

Familial Alopecia areata—Genetic Susceptibility or Coincidence?

R. VALSECCHI,¹ O. VICARI,² A. FRIGENI,¹ L. FOIADELLI,¹ L. NALDI¹ and T. CAINELLI¹

¹Department of Dermatology and ²Department of Immunohematology, Ospedali Riuniti, Bergamo, Italy

Valsecchi R, Vicari O, Frigeni A, Foiadelli L, Naldi L, Cainelli T. Familial alopecia areata, genetic susceptibility or coincidence? *Acta Derm Venereol* (Stockh) 1985; 65: 175–177.

Three generations of a not consanguineous Italian family and 40 subjects suffering from alopecia areata (AA) and residing in Northern Italy were studied. There were 321 healthy control subjects of both sexes. Six family members from three generations were affected with alopecia universalis. The subjects were HLA-phenotyped using different HLA-A, B and C antigen specificities. No significant association was found between HLA-A, B and C antigens and AA patients at the population level. Segregation analysis showed that affected members shared a common haplotype, HLA-Aw32, B18,-. *Key words: Familial alopecia areata; HLA-phenotyping; Common haplotype.* (Received September 19, 1984.)

R. Valsecchi, Department of Dermatology, ●spedali Riuniti, I-24100 Bergamo, Italy.

Alopecia areata (AA) is a common hair disease whose etiopathogenesis still remains to be elucidated. In the past few years some reports suggested the possibility that immunologic and genetic factors may play an important role in this disease (1–5). The familial incidence of AA is between 10% to 20% (6). To investigate further the importance of the genetic factors in the AA patients, we have studied 40 subjects with AA and particularly three generations of a non-consanguineous Italian family in which six members had alopecia universalis (AU). The HLA-Aw32, B18,-haplotype was noted in all affected members of three generations.

MATERIAL AND METHODS

Three generations of a non-consanguineous Italian family and other 40 AA patients residing in Northern Italy were studied. Of the six affected family members, five were men. All six affected members showed a similar clinical pattern of AA (alopecia universalis) (disease expressiveness) with early outcome in age, similar in all members (disease penetrance). Patients II-1 and II-2, on several occasions, had experienced the spontaneous regrowth and subsequent loss of their hair. All six patients showed nail pitting, a common occurring phenomenon in patients with AA. In our family there was no history of thyroid disease, vitiligo, rheumatoid arthritis, pernicious anemia, Addison's disease, diabetes mellitus connective tissue disorders or atopy. In AA patients HLA typing was performed by the microlymphocytotoxicity standard test for the following specificities: A1, A2, A28, A3, A9, A10, A11, A29, Aw30, Aw31, Aw32, Aw33; B5, B7, B8, B35, B12, B13, B40, B47, B41, B14, B18, B15, B16, B17, B21, B22, B27, B37; Cw1, Cw2, Cw3, Cw4, Cw5, Cw6.

There were 321 healthy control subjects of both sexes. None had a history of AA. All subjects lived in the same geographical area as the patients and were typed at the same time as the patients. The significance of possible deviations between the frequencies observed in the patients and in the control subjects has been evaluated by means of χ^2 analysis (2x2 contingency tables) with the correction of

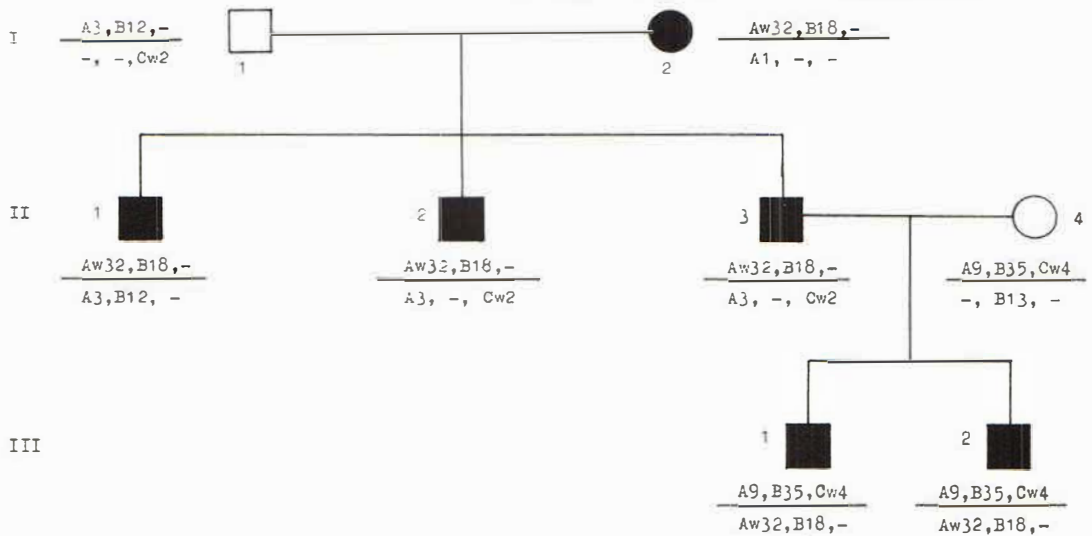


Fig. 1. Square indicates male, circle indicates female; solid square and solid circle denote affected family member. Dash (-) represents "blank".

Yates for discontinuities. The values of the strength and rank of association was obtained by calculating the relative risk (RR).

RESULTS

The frequencies of the HLA-A, B and C antigens showed no statistically significant differences between the 40 AA patients and controls. From a family study emerged that AA in the subjects examined in the three generations segregates in association with HLA-Aw32, B18,-haplotype, where the short line (-) is "blank" (Fig. 1).

DISCUSSION

The familial incidence of AA, on the different clinical patterns, has been reported to be between 10% to 20% (6). In the study by Muller & Winkelmann, a review of 736 patients, one parent and child were affected in 18 instances and siblings alone in 21 instances. Two pairs of identical twins of undetermined type were affected.

After these clinical observations, HLA phenotyping was available to examine this issue. A study of 47 unrelated Finnish patients with AA has shown an increase in the frequency of HLA-B12 with RR of 3.59 (5); moreover a study of 46 AA patients in Jerusalem showed a significant increase in the frequency of HLA-B18 (23.9%) as compared to the control population (7.4%) with RR of 3.9 (4). On the other hand, Kuntz et al. (7) studied 70 unrelated German patients with AA and found no statistically significant HLA antigen frequency. From our study the disease seems genetically determined as mendelian dominant trait. The positive segregation of AA with HLA-Aw32, B18,-haplotype suggests a non-random association between disease and HLA system. A recent report about AA association with a different haplotype (HLA-A2, B40) (2) in an American family suggests a locus mapping closely associated—without linkage disequilibrium—with a single HLA haplotype. The absence of association between AA and HLA antigen at population level is in agreement with our hypothesis. Therefore it is necessary to increase the number of

informative families from different geographical areas or from different ethnic groups to exclude a simple coincidence.

REFERENCES

1. Giannetti A, Silverio AD, Castellazzi AM, Maccario R. Evidence for defective T cell function in patients with alopecia areata. *Br J Dermatol* 1978; 98: 261.
2. Hordinsky-Kramarczuk M, Hallgren H, Nelson D, Filipovich AH. Familial alopecia areata. HLA antigens and autoantibody formation in an American family. *Arch Dermatol* 1984; 120: 464-468.
3. Filipovich AH, Hordinsky-Kramarczuk M, Nelson D, Hallgren H. The correlation between inducer-suppressor ratios, generation of concanavalin-A activated suppressor cells and mitogen-stimulated proliferation of peripheral blood lymphocytes in patients with alopecia areata and normal controls. *Clin Immunol Immunopathol* 1982; 25: 21-31.
4. Hacham-Zadeh S, Brautbar C, Cohen CA, Cohen T. HLA and alopecia areata in Jerusalem. *Tissue Antigens* 1981; 18: 71-74.
5. Kianto U, Reunala T, Karvonen J, Lassus A, Tiilikainen A. HLA-B12 in alopecia areata. *Arch Dermatol* 1977; 113: 1716.
6. Muller SA, Winkelmann RD. Alopecia areata: an evaluation of 736 patients. *Arch Dermatol* 1963; 88: 290-297.
7. Kuntz BME, Selzle D, Braun-Falco D, Scholz S, Albert ED. HLA antigens in alopecia areata. *Arch Dermatol* 1977; 113: 1717.