Acta Derm Venereol (Stockh) 1991; 71: 407–410

Stigmata of Atopic Constitution in Patients with Atopic Eczema or Atopic Respiratory Disease

BERNHARD PRZYBILLA,[1] JOHANNES RING,[2] FRIEDEMANN ENDERS[1] and HANS WINKELMANN[1]

[1] *Dermatology Clinic and Policlinic of the Ludwig-Maximilians-University, Munich, and* [2]*Dermatology Clinic of the University Hospital, Hamburg-Eppendorf, Federal Republic of Germany*

In the diagnosis of atopic eczema, minor physical markers (stigmata) frequently provide valuable clues. The prevalence of nine stigmata (dry skin, hyperlinearity of the palms or soles, infraorbital fold, white dermographism, facial pallor, orbital darkening, Hertoghe's sign, low hairline) was evaluated in 34 atopic eczema patients without atopic respiratory disease, in 16 patients with allergic rhinitis and/or asthma without atopic eczema, and in 23 controls without atopic respiratory or eczematous disease, and with negative results at prick testing with three common aeroallergens. Compared with controls, all features except Hertoghe's sign were significantly ($p < 0.01$) more frequent in atopic eczema, and, except for Hertoghe's sign, dry skin and white dermographism, they were significantly (low hairline, $p < 0.05$; others, $p < 0.01$) more frequent also in respiratory disease. The prevalence of most stigmata did not differ significantly ($p > 0.05$) in cutaneous vs. respiratory atopic disease, only dry skin being more frequent in atopic eczema ($p < 0.05$). Although not specific, most stigmata are characteristic markers not only of atopic eczema, but of atopy as such.

(Accepted March 13, 1991.)

Acta Derm Venereol (Stockh) 1991; 71: 407–410.

B. Przybilla, Dermatologische Klinik und Poliklinik, Frauenlobstraße 9–11, D-W-8000 München 2, FRG.

Up to now, there is no definite marker which would allow to decide whether atopy is present or absent in a given individual. However, there are numerous features which are characteristic, but mostly non-specific indicators of atopy. Among these, minor physical markers in particular provide clinically valuable clues. Such stigmata have been reported as markers of atopic eczema by Hanifin & Rajka (1), and also by others (2–6). Particularly in recent years the prevalence of some of these features has been studied quantitatively in atopic eczema and controls (7–16). Despite their importance in the diagnosis of atopic eczema, the presence of such stigmata in atopic respiratory disease has not yet been investigated systemically. We have compared the prevalence of nine stigmata in three groups: *a*) atopic eczema (AE) patients free from history of atopic respiratory disease; *b*) patients with allergic rhinitis and/or asthma without present or previous AE; *c*) rigorously defined controls.

MATERIALS AND METHODS

Subjects

The study population consisted of consecutive patients and clinic personnel. Individuals were included in the study if they fitted into one of the following three groups characterized on the basis of anamnesis, inspection of the entire skin surface, and skin prick testing with three common aeroallergens (grass pollen, house dust mite *D. pteronyssinus*, cat epithelium; Bencard, Neuss):

Atopic eczema patients: 34 patients (16 males, 18 females; 25.5 ± 16.6 years old) with a history of as well as current manifestations of AE (diagnosed according to [1]) and without indications of prior or current respiratory atopic disease (allergic rhinoconjunctivitis, asthma bronchiale). All patients had flexural eczema and at least one positive reaction to one of the aeroallergens tested (the latter being not an inclusion criterion).

Patients with atopic respiratory disease. This group was comprised of 16 individuals (7 males, 9 females; 17.4 ± 7.0 years old) with allergic rhinoconjunctivitis and/or asthma bronchiale without a history of previous or present manifestations of AE. Atopic respiratory diseases had been diagnosed on the basis of a typical history and the demonstration of corresponding sensitization in the skin prick test or RAST. Although not being an inclusion criterion, all patients exhibited at least one positive reaction to one of the three aeroallergens.

Controls. These were 23 individuals (11 males, 12 females; 23.0 ± 15.3 years old) without indications of a personal or family history of AE, allergic rhinoconjunctivitis or asthma and with negative results at prick testing with the aeroallergens.

Evaluation of stigmata

The following stigmata were assessed: dry skin, hyperlinearity of the palms/soles, white dermographism (testing performed with a blunt instrument on clinically normal skin, usually the upper back), facial pallor, orbital darkening, Hertoghe's sign (lateral thinning or absence of the eyebrows) and low hairline (reduced distance between

Table I. *Prevalence of stigmata of atopic constitution*

Feature	Controls (n = 23)		Atopic eczema (n = 34)		Atopic respiratory disease (n = 16)	
	% of n	$P^1<$	% of n	$P^2<$	% of n	$P^3<$
Dry skin	31	0.01	74	0.05	44	ns
Moderate at least	0	0.01	50	ns	25	0.05
Prominent	0	0.01	32	ns	13	ns
Hyperlinear palms	48	0.01	88	ns	94	0.01
Moderate at least	18	0.01	64	ns	50	0.01
Prominent	4	0.01	35	ns	25	0.01
Hyperlinear soles	30	0.01	74	ns	81	0.01
Moderate at least	8	0.01	44	ns	50	0.01
Prominent	4	ns	15	ns	6	ns
Infraorbital fold	13	0.01	82	ns	81	0.01
Moderate at least	4	0.01	59	ns	31	0.01
Prominent	0	0.05	9	ns	6	ns
White dermographism	4	0.01	38	ns	13	ns
Facial pallor	13	0.01	85	ns	75	0.01
Moderate at least	4	0.01	47	ns	19	0.05
Prominent	0	ns	6	ns	0	ns
Orbital darkening	26	0.01	85	ns	100	0.01
Moderate at least	0	0.01	41	ns	50	0.01
Prominent	0	0.01	18	ns	6	ns
Hertoghe's sign	44	ns	68	ns	69	ns
Moderate at least	14	0.05	35	ns	38	ns
Prominent	0	ns	6	ns	6	ns
Low hairline	52	0.01	88	ns	88	0.05
Moderate at least	26	0.01	65	ns	69	0.01
Prominent	9	0.01	47	ns	38	0.05

P^1: Frequency in controls compared with atopic eczema patients. P^2: Frequency in atopic eczema patients compared with patients with atopic respiratory disease. P^3: Frequency in controls compared with patients with atopic respiratory disease. ns = not significant.

scalp hairs and the upper margin of the eyebrows). Most stigmata were graded as 'absent', 'mild', 'moderate' or 'prominent'; white dermographism was graded as 'absent' or 'present' only.

Regarding dry skin, hyperlinearity of palms/soles, facial pallor and orbital darkening, grading was done on the basis of the clinical impression. The other features, if present, were graded as follows. *Infraorbital fold.* Mild: underlining at most the medial half of the palpebral fissure; moderate: underlining at most the whole palpebral fissure; prominent: going beyond the palpebral fissure; *Hertoghe's sign.* Lateral thinning or absence of the eyebrows: mild: extending not beyond the lateral corner of the palpebral fissure; moderate: involving the eyebrow above the lateral quarter of the palpebral fissure; prominent: extending to the eyebrow above the medial three-quarters of the palpebral fissure; *Low hairline.* The lowest distance between scalp hairs and the upper margin of the eyebrows was measured: mild: 1.6 to 3.0 cm; moderate: up to 1.5 cm; prominent: direct transition from scalp hair to eyebrow. For statistical analysis, Fisher's exact test was used. If $p < 0.05$, differences were regarded as significant.

RESULTS

Detailed results are given in Table I. Apart from Hertoghe's sign, all other features were significantly more common in AE patients than in controls. Patients with atopic respiratory disease and controls did not differ significantly with regard to the prevalence of dry skin, white dermographism or Hertoghe's sign. The other stigmata assessed were significantly more common in patients with atopic respiratory disease than in controls. The prevalence of most stigmata did not differ significantly between patients with atopic eczema and atopic respiratory disease, only dry skin being more frequent in AE

patients. Dry skin, hyperlinearity of the palms and low hairline were the most prevalent stigmata prominently expressed by atopic patients.

DISCUSSION

Compared with controls, the prevalence of most stigmata evaluated was significantly higher in patients with atopic diseases. Only the prevalence of Hertoghe's sign did not differ significantly within the three groups and there were no significant differences between controls and patients with atopic respiratory disease regarding the prevalence of dry skin and white dermographism. When patients with atopic cutaneous or respiratory disease were compared, no significant differences in the prevalence of most stigmata were found, only dry skin being more frequent in individuals with eczema. This indicates that most of the features are constitutional markers not only of AE, but rather of the atopic state as such. However, they are not specific for atopy, as they are present also in quite a number of presumably non-atopic individuals. Grading of the expression of stigmata evidently enhances their diagnostic value, as particularly among controls the frequency of more pronounced features is much lower than their overall prevalence. When considering only strongly expressed stigmata, a loss of sensitivity has to be accepted.

Many of the features evaluated have been found in other studies to be significantly more common in AE patients than in controls, e.g. dry skin (12, 13, 15, 16), hyperlinearity of the palms (13, 15), infraorbital fold (12, 15), white dermographism (13, 14), facial pallor (12, 13), orbital darkening (13), and Hertoghe's sign (15). No such differences were found in a few studies with regard to hyperlinearity of the palms (11), infraorbital fold (14), or white dermographism (12). To the best of our knowledge, the prevalence of hyperlinearity of the soles or of low hairline, a stigma not found mentioned in the English, but only in the German literature (2, 5, 6, 17), has not yet been evaluated.

It has been claimed that some stigmata are actually not constitutional, but that they are rather direct manifestations or sequelae of AE. This has been put forward with regard to dry skin (18, 19), infraorbital fold (10), white dermographism on non-eczematous skin (8), orbital darkening (20), and Hertoghe's sign (20, 21). The interpretation of some features as secondary to disease may be right in certain, but evidently not in all cases. This is strongly suggested by the finding that patients with respiratory or cutaneous atopic disease did not differ significantly with regard to the prevalence of all stigmata but dry skin.

Infraorbital fold and orbital darkening have been known not only as features of AE, but also of atopic respiratory disease (22–24). Interestingly, this association has been reported for infraorbital fold already in the first description of this feature (22). However, quantitative data on the prevalence of stigmata in atopic respiratory disease are scarce. White dermographism was reported to occur in 10% of patients with asthma and/or atopic rhinitis, vis-à-vis 81% in lesional skin of AE (25). In another study (12) there was a significant correlation between the absence of orbital darkening and allergic rhinitis or asthma, which contrasts with our findings and other views (23, 24). Furthermore, also at variance with our results, the same authors found an association between asthma and the absence of an infraorbital fold (12). Due to the lack of other data, these discrepant findings must await further evaluation.

As there is as yet no method allowing one to establish or to exclude the presence of an atopic state, the assessment of constitutional stigmata can aid considerably in identifying presumably atopic individuals without manifest disease so far ('silent atopy'). However, as stigmata are non-specific, atopy should be presumed only in the presence of several clear-cut features. Identification of 'silent' atopics may be of considerable value both in the clinical setting, and for research purposes.

REFERENCES

1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; Suppl 92: 44–47.
2. Korting G. Zur Pathogenese des endogenen Ekzems. Stuttgart: Thieme, 1954.
3. Kierland RR. Certain stigmata associated with atopic dermatitis. In: Baer RL, ed. Atopic dermatitis. Philadelphia: Lippincott, 1955: 43–45.
4. Lobitz WC, Dobson RL. Physical and physiological clues for diagnosing eczema. J Am Med Assoc 1956; 161: 1226–1229.
5. Keining E, Braun-Falco O. Dermatologie und Venerologie. München: Lehmanns, 1969.
6. Braun-Falco O, Plewig G, Wolff HH. Dermatologie und Venerologie. Berlin: Springer, 1984.
7. Hirth L, Schöpf E, Benkmann HG, Goedde HW. Un-

tersuchungen der Hautfurchen bei Patienten mit endogenem Ekzem mit einem Beitrag zur Technik der Daktyloskopie. Anthrop Anz 1971; 33: 26–38.
8. Uehara M, Ofuji S. Abnormal vascular reactions in atopic dermatitis. Arch Dermatol 1977; 113: 627–629.
9. Meenan FOC. The significance of Morgan's fold in children with atopic dermatitis. Acta Derm Venereol (Stockh) 1980; Suppl 92: 42–43.
10. Uehara M. Infraorbital fold in atopic dermatitis. Arch Dermatol 1981; 117: 627–629.
11. Mevorah B, Marazzi A, Frenk E. The prevalence of accentuated palmoplantar markings and keratosis pilaris in atopic dermatitis, autosomal dominant ichthyosis and control dermatological patients. Br J Dermatol 1985; 1123: 679–685.
12. Svensson Å, Edman B, Möller H. A diagnostic tool for atopic dermatitis based on clinical criteria. Acta Derm Venereol (Stockh) 1985; Suppl 114: 33–40.
13. Kang K, Tian R. Atopic dermatitis. An evaluation of clinical and laboratory findings. Int J Dermatol 1987; 26: 27–32.
14. Mevorah B, Frenk E, Wietlisbach V, Carrel CF. Minor clinical features of atopic dermatitis. Evaluation of their diagnostic significance. Dermatologica 1988; 177: 360–364.
15. Diepgen TL, Fartasch M, Hornstein OP. Evaluation and relevance of atopic basic and minor features in patients with atopic dermatitis and in the general population. Acta Derm Venereol (Stockh) 1989; Suppl 144: 50–54.
16. Werner Linde Y. 'Dry' skin in atopic dermatitis. I. Aclinical study. Acta Derm Venereol (Stockh) 1989; 69: 311–314.
17. Ring J. Angewandte Allergologie. München: MMW Medizin Verlag, 1988.
18. Finlay AY, Nicholls S, King CS, Marks R. The »dry« non-eczematous skin associated with atopic eczema. Br J Dermatol 1980; 102: 249–256.
19. Uehara M. Clinical and histological features of dry skin in atopic dermatitis. Acta Derm Venereol (Stockh) 1985; Suppl 114: 82–86.
20. Hanifin JM. Atopic dermatitis. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, eds. Allergy. Principles and practice, 3rd edn. St. Louis: Mosby, 1988: 1403–1428.
21. Urbach E. Klinik und Therapie der allergischen Krankheiten. Wien: Maudrich, 1935.
22. Morgan DB. A suggestive sign of allergy. Arch Dermatol 1948; 57: 1050.
23. Marks MB. Physical signs of allergy of the respiratory tract in children. Ann Allergy 1967; 25: 310–317.
24. Meltzer EO, Schatz M, Zeiger RS. Allergic and nonallergic rhinitis. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, eds. Allergy. Principles and practice, 3rd edn. St. Louis: Mosby, 1988: 1235–1289.
25. Rajka G. Prurigo Besnier (atopic dermatitis) with special reference to the role of allergic factors. 1. The influence of atopic hereditary factors. Acta Derm Venereol (Stockh) 1960; 40: 285–306.