LAA, localized alopecia areata; AT, alopecia totalis, AU, alopecia universalis

DISCUSSION

AA is an ancient disease that was known to Egyptians even in the pre-Christian time (14). Despite its long history, our knowledge is actually limited. Of the numerous pathogenic processes which have been proposed as the underlaying pathogenic causes of AA, immune, environmental and genetic factors (2,5,15) are the most powerful explanation. The possible association of serum IgE levels and AA has been previously reported (16-18). Our study clearly demonstrated that total serum IgE was significantly increased in AA

patients (36.6%) in comparison to healthy subjects (16%). These results are consistent with a clinical study performed by O'Loughlin *et al.* (16). They analyzed serum IgE levels in 497 Mayo Clinic patients with various forms of dermatitis and common dermatoses, and found serum levels of IgE to be elevated in 30% of AA patients. Our findings are similar to the study of Bork *et al.* (17), who also recorded a significant increase in serum IgE (32%) in children with AA. Similar results have been reported by Przybilla *et al.* (18), who found elevated total serum IgE in 19.7% of AA patients. Nevertheless, our observations of serum IgE concentrations in AA patients were in contrast to some previous studies (19,20), which did not find an increase in IgE levels.

Accordingly, our results suggest that elevation of total serum IgE might be a common feature in AA. Unfortunately, the mechanism by which IgE might interact in the pathogenesis of AA is unknown. An attractive explanation is supported by genetic linkage analyses, which have revealed a possible co-inheritance of the genetic loci. Multiple genetic studies on total IgE regulation have been performed. IgE responsiveness has recently been linked to a locus on chromosome 11q13 close to a gene encoding β-subunit of the high-affinity IgE receptor (21). A hereditary component has also been identified in patients with AA, and on the basis of present information it most likely represents a polygenic disease (4). Tarlow *et al.* (22) demonstrated an association between the severity of AA and the frequency of allele 2 of the 5 allele polymorphism in intron 2 of the interleukin 1 receptor antagonist gene. This allele is also associated with severity in other chronic inflammatory disorders. Associations have also been reported with immunoglobulin heavy chain (Gm) and light chain (Km) allotypes in AA (23), raising the possibility of involvement of genes on chromosome 2 or 14 (15). The importance of genetic factors in the etiology of AA is underlined by the frequency of positive family history in affected individuals. In most reports, it ranges from 10% to 20% of cases (15,24). There also are several reports of AA in twins, sometimes with concurrent onset (25).

The evidence suggests that AA is a clinical reaction pattern that is the result of combinations of genetic and environmental factors. Each of these factors plays a role but none, on its own, is sufficient to cause the disease (15). In our opinion, the investigation of this mechanism is very important because it should provide information on the pathogenesis of AA.

CONCLUSION

In summary, this study supports the evidence that elevation of total serum IgE is associated with AA, although this association may be limited to a selected patient population. Additional studies are clearly warranted to elucidate whether these observations represent a causal, pathogenic, or non-causal association.

References

1. Safavi KH, Muller SA, Suman VJ, Moshell AN, Melton IJ. Incidence of alopecia areata in Olmsted County, Minnesota, 1975-1989. Mayo Clin Proc 1995;70:628-33.
2. Madani S, Shapiro J. Alopecia areata update. J Am Acad Dermatol 2000;42:549-66.
3. Hoffmann R. The potential role of cytokines and T cells in alopecia areata. J Invest Dermatol Symp Proc 1999;4:235-8.
4. McElwee KJ, Freyschmidt-Paul P, Ziegler A, Happle R, Hoffmann R. Genetic susceptibility and severity of alopecia areata in human and animal models. Eur J Dermatol 2001;11:11-6.
5. Alexis AF, Dudda-Subramanya R, Sinha AA. Alopecia areata: autoimmune basis of hair loss. Eur J Dermatol 2004;14:364-70.
6. Ishizaka K, Ishizaka T, Hornhbrook MM. Physicochemical properties of reaginic antibody. IV. Presence of a unique immunoglobulin as a carrier of reaginic activity. J Immunol 1966;97: 75-85.
7. Sutton BJ, Gould HJ. The human IgE network. Nature 1993;366:421-8.
8. Mazza DS, Grieco MH, Reddy MM, Meriney D. Serum IgE in patients with human immunodeficiency virus infection. Ann Allergy Asthma Immunol 1995;74:411-4.
9. Gurevitch AW, Heiner DC, Reisner RM. IgE in atopic dermatitis and other common dermatoses. Arch Dermatol 1973;107:712-5.
10. Krueger GG, Kahn G, Weston WL, Mendel MJ. IgE levels in nummular eczema and ichthyosis. Arch Dermatol 1973;107:56-8.
11. Mikecz K, Sonkoly I, Meszaros C, Szegedi G. Serum IgE level in systemic lupus erythematosus. Acta Med Hung 1985;42:59-65.
12. Li LF, Sujan SA, Yang H, Wang WH. Serum immunoglobulins in psoriatic erythroderma. Clin Exp Dermatol 2005;30:125-7.

13. Olsen E, Hordinsky M, McDonald-Hull S, Price V, Roberts J, Shapiro J. Alopecia areata investigational assessment guidelines. J Am Acad Dermatol 1999;40:242-6.
14. Ebel B. The papyrus Ebers: The greatest Egyptian medical document. Copenhagen: Leivin and Munksgaard; 1937.
15. McDonagh AJG, Messenger AG. The pathogenesis of alopecia areata. Dermatol Clin 1996;14:661-70.
16. O'Loughlin S, Diaz-Perez JL, Gleich GJ, Winkelmann RK. Serum IgE in dermatitis and dermatosis. Arch Dermatol 1977;113:309-15.
17. Bork J, Dallaire M, Lewis S, Boeck C, Hordinsky M. Childhood alopecia areata and atopy: a significant disease association. Am J Hum Genet 1995;57:619-28.
18. Przybilla B, Ring J, Volk M. Total IgE levels in the serum in dermatologic diseases. Hautarzt 1986;37:77-82.
19. Roselino AM, Almeida AM, Hippolito MA, Cerqueira BC, Maffei CM, Menzes JB, *et al.* Clinical-epidemiologic study of alopecia areata. Int J Dermatol 1996;35:181-4.
20. Whitmont KJ, Cooper AJ. PUVA treatment of alopecia totalis and universalis: a retrospective study. Australas J Dermatol 2003;44:106-9.
21. Sandford AJ, Shirakawa T, Moffat MF, Daniels SE, Ra C, Faux JA, *et al.* Localisation of atopy and β subunit of high-affinity IgE receptor (FcεRI) on chromosome 11q. Lancet 1993;341:332-4.
22. Tarlow JK, Clay FE, Cork MJ, Blakemore AI, McDonagh AJ, Messenger AG. Severity of alopecia areata is associated with a polymorphism in the interleukin-1 receptor antagonist gene. J Invest Dermatol 1994;103:387-90.
23. Galbraith GM, Pendey JP. Km1 allotype association with one subgroup of alopecia areata. Am J Hum Genet 1989;44:426-8.
24. Colombe BW, Lou CD, Price VH. The genetic basis of alopecia areata: HLA associations with patchy alopecia areata versus alopecia totalis and alopecia universalis. J Invest Dermatol Symp Proc 1999;4:216-9.
25. Scerri L, Pace JL. Identical twins with identical alopecia areata. J Am Acad Dermatol 1992;27:766-7.

Loosing your hair? Trilysin used every day helps! Year 1935.
(from the collection of Mr. Zlatko Puntijar)