REVIEW ARTICLE

Dermoscopy pathology correlation in melanoma

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ABSTRACT

Dermoscopy is a widely used technique whose role in the clinical (and preoperative) diagnosis of melanocytic and non-melanocytic skin lesions has been well established in recent years. The aim of this paper is to clarify the correlations between the “local” dermoscopic findings in melanoma and the underlying histology, in order to help clinicians in routine practice.

Key words: correlation, dermatoscopy, dermoscopy, melanoma, pathology.

INTRODUCTION

The dermatoscope has currently become a primary tool for dermatologists, because it allows a rapid in vivo evaluation of structures of the epidermis and dermis which are not visible to the naked eye. Given that many dermoscopic structures have been correlated with the underlying histopathological alterations, dermoscopy has been regarded as a bridge between clinical and histopathological examination.

The most important purpose of dermoscopy remains the identification of specific criteria that allow melanoma to be distinguished from non-melanoma skin lesions. In the last few years, many specific dermoscopic features have been identified in order to improve the early melanoma detection, which represents the only way to improve the patients’ prognosis. Although many “local” dermoscopic features of melanoma have been clearly related to the respective histopathological findings, a direct and accurate dermoscopy-pathology relationship is not always simple because the dermoscopic horizontal images have to be correlated with the traditional histopathological vertical sections. Many authors have tried to use different techniques to solve the problem and improve this correlation. In 1993, Yadav et al. published a study on histopathological correlation of dermoscopic structures. They documented the lesions with a clinical and dermoscopic image prior to surgical excision and after placing an orienting suture at one pole of the specimen. Then, clinical and dermoscopic images were compared with histopathological slides according to a right orientation. The limitation of this method was that the authors did not perform a case-by-case correlation. In 2000, Soyer et al. reported a different sophisticated method involving digital dermoscopy followed by a standardized gross pathology for a case-by-case correlation; nevertheless, this procedure did still not allow a “direct” correlation between histopathological and dermoscopic findings with a visual control. In 2002, one of us (G. F.) proposed a simplified dermoscopic-pathological protocol (based on dermoscopic images and three orienting sutures of the excision biopsy sample that were photographed also in vivo) with a following case-by-case correlation to illustrate some dermoscopic-pathological features of both melanoma and non-melanoma skin lesions. In 2006, Rezze et al. proposed to study the dermoscopic-pathological correlation using histological transverse sections. This procedure, however, can be applied only in selected areas of any given lesion because horizontal sections in melanoma can hamper the diagnostic and prognostic (Breslow’s thickness) evaluation. More recently, Braun et al. proposed the “micropunch technique” to allow a direct correlation. The lesions were systematically documented with dermoscopy prior to surgery and then a 1-mm micro-punch (usually used for hair transplantation) was made in the area of interest.

In contrast, Amin and Fraga proposed the use of ex vivo dermoscopy with “derm dotting” to correlate the dermoscopic pattern with the microscopic findings. According to them, this technique would be useful especially to study the focal changes in the lesions and to enable the technician to include the diagnostic zones in the chosen tissue block, thanks to a nail varnish color dot that marks the suspicious section immediately after their detection with the dermoscope and that allows easy detection of the area of interest under the microscope.

In a recent study by Pellacani et al., a series of dermoscopic features in 202 melanocytic lesions have been evaluated and correlated with their histopathological and confocal microscopic findings. In 2014, Rstom et al., described the
correlation between some dermoscopic findings and histopathological ones in melanoma using the reflectance confocal microscopy (RCM) evaluation.10

Nowadays, in vivo RCM — by producing horizontal images like dermoscopy — is most likely the best method to link dermoscopic to histopathological findings, even more if associated with the punch technique.

The aim of this article is to provide a review of the dermoscopic–pathological relationship in melanoma according to the published work and our experience based on selected cases.

SEVEN-POINT CHECKLIST: DERMOSCOPIC–PATHOLOGICAL CORRELATION

Each melanoma, according to its anatomical site, degree of pigmentation, rate of growth, biological behavior, thickness and histopathological subtype, shows specific dermoscopic features. Superficial spreading melanoma (SSM) of the trunk and limbs is the most common type of melanoma in Caucasians. It is characterized by an early radial growth phase, followed by vertical proliferation after invasion. The list of SSM-specific dermoscopic criteria of the trunk and extremities includes the criteria of the 7-point checklist: (i) atypical network; (ii) blue whitish veil; (iii) atypical vascular pattern; (iv) irregular dots/globules; (v) irregular streaks; (vi) irregular blotches; and (vii) regression structures. The 7-point checklist is a well-known algorithm useful to simplify melanoma detection: a score of 2 is given to each of the first three criteria (major criteria), whereas a score of 1 is given to each of the last four criteria (minor criteria). A lesion scoring a total of 3 points or greater should be considered suspicious enough to warrant excision. According to the revised 7-point checklist of Argenziano et al., the presence of only one of these criteria is sufficient to warrant excision.11 This new method better reflects also the clinical practice, avoiding a scoring system and allowing to keep in mind only a list of features that warrant the excision.

Based on the published work review and our experience, here we report the dermoscopic–pathological relationship for the 7-point criteria.

The atypical network, presenting at dermoscopy as a combination of at least two types of pigmented network (in terms of color and thickness of the lines) asymmetrically distributed throughout the lesion, corresponds histopathologically to a disarrangement of the rete ridge with an increased number of atypical melanocytes (Fig. 1). The blue-white veil, defined as an irregular structureless area of confluent blue pigmentation with an overlying white “ground-glass” film, usually fitting clinically with the most raised part of the lesion, histopathologically corresponds to an epidermal acanthosis associated with pigment deposition in the superficial dermis (Fig. 2).

Atypical vascular pattern, observed as several combinations of linear–irregular vessels, dotted vessels, irregular hairpin vessels and/or milky red areas, corresponds histologically to a chaotic neoangiogenesis.

Irregular dots/globules, consisting of more than three round to oval structures, brown to black, asymmetrically distributed within the lesion, correlate histologically with compact aggregates of pleomorphic melanocytes, free melanin clumps and clusters of melanophages (Fig. 3).

Irregular streaks, defined as more than three, brown or black, bulbous or finger-like projections asymmetrically distributed at the lesion border and not clearly connected to the lesion network, are histopathologically represented by confluent melanocytic nests located at the tips of irregularly oriented rete ridges (Fig. 3).

Irregular blotches, appearing as black, brown and/or gray structureless areas asymmetrically distributed within lesions,
correspond histologically to pigmented keratinocytes, transepidermal melanin loss, pagetoid melanocytosis and/or a large melanin-containing dermal area (Fig. 4).

Regression structures, namely, white scar-like depigmentation and/or blue pepper-like granules usually corresponding to a clinically flat portion of the lesion, are histopathologically represented by a thin epidermis, covering areas of fibroplasia with inflammatory infiltrate of leukocytes and few melanophages (Fig. 5).

**Figure 2.** (a) This melanoma shows as the predominant feature the blue-white veil, detectable as an irregular structureless area of confluent blue pigmentation with an overlying white “ground-glass” film. (b) At histopathology, it corresponds to a marked and irregular epidermal hyperplasia overlying dermal sheets of pigmented epithelioid melanocytes and melanophages (hematoxylin–eosin, original magnification ×40).

**Figure 3.** (a) Dermoscopy shows a combination of irregular dots/globules and peripheral irregular streaks, both typical of melanoma. (b) Irregular dots/globules correlate histologically with a striking pagetoid configuration (hematoxylin–eosin [HE], original magnification ×630). (c) On the other hand, streaks are histopathologically represented by peripheral confluent junctional nests of melanocytes (HE, ×100).

BLUE-BLACK COLOR IN NODULAR PIGMENTED MELANOMA: DERMOSCOPY–PATHOLOGY RELATIONSHIP

Nodular melanoma (NM) is a rapidly progressing neoplasm that accounts for 10–30% of all melanomas and nearly 50% of all melanomas thicker than 2 mm. It has a very aggressive biological behavior (rapidly progressing, or even starting with a vertical growth phase) and a high metastatic potential (even in its...
At the time of diagnosis NM is often already a deep and ulcerated tumor. In NM, classic clinical criteria for diagnosis of melanoma fail because it is often small, round and symmetrical. Also, dermoscopy of NM is difficult because the asymmetrical pattern is less marked than SSM. NM is commonly featureless on dermoscopy; nevertheless, in some instances, it exhibits dermoscopic findings associated with deep tumors such as multiple colors, blue-white veil and atypical vessels caused by angiogenesis. In the last years, Argenziano et al. introduced the “blue-back rule”, suggesting that the simultaneous presence of blue and black areas involving at least 10% of the lesion surface each were significantly associated with pigmented NM. The blue color is usually imparted by an aggregation of pigmented melanocytes in the deep dermis. The black color, seen as dots, globules or blotsches, results either from superficial (intraepidermal) melanin or from heavily pigmented melanocytes under a thinned epidermis. This is in keeping with the observation that ulceration is more frequent in NM compared with SSM.1,12

In a recent study by Segura et al., a case series of NM and SSM with a nodular area or a blue palpable area were
compared using dermoscopy and confocal microscopy in order to obtain a correlation with histopathology. This study showed that the moderate to massive presence of pagetoid cells, often distributed throughout the entire lesion, was more frequently observed in SSM; instead, in NM a pagetoid configuration was absent or made by few sporadically distributed small dendritic cells. Concerning the dermoepidermal junction, it was sometimes visible in SSM and almost never visible in NM because of the total architectural disarrangement and the epidermal flattening induced by the massive dermal proliferation of melanocytes. Moreover, NM and advanced SSM showed no relevant difference in the cellularity of the dermal component. Based on these findings, it can be speculated that in SSM the vertical growth arises within a predominantly horizontally growing neoplastic component which is still detectable when the tumor becomes nodular; by contrast, a vertical growth of pleomorphic cells seems to be present since the beginning in pure NM.13

ATYPICAL VASCULAR PATTERN IN AMELANOTIC/HYPOMELANOTIC MELANOMA: DERMOSCOPY–PATHOLOGY RELATIONSHIP

Amelanotic and hypomelanotic melanoma, accounting for less than 2% of all melanomas, is very difficult to diagnose both clinically and dermoscopically. Amelanotic melanoma can develop as a reddish to pinkish macule, papule, plaque or nodule that rapidly changes in size, shape and color; instead, hypopigmented melanoma usually displays small foci of pigmentation, more frequently located at the periphery of lesions. The dermoscopic diagnosis is based on the presence of an atypical vascular pattern, including polymorphic vessels, milky red areas, and homogeneous red areas that histopathologically correspond to irregularly grouped polymorphous vessels within the dermis (Fig. 6). The “atypical” vascular structures have been significantly associated with NM by Zalaudek et al.14

The residual pigmentation of hypopigmented melanoma, usually visible as peripheral area of blue, white blue or grayish color histopathologically corresponds to a pagetoid spread of atypical melanocytes within a flattened epidermis. Recognition of a flat amelanotic melanoma is very difficult because of the absence of specific dermoscopic criteria coupled with the paucity of the available anamnestic data about the tumor growth. However, according to Argenziano et al., dermoscopy of amelanotic flat melanoma may be characterized by crystalline structures, namely: fine, white, shine lines, usually arranged in an orthogonal manner, visible only on polarized light, and corresponding histologically to remodeled or new dermal collagen.15,16 The crystalline structures or chrysalis structures, behind the invasive melanoma, could be observed also in other skin tumors, such as basal cell carcinoma, dermatofibromas, scars and, rarely, even in (desmoplastic) nevi.17

GRAY COLOR IN FACIAL MELANOMA: DERMOSCOPY–PATHOLOGY RELATIONSHIP

Nowadays, it is well known that dermoscopy of melanoma varies depending on each anatomical site. Although the head area is usually described as a single anatomical region, significant differences exist between melanoma of the face and the scalp in terms of dermoscopic features and prognosis.
Lentigo maligna (LM) accounts for 4–15% of all melanomas and represents the most common tumor subtype on the face; its natural course is characterized by a long period of very slow horizontal growth within the epidermis, followed by the invasion of the underlying dermis. After invasion, the prognosis of LM melanoma is not different from the other subtypes of melanoma. Recognition of LM is a true diagnostic challenge because it has an overlapping morphology with other pigmented macules arising on sun-damaged skin of the face (solar lentigo, flat seborrheic keratosis, freckles, lichen planus-like keratosis and pigmented actinic keratosis). The common dermoscopic pattern of melanocytic and non-melanocytic pigmented macules of the face is called a “pseudo-network pattern”: a structureless diffuse brown pigmentation with regularly spaced follicular openings due to pigmented keratinocytes and melanocytes arranged along a flattened dermoepidermal junction and around wide follicular openings. Because this aspect is not due to a retiform epidermal hyperplasia, dermoscopists have coined the term “pseudo-network” (Fig. 7).18

According to Schiffner et al., the progression of LM can be evaluated by means of the evolution of some dermoscopic features. Asymmetrical pigmented follicular openings (also called gray circles) and gray dots in the follicular openings (also called circles in the circle) represent the initial dermoscopic criteria for the early diagnosis of LM. These structures subsequently evolve into a granular–annular pattern, that corresponds to fine gray dots, globules and streaks around the follicles. Finally, melanocytes surround and completely obliterate the follicular openings producing the dermoscopy feature of the rhomboidal structures and the black/gray blotches, respectively.19 The gray color, irrespective of its shape, is the single most important criterion to differentiate LM from other facial pigmented macules.20 The gray color of structures typically seen in LM, histologically, corresponds to free or intercellular melanin in the upper dermis and/or to intrafollicular melanin (Fig. 7).19,20

Melanoma of the scalp represents an invisible killer because the hairs hiding the tumor are often responsible for a delayed diagnosis which turns into a bad prognosis. Interestingly, melanoma occurring on the posterior scalp reveals the same dermoscopic features of melanoma of the trunk or limbs, whereas melanoma on the frontal scalp frequently reveals the same dermoscopic features as LM.21

ACRAL MELANOMA AND MELANOMA OF THE NAIL APPARATUS: DERMOSCOPY–PATHOLOGY RELATIONSHIP

Acral melanoma affects acral skin and typically develops in the elderly patients with a female predilection. In its early growth phase, dermoscopy shows a parallel ridge pattern histopathologically corresponding to an involvement of the preferential growth of melanocytes along the cristae intermediate, with obliteration of the acrosyringia. Advanced acral melanoma loses any relationship with furrows and ridges and shows a diffuse variegate pigmentation, with black/brown blotches due to a diffuse and untidy distribution of melanocytes in the epidermis and the dermis (Fig. 8). Acral melanoma can sometimes exhibit areas with benign pattern (fibrillary, parallel furrow or lattice-like), in spite of the absence of any histopathological evidence of association with a nevus. Amelanotic/hypomelanotic acral melanoma often presents milky red areas.22,23

Melanoma of the nail matrix is one of the most challenging diagnoses in dermatology because it is prone to be confused with other common benign or malignant ungual and subungual lesions. Dermoscopic patterns of melanoma of the nail apparatus include: light-to-dark brown background color; brown to black longitudinal lines (irregular in color and thickness); subungual hemorrhage (appearing as blood spots or linear microhemorrhages); and micro-Hutchinson’s sign, defined as a pigmentation of the cuticle invisible to the naked eye.22,23

**Figure 7.** (a) Dermoscopy of typical lentigo maligna showing a predominant gray color distributed in the characteristic granular–annular pattern and rhomboidal structures. (b) Histopathology of a lentiginous proliferation of pleomorphic melanocytes with involvement of the adnexa and perifollicular pigmentation (hematoxylin–eosin, original magnification ×200).
Melanoma of the nail matrix has a lentiginous growth; thus, as for any other lentiginous melanocytic proliferation, the histopathological diagnosis is based on the relative predominance of irregularly spaced single melanocytes in large or relatively large lesions; this is why the breadth of the band and the irregular architecture of the pigment lines are the main dermoscopic features to be checked for the clinical diagnosis of nail matrix melanoma.

OTHER NON-SPECIFIC DERMOSCOPIC MELANOMA FEATURES AND THEIR HISTOPATHOLOGICAL CORRELATES

The negative pigment network (reticular depigmentation) is reported as a melanoma-specific structure; however, it is also strongly correlated with Spitz nevi and can also be seen in other benign lesions such as dermatofibromas. The negative pigment network consists of relatively light areas making up the “cords” of the network, and darker areas filling the holes. Recently, Pizzichetta et al., by assessing 679 skin lesions with histopathological diagnosis, noticed that a negative pigment network with an irregular or peripheral distribution and associated with a multicomponent pattern or an asymmetric pigmentation is significantly correlated with melanoma. Therefore, according to these authors, the negative pigment network can be used as an additional feature in distinguishing melanoma from Spitz nevus and other benign lesions.24 Although a clear-cut histopathological substrate for the negative pigment network is difficult to be established, some authors believe that it corresponds to thick and

Figure 8. (a) Dermoscopy of acral melanoma showing a parallel ridge pattern (b,c) histopathologically corresponding to a lentiginous and pagetoid pattern made by pleomorphic hyperchromatic melanocytes (hematoxylin–eosin, original magnifications: [b] ×200; [c] ×630).

Figure 9. (a) Dermoscopy of a clear-cut melanoma showing negative pigment network as the predominant feature, consisting of relatively light areas making up the “cords” of the network, and darker areas filling the holes. (b) It corresponds at histopathology to a relatively regular epidermal hyperplasia with hyperkeratosis/hypergranulosis associated with an irregular junctional nesting of melanocytes (hematoxylin–eosin, original magnification ×200).
elongated rete ridges with hyperkeratosis/hypergranulosis and dermal fibrosis (Fig. 9).

Ulcerations and blood crusts are often present in thick melanomas. These features are not specific of melanoma, but, when present, histologically correspond to a confluent dermal growth, with or without pagetoid pattern, which induces progressive thinning of the epidermis.3,12

The rainbow pattern, detectable under polarized light, represents a specific dermoscopic feature of Kaposi sarcoma, but can be seen as a non-specific feature also in melanoma. The rainbow pattern is characterized by multiple whitish areas with some variations of colors resembling the rainbow shades (whitish, yellowish, reddish, bluish). Probably, this feature histopathologically corresponds to a dense and irregular vascular network.25

Rosette structures are another dermoscopic sign visible under polarized lights and characterized by four white points arranged as a four-leaf clover. These have been mainly described in actinic keratosis, and squamous and basal cell carcinomas; a few cases of melanoma can show rosette structure as well. On histological examination, rosettes correspond to focal hyperkeratosis alternating with a normal-appearing horny layer and with keratin-filled acrosyringeal structures.26

CONCLUSIONS

Dermoscopy is a wonderful bridge between the clinician and the pathologist; thus, a deep understanding of the underlying histopathological substrate of each dermoscopic criterion is of uppermost importance for a better understanding of morphological and biological features of melanoma.

CONFLICT OF INTEREST: None declared.

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