



PROFESSOR ALESSANDRO BORGHI (Orcid ID : 0000-0001-9163-9691)

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**Dermoscopy of patch test reactions. Study of applicability in differential diagnosis between allergic and irritant reactions**

**Running head:** Dermoscopy of patch test reactions

M. Corazza, G. Toni, D. Musmeci, V. Scuderi, G. Amendolagine, A. Borghi

Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University

of Ferrara

via L. Ariosto 35,

44121 Ferrara, Italy

Phone: +39 0532239684

**Corresponding Author:**

Prof. Alessandro Borghi

Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University

of Ferrara

via L. Ariosto 35, 44121 Ferrara, Italy

Phone: +39 0532/239684

e-mail: [alessandro.borghi@unife.it](mailto:alessandro.borghi@unife.it)

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Correct interpretation of patch test reactions is of paramount importance for differentiating allergic from irritant contact dermatitis (ICD). Differentiating weak positive and/or doubtful allergic patch test reactions from irritant reactions can be difficult.

The aim of the present study was to describe the main dermoscopic features of patch test reactions and to assess the suitability of dermoscopy in differentiating allergic from irritant reactions in clinical setting.

In this observational, cross-sectional study, all consecutive adult outpatients patch tested at our Allergy Unit during a 6-month period for suspected allergic contact dermatitis who developed any reaction at patch testing were eligible for inclusion. Since this was the first, pilot analysis of the dermoscopic features of skin reactions to patch tests and with the aim of comparing allergic and irritant reactions, it was necessary to select only those reactions clearly definable and classifiable in either category, according to clinical assessment.

Patients were patch tested with the Italian baseline Società Italiana di Dermatologia Allergologica Professionale ed Ambientale (SIDAPA) series (Lofarma, Milano, Italy). Test allergens were applied to the upper back of patients for 48 hrs, using patch test Finn Chambers<sup>®</sup> on Scanpor<sup>®</sup>. Test sites were evaluated after 48 and 72 hrs by an experienced dermatologist (M.C.).<sup>1</sup>

At the 72-hour reading, the patch test reactions were captured with a digital dermoscopic system (Vidix Dermoscope 7, Medici Medical srl, Italy). Two dermatologists (A.B., G.T.), unaware of the clinical diagnosis, assessed in consensus the dermoscopic images of each reaction. A selection of dermoscopic variables was evaluated; each variable was arbitrarily graded according to a 4-point scale (0–3, where 0 represents absent or normal variable and 3 represents most present or abnormal variable).

T-test was used for comparing quantitative variables, while Pearson's chi-squared test or the Fisher exact test were used for qualitative variables;  $p < 0.05$  was considered significant.

Seventy-six patients were included, 56 females and 20 males, for overall 94 allergic reactions (in 57 patients) and 33 irritant reactions (in 29 patients). In all allergic reactions dermoscopy showed a quite intense erythema [mean score 1.90, s.d. 0.64] and an evident vesiculation was observed in 90 (95.7%) reactions. The latter appeared as whitish circular elements, varying in size and number, either sharp or slightly blurred, similar to soap bubbles. Vesicles were isolated within the lesion or distributed in clusters or both; less frequently, they had follicular distribution. Orange-yellowish patchy areas and crusts, similar to those observed in other dermatitis,<sup>2,3</sup> were found in 35% of reactions. Dense vessels with different shapes, mainly dotted (81.9%) and linear (71.3%), were another almost constant feature (97.9%). Pustules were observed in 16 (17%) reactions (Fig. 1).

In irritant reactions, erythema was on average less intense than in allergic reactions (mean score 1.12, s.d. 0.54,  $p < 0.001$ ). White vesicles were a sporadic dermoscopic finding (9%) whereas orange-yellowish patches and crusts were observed in one reaction. In all but one irritant reaction to cobalt, a "poral pattern" was observed,<sup>4</sup> which is the dermoscopic

counterpart of the "poral" reaction described as the consequence of the toxic effect of cobalt on the acrosyringium.<sup>5</sup> This "poral" pattern consisted in diffusely distributed punctate brown pigment deposition of various sizes surrounded by yellowish halo and resulted greatly enhanced by the dermoscopic observation (mean score 2.17). Vessels were detected in 75.8% of irritant reactions; mean vessel scores were significantly lower than those of allergic reactions ( $p=0.004$ ).

Erythema (OR 27.89 [95%CI 1.46-532.86],  $p=0.02$ ), vesicles (OR 225 [95%CI 47.61-1063.22],  $p<0.001$ ), orange-yellowish patchy areas (OR 17.31 [95%CI 2.26-132.47],  $p=0.006$ ) and vessels (OR 14.72 [95%CI 2.94-73.74],  $p=0.001$ ) were found to be strongly associated with allergic reactions. Erythema (100%), vesicles (95.74%), and vessels (92.52%) had high sensitivity for the correct differential diagnosis of allergic reactions whereas vesicles (90.91%) and orange-yellowish areas/crusts (96.97%) had high specificity (complete data available on request).

These results indicate that patch test reactions exhibit characteristic dermoscopic patterns, which significantly differ according to their allergic or irritant nature. Dermoscopic features found in allergic reactions correspond to skin changes which are typical of these reactions.<sup>6</sup>

In particular, dermoscopy seems to greatly enhance the visualization of the intense inflammatory process leading to both spongiosis, which in turn results in the formation and exudation of vesicles, and congestion and dilatation of papillary capillaries.

Dermoscopic features of irritant reactions were less definite than those of allergic reactions, probably due to a wider range of epidermal changes in ICD.

Our study has limitations. Only cases that could be clinically defined as allergic or irritant beyond any reasonable doubt were included; therefore, it is not possible to state with certainty that our findings can also be extended to cases of doubtful clinical interpretation. Further assessment of doubtful cases, e.g. weak reactions artificially induced, may represent the next step in an even more accurate definition of dermoscopic patterns of patch test reactions. In the analysis of sensitivity and specificity of the observed dermoscopic features, we did not include a comparison with dermoscopic images of normal skin. Both clinical and dermoscopic features were captured at the 72-hour reading, thus they are not representative of either early or late phases of the reactions.

In conclusion, dermoscopy could be a useful tool in differentiating allergic from irritant patch test reactions by allowing the identification of sensitive and/or specific markers.

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## Figure Legend

**Figure 1.** *Left side, a-d:* representative dermoscopic images of four patch test allergic reactions; (a) in this allergic reaction to Myroxylon pereirae 25%, numerous whitish soap bubbles-like vesicles, both isolated and distributed in clusters, were present over an erythematous background. Few dotted vessels were observable (original magnification x10); (b) at a higher magnification (x20), in this allergic reaction to methylisothiazolinone 0.2% it was possible to observe whitish vesicles, both isolated and follicular, dense dotted vessels, orange patchy areas and crusts; (c) allergic reaction to benzocaine 5%: we can observe intense erythema, rich vascularization, mostly dotted in shape, and isolated vesicles, both sharp or slightly blurred (original magnification x10); (d) in this reaction to nickel sulphate 5%, the clustered vesicles tended to coalesce forming larger, irregular figures (original magnification x10). *Right side, e-h:* dermoscopic images of four patch test irritant reactions (e, isobornyl acrilate 0.1%; f, methylchloroisothiazolinone/methylisothiazolinone 0.02%; g and h, cobalt chloride 1%) which show erythema, which was in general less intense than in allergic reactions, and vessels, mostly linear in shape. In the irritant reaction to cobalt reported in (g) a typical “poral pattern” was observed (original magnification x10 for all images).

