

Original article

Vascular pattern of the palms – a clinical feature of atopic skin diathesis

Background: Atopic skin diathesis is a clinical term to describe skin atopics with previous, present or future atopic eczema/dermatitis syndrome (AEDS). In clinical practice, an unequivocal assessment of atopic skin diathesis in non-eczematous patients may be difficult. The majority of the known clinical features included in diagnostic scores are characteristic, but not specific markers of atopy. Especially, the vasoreactivity of atopic skin is disturbed. This is manifested by white dermographism, an irregular vascular response to thermal stimuli, and paradoxical skin reactions to histamine, cholinergic agents, and nicotines.

Objective: The aims of our study were to investigate the clinical morphology of palmar vascular reactions in skin atopic and non-atopic individuals, and to determine whether this abnormal vascular reaction is more pronounced in skin atopic individuals.

Methods: Forty persons, 20 of them skin atopics, assessed by the Erlangen Atopy Score and an elevated serum IgE level (> 150 U/ml), were included in a prospective single-centre study. Standardized digital photographs of the palms were presented in a blinded manner to five dermatologists in random order by means of the computerized imaging analysis system KS400 3.0.

Results: Evaluation of the original rgb (red, green, blue) color images and modified gray-level images showed that a pronounced reticular pattern of erythema of the palms was significantly ($P < 0.0001$) more common in skin atopics (72% and 69.6%, respectively).

Conclusion: The gross vascular pattern of the palm might be an additional diagnostic feature of atopy, and further studies are needed to establish its exact prevalence.

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The prevalence of atopic diseases such as asthma, rhinoconjunctivitis, and atopic eczema/dermatitis syndrome (AEDS) is rising in industrialized nations, considerably adding to the burden of healthcare costs (1, 2). Although atopy is a poorly defined condition, it is commonly recognized as a genotypic diathesis that causes a syndrome of immunologic aberrations (3, 4). Atopic individuals show a multitude of combinations and permutations of commonly associated genotypic findings, i.e. which are presented as xerosis and vascular abnormalities in the phenotype, referred to as minor features or associated criteria (3, 5, 6). Atopic skin diathesis is a clinical term to describe skin atopics with previous, present, or future AEDS (7, 8). Usually, the diagnosis of atopic diseases is based on the patient's history, and clinical and laboratory findings as proposed by different authors (5, 6, 9, 10). The frequency and significance of basic and minor features of atopy have been evaluated in the past, and diagnostic scores, such as the Erlangen Atopy Score by Diepgen et al.,

have been designed (7, 9, 11). This atopy score is a summary measure of anamnestic and clinical cutaneous features as well as symptoms of atopy (see Tables 1 and 2). According to Diepgen et al. (7) and Berndt et al. (12), an individual with an Erlangen Atopy Score ≥ 10 points, suffers from atopic skin diathesis. Well known vascular abnormalities in atopic persons are facial pallor, white dermographism following light or firm stroking of the skin, an irregular vascular pattern in response to thermal stimuli, and paradoxical skin reactions to histamine, cholinergic agents, and nicotines (3). In particular, pronounced erythematous maculae or reticulated erythema surrounding pale, angiospastic foci may be seen on the palms. We investigated this particular vascular reaction by comparing the palms of skin atopic and non-atopic patients under standardized conditions. The purpose of the study was to determine whether an abnormal vascular reaction of the palms is more prominent in skin atopics.

Table 1. The Erlangen Atopy Score proposed by Diepgen et al. (7) – a diagnostic scoring system based on anamnestic and clinical criteria of atopic symptoms and signs from the skin

Family history of atopy (first-degree relatives)	1 point
Personal history of allergic rhinitis	1 point
Personal history of allergic asthma	1 point
Cradle cap in the newborn period	1 point
Itch when sweating	3 points
Wool intolerance	3 points
Metal intolerance (e.g. nickel sensitivity)	1 point
Photophobia	1 point
Xerosis	3 points
Ear rhagades	2 points
Dyshidrosis/pompholyx	2 points
Pityriasis alba	2 points
Atopic winter feet/pulpitis sicca	2 points
Nipple eczema	2 points
Cheilitis sicca/perléche	1 point
Hyperlinear palms	2 points
Hertoghe's sign	2 points
Dirty neck	2 points
Keratosis pilaris	1 point
White dermographism	3 points
Acrocyanosis	1 point
Total serum IgE > 150 U/ml	1 point
Total serum IgE > 400 U/ml	2 points
Positive Phadiatop® test	1 point

Radioallergosorbent screening test for IgE-mediated allergy; Pharmacia Diagnostics.

Table 2. The number of patients with AEDS in percentage related to the summarized points in the Erlangen Atopy Score, without an inclusion of the laboratory results – according to Diepgen et al. (7)

Atopy points	Percentage of AEDS	Assessment
0–3	0	No atopic skin diathesis
4–7	5	Improbable atopic skin diathesis
8–9	34	Indistinct atopic skin diathesis
10–14	78	Atopic skin diathesis
15–19	97	Atopic skin diathesis
>20	100	Atopic skin diathesis

Methods

Study population

In a prospective single-center study, 40 Caucasian individuals aged between 18 and 50 years (average age: 32.18) were investigated over a 6-month period (March to August 2004). We enrolled 20 skin atopic individuals with more than 10 points in the Erlangen Atopy Score (see Tables 1 and 2) and an elevated serum IgE level (>150 U/ml), but no history of AEDS. Previous or present atopic symptoms from mucous membranes like allergic rhinitis, allergic conjunctivitis, or allergic asthma were not considered. In the control group, 20 persons were enrolled with <5 points in the Erlangen Atopy Score and no history of atopic respiratory disease. Exclusion criteria were as follows: intake of vasoactive drugs, consumption of nicotine, caffeine or alcohol within 2 h prior to the examination, and skin disease involving the palms.

Study measurements

Immunoglobulin E levels were measured in duplicate with Uni-CAP Technology in accordance with the specifications of the manufactures (Pharmacia Diagnostics, Uppsala, Sweden). For the purpose of acclimatization, the patients were allowed to sit in a draught-free room with a constant ambient temperature of 20–22°C for 15 min. The subject's right forearm was placed horizontally and in supination 20 cm below the level of the heart in order to avoid orthostatic effects. The right hand was also placed in a standardized horizontal position with the interphalangeal joints flexed at an angle of 35° and kept motionless for at least 3 min. The examination room was darkened. An electric daylight lamp (Daylight 100; Philips, Eindhoven, the Netherlands) placed at a distance of 100 cm above the test site served as a source of homogeneous illumination. Gross images of the palms (examination area 7.5 × 3.5 cm) were taken with a standard digital camera (Coolpix 990; Nikon, Tokyo, Japan) fixed on a tripod and the images were stored as JPEG files. A digital image of the right palm of each patient was transferred to the image analysis System KS400 3.0 (Zeiss Vision, Halbergmoos, Germany) and stored for further evaluation. Image analysis was performed with the red, green, blue (rgb) color system. A sequence of 100 image pairs was created; each pair consisted of one image of a skin atopic individual and a randomly selected counterpart of a non-atopic individual and was presented in a blinded manner to five independent observers. Each pair was displayed randomly; in other words, the observer was unaware of whether the image of the skin atopic individual was placed on the left or the right side of the screen. For each image pair, the observers had to judge whether the left or the right image showed a more pronounced vascular pattern than the counterpart image. The assessment was performed twice. In the first run, the original rgb color images were evaluated (see Fig. 1). In the second run, only the green channel was selected, submitted to digital contrast enhancement and presented as a gray-level image. This increased the visibility of erythematous structures that appear as dark areas (see Fig. 2).

Statistical evaluation

Statistical analysis was performed with SPSS 10.0 for Windows. The results of the five observers were collected and the number of pairs, in which the palm of the skin atopic individual was considered to show the more prominent pattern was recorded. In terms of mathematical probability, the palm of the skin atopic individual would be selected in about 50% of all image pairs. The chi-squared test was used to evaluate whether the judgment of the observers differs significantly from the 50% value. A *P*-value <0.05 was considered significant.

Results

When the results of the color images and the modified gray-level images were combined, the image of the skin atopic individual was considered to present a more pronounced vascular pattern in 708 of 1000 comparisons (70.8%; chi-squared test: *P* < 0.00001). When the analysis was limited to the original color images, 360 of 500 comparisons (72.0%; chi-squared test: *P* < 0.0001) were in favor of the skin atopic image. When the modified gray-level images were analysed, the vascular pattern was deemed more prominent on the skin atopic image in

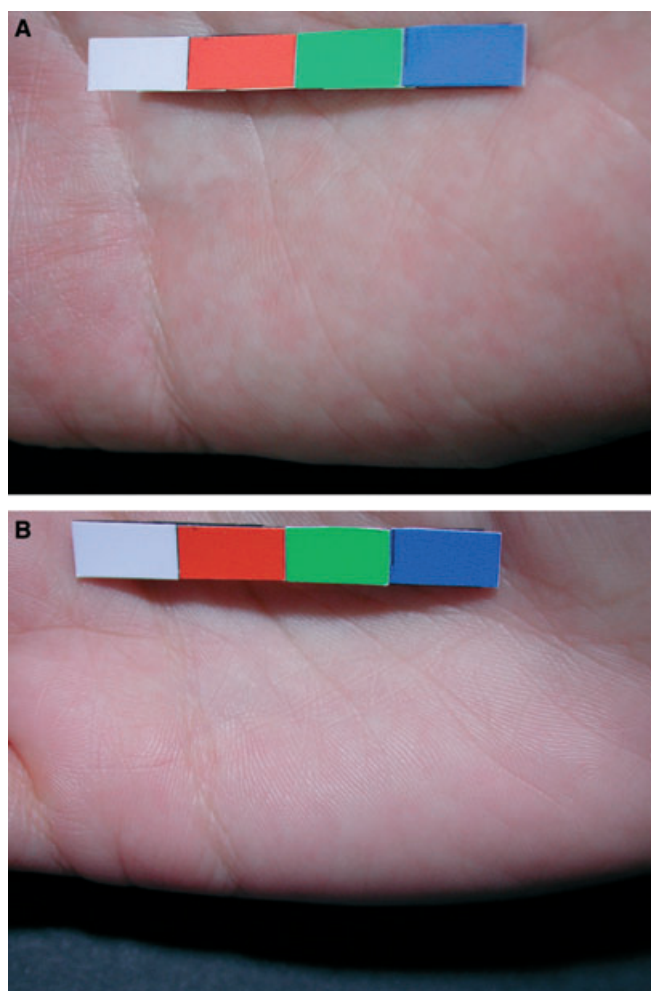


Figure 1. Color image of a skin atopic (A) and a non-atopic (B) individual.

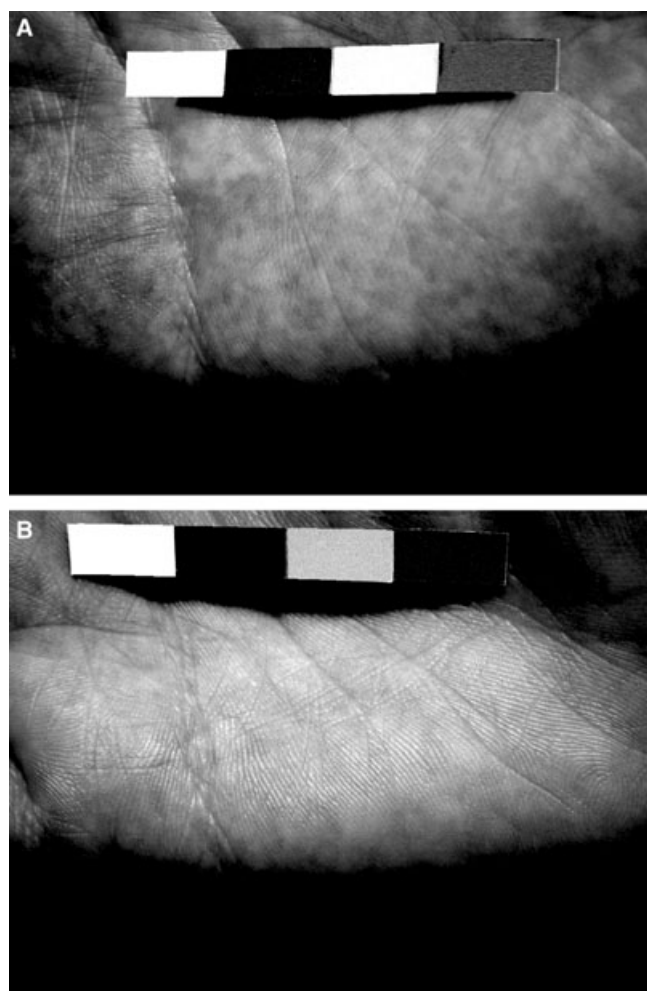


Figure 2. Gray-level image of a skin atopic (A) and a non-atopic (B) individual.

348 of 500 comparisons (69.6%; chi-squared test: $P < 0.0001$) (see Table 3).

Discussion

In clinical practice, it may be difficult to assess atopic skin diathesis in patients with no history of skin problems or eczema. Most of the known clinical features of diagnostic scoring systems are characteristic, but not specific, for the assessment of atopy (13). Several authors have tried to evaluate the significance of minor features in relation to their occurrence or presence in control groups of healthy individuals (9, 14–16). However, there is still no international consensus about diagnostic sets of atopic criteria (6). The presence of allergen-specific IgE is generally regarded as an important criterion for the diagnosis of atopy (6). However, some atopic patients lack any sensitization to food or aeroallergens and have serum IgE levels within the normal range (17, 18). Atopic skin is

characterized by an altered cutaneous vascular response, as demonstrated by the delayed blanch to cholinergic stimuli and nicotines (19). The greater prevalence of white dermographism and the paradoxical vascular reaction to thermal stimuli in atopic individuals are attributed to the fact that these individuals are more prone to vasoconstriction (20). The vascular mechanisms producing white dermographism and delayed blanching remain controversial. Some authors regard white dermographism as a consequence of superficial edema over dilated cutaneous vessels, while others attribute it to vasoconstriction based on the organism's paradoxical response to acetylcholine-like drugs (19, 21, 22). Non-invasive measurement of the vascular dynamics of dermographism by laser Doppler flowmetry and an infrared thermocamera support the hypothesis that white dermographism depends on the degree of local vasoconstriction, possibly in combination with altered blood flow in cutaneous shunt vessels (23). Furthermore, the individual's sensitivity to thermal stimuli and paradoxical reactions to

Table 3. The pronounced vascular pattern of the palm assessed by five independent observers in a sequence of 100 pairs of original rgb color images and in a sequence of 100 pairs of gray-level images

	Pronounced vascular pattern			Chi-squared test
	Yes	No	Total	
Original color images	360	140	500	96.800
Gray-level images	348	152	500	76.832
Original color images and gray-level images together	708	292	1000	173.056

temperature changes are well known phenomena (24–26). Borelli and Kopecka (27) as well as Koscard et al. (28) observed that, in atopic patients, heating of one arm caused cooling of the other unaffected arm, as a result of vasoconstriction of the skin vessels. The abnormal pattern of thermoregulation may reflect an intrinsic disturbance of the peripheral and hypothalamic autonomous system (26, 28). According to Szentivanyi's hypothetical model for atopy, atopic skin is more susceptible to vasoconstriction because of a deficit of β -adrenergic receptors, which on the other hand reduce the cyclic adenosine monophosphate level (cAMP) (29, 30). The latter plays an important role in the inhibition of cellular processes. As a result, the activity of several types of cells is increased. In particular, it leads to the release of mediators from mast cells or a greater release of interleukin-4 from monocytes (31, 32). The increased tendency to vasoconstriction and decreased circulation of the small blood vessels was found in AEDS affected skin areas as well as disease-free skin areas (20, 33). In the literature, there is no report on any correlation between the vascular mechanisms because of a disturbed vasoreactivity of atopic skin and other erythematous skin conditions. The herein described vascular pattern of the palms is not associated with other clinico-morphological features like inflammatory infiltration, papules, vesicles or clinical symptoms like itching or burning, with the exception that the individual suffers from AEDS at the same time.

In clinical assessment, the vascular pattern of the palms has to be differentiated from other erythematous skin conditions like livedo reticularis, livedo racemosa, pernio, Raynaud's phenomenon, and any kind of erythrodermia. For clinical and socioeconomic purposes, the estimation of atopic risk is of great importance, particularly in pre-employment examinations and in the assessment of probable occupational dermatoses (34). Workers with atopic skin diathesis are known to develop occupational skin disease more often, especially in jobs related to the food industry, health service, metal industry, and hair-dressing salons, because of intensive exposure to wet work and skin irritants (34).

Despite the fact that the relevance of some minor or additional features of atopy has changed over time, they are still a source of help in case of doubt (6, 35). Our findings demonstrate that the defined vascular pattern of the palm is more common in skin atopic than in non-atopic persons. This gross feature provides an inexpensive and practical method for clinical assessment of atopic skin diathesis by experienced physicians. The clinical pattern of numerous small red maculae or reticular erythema and pale maculae in the palms of skin atopic persons may be an additional diagnostic feature and serve as the first clue for the evaluation of atopic risk in individuals, viewed in conjunction with the person's medical history and the hyperlinearity of the palms. Subsequently, the presence of allergen-specific IgE could support the diagnosis of atopy. Further investigations of the frequency of this phenomenon in larger numbers of patients will throw light on the diagnostic significance of this clinico-morphological criterion in clinical practice.

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