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A risk scoring system for the differentiation between melanoma with regression and regressing nevi

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ABSTRACT

Background: Spontaneous regression of melanomas is relatively common, its prevalence ranging from 10 to 35%. However, regressing nevi can exhibit worrisome feature and simulate melanoma both clinically and dermoscopically. Thus, the presence of regression can represent a confounding factor.
Objective: To investigate the frequency of dermoscopic patterns of "regression" in a series of benign and malignant melanocytic skin lesions, and to design an integrated scoring system. Scoring classifiers are very effective in selecting the significant parameters for discriminating two clinical conditions, thus can rapidly calculate a patient's risk for a given disease.
Methods: We selected a series of 95 regressing melanocytic lesions, including 50 regressing nevi and 45 melanomas with regression. For each lesion, 12 dermoscopic variables (i.e. five types of regression structures, five atypical pigmentation structures, atypical vascular pattern and pink areas) were examined by three expert in dermoscopy (blinded to the histological diagnosis). The dermoscopic evaluation was then combined with patient age, gender, body site and the maximum diameter of lesion. Concordance analysis with Cohen's kappa was performed between the three clinicians. A risk scoring system was designed by the leave-one-out cross-validation procedure to ensure model prediction power.
Results: The predictive score model revealed a sensitivity of 97.8% and a specificity of 75.5% in discriminating nevi and melanomas with regression. Using the score model, the diagnostic performance of the examiners increased by an average of 23.7% in sensitivity and 5.9% in specificity, compared with standard dermoscopic pattern analysis.
Conclusions: We assessed the validity of an integrated risk scoring model as a new methodological approach that could help the dermatologist in the differentiation between melanoma with regression and regressing nevus. Future studies could test the setting up of a score model over an even more complex pool of data obtained from different skin lesions with various diagnostic devices.

1. Introduction

Some clinical and dermoscopic changes typically associated with melanoma are not infrequently observed in benign melanocytic nevi. Regression of nevi can occur spontaneously (e.g. halo nevus) or after repeated trauma, and regression with or without halo has an incidence of 1% in the general population [1,2]. On the other hand, spontaneous regression of melanomas is not uncommon, the prevalence ranging from 10 to 35% [3,4]. The microscopic features of regression in melanoma are well recognized being originally described by McGovern in Sydney [5].

Non-invasive imaging methods and technologies may facilitate early melanoma detection. Dermoscopy is a useful adjunctive tool that can help identify melanocytic lesions, increase confidence that a lesion may be benign or malignant, and increase diagnostic sensitivity in experienced users. The interest in dermoscopy in the modern era had initially focused on its diagnostic utility in discriminating between melanomas and the very common yet diverse melanocytic nevi and other pigmented lesions. More

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recently, however, its diagnostic utility has expanded to include a wide range of difficult to diagnose subset melanocytic lesions: i.e. melanoma with regression [4]. In particular, a series of dermoscopic patterns have been correlated with the regression process, including white scar-like areas, blue-white veil, pepper-like granules, blue-grey granules/globules, shiny white streaks and hypopigmented areas [3,4,6]. All these patterns are correlated to dermal fibrosis, pigment incontinence and presence of melanophages and can be found in both melanoma with regression and regressing nevi [3].

On these bases, the first aim of our study was to investigate the frequency of established dermoscopic criteria of regression in a series of benign and malignant melanocytic skin lesions (MSLs) and to test their ability to separate regressing nevi (also termed *nevi with regression*-NwR) from melanomas with regression (MwR). A further aim was to design, develop and validate a "risk scoring system" for a rational diagnostic approach to these lesions. We compared the performance of the score-based model with that of pattern analysis performed on the same lesions by three experts in dermoscopy.

2. Materials and methods

2.1. Study population

We retrospectively selected a series of 95 consecutive MSLs showing clear-cut dermoscopic features of regression, according to three experienced dermatologists (M.F., N.N. and E.C.) (Fig. 1). All lesions were excised in the period 2010–2014 for suspected malignancy. Every histological diagnosis was confirmed by 2 out of 3 expert dermopathologists (C.M., M:F. and E.C.).

For each lesion, we collected data on morphology, such as the maximum diameter (mm), and lesion site (head/neck/shoulder/chest-breast/abdomen/back/side/buttock/arm/leg/foot). For statistical purposes, body areas were grouped into three macro-areas as follows: group A, head and neck; group B, trunk; group C, arms and legs. We also recorded gender and age (years).

2.2. Dermoscopic pattern analysis

The 95 images were randomly allocated to a training dermoscopic dataset for evaluation by three experienced dermoscopists (G.A., P.R. and N.N.) in blind to histopathological diagnosis. These independent examiners (D1, D2 and D3) were asked to assess the presence or absence of 12 dermoscopic structures (Table 1) that were selected according to the literature [3,6]. We evaluated dermoscopic structures suggestive of regression, including blue-grey areas (BGA), blue-whitish veil (BWV), blue globules and blue-grey peppering (BGP), white scar-like areas (WSA), white shiny streaks (WSS), atypical network (AN) and hypopigmented areas (HA). Irregular dots and globules (IDG), irregular streaks (IS), irregular pigmented blotches (IPB) and pink areas (PA) were also evaluated. The presence of atypical vascular pattern (AVP) was assessed when ≥ 2 of the following vascular structures were detected: hairpins, dots, corkscrews, irregular linear and polymorphic vessels. Furthermore, for 6 out of 12 dermoscopic variables, the number, extent, site and subtypes were assessed, obtaining a series of 27 specific variables (Table 1). The dermatologists were asked to assess the presence or absence of the 27 specific variables as well. Finally, they were invited to suggest the diagnosis of nevus or melanoma.

2.3. Statistical analysis

2.3.1. Univariate analysis

All separate dermoscopic variables were included in the analysis and examined as possible predictors of malignancy (i.e. of MwR). We evaluated correlations between the histological diagnosis of melanoma and 12 dermoscopic variables by 2×2 contingency tables and the Fisher exact test. The performance of the dermatologists in dermoscopic pattern analysis was calculated in terms of sensitivity and specificity.

Inter-observer agreement was examined by Cohen's kappa for each pair of examiners (D1 vs. D2, D2 vs. D3 and D3 vs. D1). The average value of kappa and its standard deviation were used to

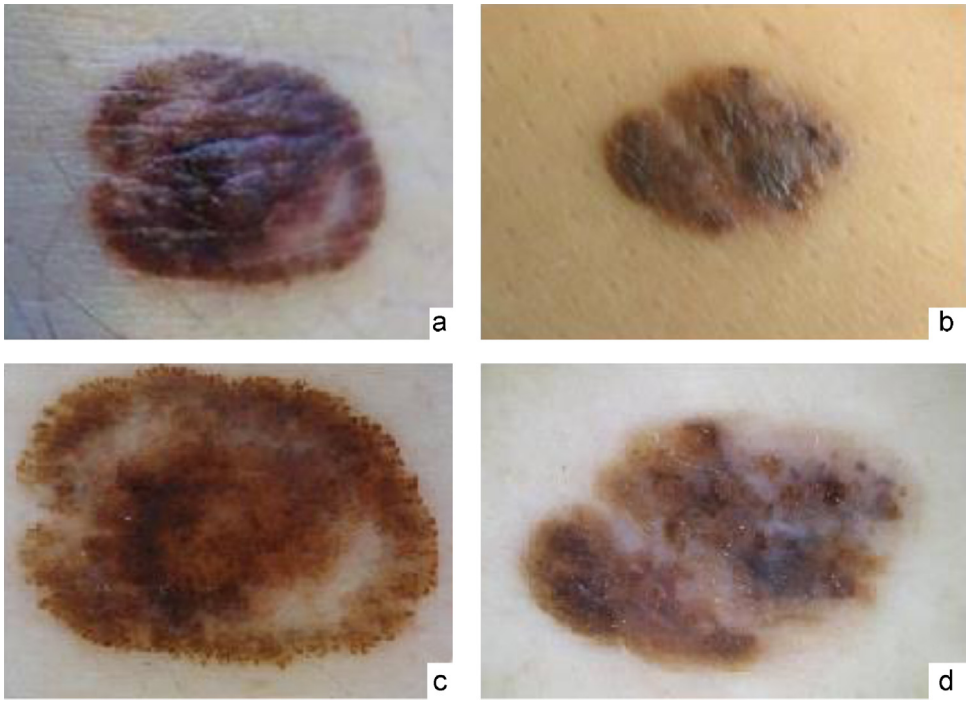

Fig. 1. Clinical (a,b) and dermoscopical (c,d) images (17×) of a regressing nevus and a melanoma with regression. Regression features, including blue-grey veil, blue grey globules and white scar-like areas, hypopigmented areas and atypical network, are observable in both benign (a,c) and malignant (b,d) melanocytic regressing lesions.