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Advances in dermoscopy for detecting melanocytic lesions

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Abstract

Over the last 30 years dermatological approaches to diagnosis and management of melanocytic lesions have been revolutionized by the introduction of dermoscopy. Continuous improvements are being made in applying the technique, mostly in melanoma diagnosis, follow-up of melanocytic lesions and nevogenesis. Identification of new dermoscopic criteria, such as the dermoscopic island and the blue-black color for thin and nodular melanoma, respectively, further add two new weapons in the dermoscopical armamentarium for diagnosis of otherwise featureless melanoma. Recent advances show that short-term, 3-month, follow-up is the optimum time interval to identify minimal changes in initially featureless melanomas. Nevertheless, long-term follow-up is still useful for the recognition of changes in melanomas with a very low-rate of growth. Dermoscopy greatly improves diagnosis and early excision of melanomas and reduces the number of unnecessary excisions.

Introduction

In the pre-dermoscopic era, melanoma diagnosis was based only on clinical morphology and on the simple "ABCD" rule (asymmetry, border irregularity, color, diameter) [1,2]. Dermoscopy or dermatoscopy [3,4] is a non-invasive technique that consists of viewing pigmented skin lesions through a hand-held lens, a dermatoscope or a video imaging system [5]. This procedure allows physicians to observe structures and colors not otherwise visible to the unaided eye, increasing melanoma diagnostic accuracy by up to 35% [3,6,7]. The conventional dermoscopic diagnosis is based on the assessment of specific criteria and on the application of different diagnostic algorithms [5]. In recent years, polarized light dermatoscopes gradually overtook non-polarized light devices, which were introduced in the 1990s and are still used today [8].

Since its introduction in the mid-1980s, and thanks to more than 1500 publications, dermoscopy has developed and dramatically become a well-established, routine technique in many European countries and Australia [9,10]. Nevertheless, in other countries, like the United States, dermoscopy still struggles to be accepted in daily clinical practice [11]. Herein, we reviewed the most recent important advances in dermoscopy of melanocytic lesions published in the last three years in English literature. Other applications of dermoscopy for non-melanoma skin cancers and other skin conditions are beyond the scope of this review [6,12,13].

New advances in melanoma diagnostics

First, dermoscopy is not too time-consuming. The time for dermoscopic examination of nevi is basically double that required for a naked-eye examination (142 vs 70 seconds), but still under 3 minutes - a reasonable time for a correct skin cancer screening [14].

Dermoscopy reduces the number of unnecessary excisions [3,15,16], thanks to the improvement of diagnostic accuracy [3]. Argenziano et al. showed that, in specialized clinical settings, the introduction of dermoscopy leads to a reduction of excised nevi and to an increased number of diagnosed and excised melanomas [16]. With

dermoscopy, non-specialist clinicians are able to improve the malignant/benign ratio of excised lesions [15,17] and even non-clinicians can identify suspicious lesions [18] simply by applying a simple method like the AC rule (asymmetry and color variation) [19].

Recently, several groups analyzed the most commonly used dermoscopic algorithms [7,20,21]. Haenssle et al. [7] and others [22] revised the 7-point checklist in a 10-year prospective study and found this method highly specific but less sensitive. In fact, 38% of melanomas scored less than 3 points (*in situ* melanomas frequently only scored 1 point) using the checklist and were identified only thanks to additional information such as anamnestic data, the ugly-duckling sign and signature nevi [7,23] or changes at digital follow-up [24]. Regression patterns, atypical vascular patterns and radial streaming were associated with the highest relative risk for melanoma [7]. Argenziano et al. revised the 7-point checklist, reducing the original 3-point threshold to 1-point in order to identify more melanomas. This gave higher mean rates of excision with an increased sensitivity but a lower specificity compared with the original 7-point checklist and pattern analysis. The authors recommend using the revised algorithm in a daily clinical setting, integrating dermoscopy with clinical information and follow-up [20].

Borsari et al. recently described a new melanoma predictor, the dermoscopic island [25], which differs from the eccentric pigmentation described by Arevalo et al. [26]. The dermoscopic island is defined as a circumscribed area showing a different dermoscopic pattern from the rest of the lesion (reticular, globular, homogeneous or starburst pattern) located at the periphery or in a paracentral position. It is more frequently observed in *in situ* and thin melanomas than in nevi, and represents the morphological aspect of initial malignant transformation. Lesions showing this feature should be referred for excision [25]. Eccentric pigmentation represents an area of asymmetrical pigment distribution and lesions showing this feature, but lacking other specific criteria for melanoma, do not require closer follow-up than other nevi [26].

The use of polarized light in dermoscopy allows the recognition of some structures not visible with non-polarized light [8,27,28]. Shiny white streaks arranged in an orthogonal organization are known as chrysalis structures [29,30]. Some authors proposed changing this term to crystalline structures, to include short white lines, white strands, white clods or white areas and rosettes [31]. Short white lines arranged in an orthogonal fashion may be observed not just in melanomas and Spitz nevi but also in basal cell carcinomas, squamous cell carcinomas and dermatofibromas [29,31,32].

Argenziano et al. [33] described a new predictor of nodular melanoma, the blue-black color due to the combination of pigment localized in the mid-deep dermis (blue) and, in atypical melanocytes, in the epidermis (black). The authors found a higher sensitivity for blue-black color with respect to standard criteria in the diagnosis of nodular melanoma (78.2% vs 43.6% respectively). Combination of the two reaches 84.6% sensitivity with 80.5% specificity. The blue-black color is a useful new feature allowing the diagnosis of some melanomas lacking standard criteria.

Few studies have been performed on hypopigmented lesions. Menzies et al. [34] looked at hypomelanotic and amelanotic melanoma and found blue-white veil, scar-like depigmentation, multiple blue-gray dots, irregular-shaped depigmentation, brown dots/globules irregular in size or distribution, five to six colors and predominant central vessels to be the most positive predictors of melanoma. In contrast, three or more milia-like cysts, comma vessels with regular distribution or the predominant vessel type, symmetrical pigment distribution, irregular or multiple blue-gray globules are the most significant negative predictive factors in melanoma diagnosis [34]. Accuracy of dermoscopic criteria is lower for hypomelanotic-amelanotic melanoma than with pigmented melanoma, but still superior to naked-eye examination [34].

Advances in digital follow-up

Sequential digital dermoscopy imaging (SDDI) is crucial in identifying melanomas lacking the specific criteria of malignancy. Unlike long-term follow-up (6-12 months), any morphologic change detected on short-term 3-month follow-up serves as a reliable prompt for the physician to excise the lesion. In contrast, lesions not showing dermoscopic changes on follow-up imaging can be left to avoid unnecessary excision [24,35,36]. Three-month follow-up remains the correct interval (rather than 6 weeks) to diagnose featureless melanoma [35]. Three months is also the recommended follow-up period for high-risk patients, such as those with familial atypical mole and multiple melanoma (FAMMM) syndrome, but 6-12 months is better for those with atypical mole syndrome [37,38].

Short-term follow-up is also the best strategy to optimize patient compliance. Patients addressed to a short-term follow-up are more likely to return compared with long-term follow-up patients, probably because of the major concern about a lesion to be checked after only 3 months [36]. Unfortunately, not all melanomas are clearly detected at 3-months follow-up. Sometimes long-term follow-up visits are needed to detect suspect changes [39].

Argenziano et al. [39] described a series of 103 melanomas diagnosed and excised after long-term follow-up with

minimal dermoscopic changes, with respect to the baseline visit (mean follow-up time: 20 months) and still *in situ* or thin at the time of histopathological diagnosis. Melanomas showing a reticular pattern on baseline image are more likely to remain *in situ*, whereas those with a non-reticular pattern usually show major changes at follow-up control. This supports the theory that melanoma represent a family of tumors: rapidly growing melanomas with a high capacity to metastasize, on the one hand, and slowly growing lesions often detectable only after repeated follow-up visits, on the other. Correct use of SDDI allows us to increase diagnostic accuracy, and reduce the number of undetected melanomas and also unnecessary excisions [24,38].

Advances in understanding melanocytic nevi and nevogenesis

Dermoscopy also allows us to study the physiology of nevi (clusters of pigmented skin cells). Some people have a high propensity to develop nevi, others lower, and this propensity is genetically established and, in part, due to environmental factors. The number of nevi is small in childhood, increases during adolescence and mid-life, and finally decreases during late adulthood [40-42]. The dermoscopic pattern of nevi seems to be age- and site-related, with a prevalence of globular nevi on the trunk in childhood (which tend to persist), and reticular nevi appearing on the upper back and extremities in adulthood (which tend to fade over time) [40,41,43,44].

These data led Zalaudek et al. to prepare two different pathways for nevogenesis [40,45]: the constitutional pathway gives rise to congenital globular nevi in childhood; and the acquired pathway is responsible for arising nevi with a prevalent reticular pattern in adolescence and adulthood. Based on these and other observations, Argenziano et al. proposed a new dermoscopic classification of melanocytic nevi into seven groups based on specific dermoscopic features that identify those lesions as specific entities (Table 1) [46].

Spitz/Reed nevi received particular attention. The original clinical description of a pink-red papulonodular lesions on the face and extremities of children or black (Reed nevus) papules or plaques on the extremities is no longer optimal for diagnosis [47,48]. Dermoscopy completely changed this view by identifying three main dermoscopic patterns: globular, starburst and multicomponent (atypical, melanoma-like) [48,49]. Similar to acquired nevi, Spitz/Reed nevi follow an evolution/involution process [50]. In the evolution, or growing phase, Spitz/Reed nevi show the classical starburst pattern, which is subsequently replaced after a variable number of months by a homogenous pattern observed during the stability phase. After some years, lesions gradually lose pigment and finally disappear, indicating that involution is common [50]. However, the recommendation is to excise nevi with spitzoid features in patients older than 12 years [48].

The BRAF oncogene is highly expressed in acquired nevi, whereas other types of melanocytic nevi – such as congenital dermal nevi, Spitz, and blue nevi – are usually characterized by mutations in other genes. BRAF mutations induce melanocyte proliferation, forming neoplastic

Table 1. Nevus dermoscopic subtypes

Nevus type	Clinical features	Dermoscopic features
Globular (congenital) nevus	Present at birth or appearing before puberty	Globular pattern in children; cobblestone or fried-egg pattern in adults
Reticular (acquired) nevus	Onset after puberty or in adulthood	Reticular pattern with or without hypopigmented or structureless area. Occasionally atypical features
Starburst (Spitz/Reed) nevus	Onset mostly during childhood or adolescence	Peripheral pigmented streaks or globules symmetrically distributed. Dotted vessels and reticular depigmentation in non-pigmented lesions
Blue (homogeneous) nevus	Congenital or acquired	Homogeneous structureless blue coloration. Sometimes white areas of fibrosis or hypomelanosis
Site-related nevi		
a. Acral nevus	Congenital or acquired	Parallel furrow, lattice-like, fibrillar pattern and other minor patterns
b. Facial nevus	Congenital or early-acquired	Children: pseudoreticular pattern Adults: remnants of pigmentation and comma vessels
Nevi with special features		
a. Combined nevus	Congenital or acquired	Combination of two or more patterns: reticular, globular, homogeneous and starburst
b. Halo nevus	Congenital or acquired	Globular pattern with blue granules and/or with scar-like areas
c. Irritated nevus	Congenital or acquired	Reticular, globular or structureless with variable grey or red areas
d. Nevus with eczematous halo	Congenital or acquired	Reticular, globular or structureless with yellowish areas
c. Recurrent nevus	Congenital or acquired (previous excision or trauma)	Atypical pigmentation and scar-like areas
Unclassifiable melanocytic lesions	One of the previous nevi with atypical features	One of the previous patterns with atypical features. Melanoma cannot be ruled out

clones. Without any other genetic alteration, such as that induced by intermittent UV exposure, proliferation stops and cells enter a senescent phase [40]. BRAF mutations are probably acquired early in nevogenesis and their level of expression is correlated with the phase of growth [51]. Based on this theory, it seems that young benign reticular nevi express high levels of BRAF mutations, slowly decreasing with nevus growth, followed by a final low rate in senescence [40].

Conclusions

Dermoscopy has dramatically improved the diagnostic accuracy of melanocytic skin lesions and, more recently, is helping us understand nevogenesis mechanisms and nevus physiology. New advances in terms of optimal application and follow-up and newly described criteria have gradually allowed us to correctly diagnose melanoma even in very early stages, where rates of curability and survival are high. This success may be an argument for a more widespread application of dermoscopy to screen the wider asymptomatic community on a routine basis.

Abbreviations

FAMMM, familial atypical mole and multiple melanoma; SDDI, sequential digital dermoscopy imaging.

Competing interests

The authors declare that they have no competing interests.

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