

Correlation of dermatoscopy with the histopathological changes in the diagnosis of thin melanoma

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Abstract

Dermatoscopy is a non-invasive technique that enables the early diagnosis of melanoma. The purpose of the present study is to identify the dermatoscopic structures or changes that can indicate the presence of thin melanoma and their correlation with the histopathological aspect. **Materials and Methods:** Twenty-four thin melanomas diagnosed at the Department of Dermatology in Cluj-Napoca, Romania, have been assessed from the point of view of the presence of dermatoscopic structures likely to indicate malignancy. The lesions have been excised and serially sectioned to identify the histopathological correspondent of the various dermatoscopic structures. **Results:** The dermatoscopic analysis has indicated the following characteristics that suggest the presence of thin melanoma: irregular dots or globules, small white or grey-blue areas, some peripheral pseudopods or radial streaming, red dots at the level of the lesion or the presence of an atypical vascular pattern. As far as lesions under dermatoscopic follow-up are concerned, the following may be signs of malignant transformation: changes of the pigment network, newly appeared small white or red-blue areas or irregularly distributed dots or globules. All these structures are correlated with the histopathological changes that characterize thin melanoma. **Conclusions:** Slight dermatoscopic changes are extremely important in diagnosing thin melanomas as they correlate with the histopathological aspect.

Keywords: melanoma, dermatoscopy, histopathology.

Introduction

The incidence of cutaneous melanoma (CM) has grown in the last decades in many countries. Despite the existing methods for diagnosis and treatment, the prognosis of the patients with thick melanomas is quite reserved [1]. Currently, the most efficient treatment for CM is the surgical excision in its early stage [2]. For an early diagnosis, establishing the main criteria for identifying a CM in its early stage (when it is just a small and plane lesion) is crucial. Clinical criteria, such as the ABCD rule are not useful for thin melanomas [2].

Although surgical excision is the only strategy that can reduce the mortality associated with melanoma, the unnecessary excision of benign lesions may increase morbidity and medical costs [3]. The introduction of dermatoscopy in clinical practice was intended to improve the diagnostic performance of pigmentary lesions, enabling the early excision of malignant lesions and severely atypical nevi, while, at the same time, limiting unneeded interventions [2].

Dermatoscopy is an *in vivo*, non-invasive technique that allows a 10× magnification of the skin which enables the clinician to analyze the morphological structures within pigmented lesions that are not visible with the naked eye, structures with a well-defined histological correspondent. Various studies have demonstrated the improved capacity of dermatoscopy in differentiating

benign lesions from malignant ones, bringing a valuable contribution to the early diagnosis of melanoma [4–7].

However, a diagnosis that would differentiate between thin melanomas (*in situ* and thin invasive forms) and dysplastic melanocytic nevi is very difficult, though not impossible. Friedman RJ *et al.* have underlined the limitation of dermatoscopy in diagnosing small melanomas [8]. The reported correct melanoma diagnosis was only 39% [8]. This disappointing result is in agreement with previous observations of Skvara H *et al.* who appreciated that the sensitivity of dermatoscopy in diagnosing thin melanomas is no more than 27% [9]. Consequently, dermatoscopy is more efficient than naked eye examination, though not sufficient for small lesions. Dermatoscopic criteria that would accurately diagnose all melanocytic lesions have not been established yet. It is certainly more important to identify and excise suspicious lesions than to diagnose *in vivo*.

The golden standard in the diagnosis of cutaneous tumors is the histopathological exam. However, a diagnosis that differentiates between dysplastic nevi and thin melanomas is subjective and it usually resides in the degree of the dysplasia [10, 11]. Severely dysplastic melanocytic nevi make a continuous histopathological spectrum with thin melanoma. There are no unbeatable morphological criteria that would enable this distinction [10]. Several criteria to use in the histopathological

diagnosis of the melanoma have been reported, such as asymmetry, unclear borders, cytological dysplasia, mitotic activity and the lack of profound cell maturation. Although these criteria are used in the diagnosis of melanoma, none can enable the diagnosis by itself. Consequently, there are still controversies related to the differentiation between benign and malignant lesions [10].

Objectives

Taking into account the importance of early diagnosis, the purpose of this study was to identify the dermatoscopic structures or changes that appear in time and can indicate the presence of a thin melanoma. Moreover, we correlated the observed dermatoscopic structures with the histopathological characteristics of thin melanoma.

Materials and Methods

Twenty-four thin melanomas (*in situ* and T<1 mm) which have been diagnosed and treated in the Department of Dermatology in Cluj-Napoca, Romania, between January 2008 and June 2012, were assessed from the point of view of the clinical picture and dermatoscopic structures. Lesions located on the face, palms, soles, nail bed and mucous membranes were excluded due to the special dermatoscopic structures described in these sites. Suspicious lesions were diagnosed based on dermatoscopic examination.

The following structures were monitored: atypical pigment network, radial streaming, grey or black dots and globules, grey-blue areas or white-blue veil as well as the irregular or polymorphous vascular pattern. Lesions were excised and underwent histopathological examination, which included identifying the Breslow index. The biopsy specimens were processed using the paraffin embedding sectioning and Hematoxylin-Eosin (HE) staining method. Excised lesions were serially sectioned in order to correlate the various dermatoscopic structures with the histopathological changes.

Results

Out of the 24 cases, 18 (75%) were associated with melanoma suspicion at the first examination of the patient, while the other six (25%) were identified in patients with multiple dysplastic nevi which presented dermatoscopic changes at the level of one of the lesion (four cases – 16.6%) or developed a new melanocytic lesion (two cases – 8.33%) during follow-up.

The clinical diagnosis was melanoma just in three (12.5%) cases, while in 20 (83.3%) cases the clinical suspicion was that of melanocytic nevus. One case (4.16%) was interpreted as an actinic keratosis.

The clinical naked-eye evaluation showed that 18 (75%) of the lesions had the largest diameter under 6 mm, only six (25%) lesions being larger than 6 mm, the known diameter criterion suggestive for melanoma of the ABCD rule. All of the melanomas were flat, macular lesions, with well-defined borders. Regarding clinical color, 20 (83.3%) melanomas presented as a

light-brown or/and dark-brown lesion, while four (16.6%) melanomas presented red color too.

The histopathological exam indicated 11 (45.83%) cases of *in situ* melanoma, whereas the other 13 (54.16%) were thin melanoma with a Breslow index below 1 mm.

The dermatoscopic evaluation showed that the most frequent dermatoscopic structures present in 21 (87.5%), of the cases were irregular black dots and globules spread within the lesion. Small grey-blue areas were present in 19 (79.16%) cases, peripheral pseudopods or radial streaming in 17 (70.83%) cases and small areas of atypical network in 15 (62.5%) cases. Irregular or polymorphous vascularization (eight cases – 33.3%) as well as peripheral globules were also reported (six cases – 25%) (Figure 1).

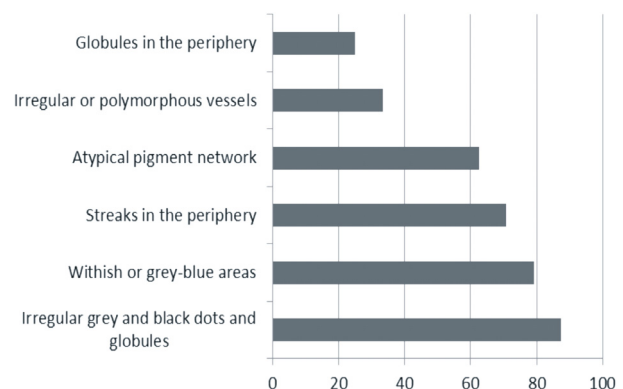


Figure 1 – The frequency of dermatoscopic structures in incipient melanomas.

Histopathological examination underlined the correspondence between the dermatoscopic and the microscopic structures in all melanomas. Thus, pigment globules (Figures 2a and 3a) indicate the presence of atypical melanocytic nests in the lower epidermis or in the papillary dermis (Figures 2b and 3b).

The black or grey dots indicate the presence of intensely pigmented macrophages in the dermis. The grey-blue areas (Figure 3a) correlate with the presence of lymphocytes and melanophages at the level of the dermis (Figure 3b).

Atypical pigment network (Figure 4a) is related to the atypical melanocytic hyperplasia along the dermis-epidermis junction associated with the prolonged epidermal crests (Figure 4b).

Radial streaming and pseudopods (Figure 5a) represent melanocytic nests confluent at junction level with atypical melanocytic pagetoid spread (Figure 5b).

A polymorphous vascular aspect consisting of red dots, red-milky areas and irregular vessels (Figure 6a) is histopathologically associated with intense vascularization, with vessels of different forms and sizes (Figure 6b).

Regarding the lesions under dermatoscopic follow-up, the indication for excision was based on the change of size and shape (one case) or on the presence of some structures characteristic to melanoma, such as: modified pigment network, which became atypical, newly developed small grey-blue areas, new small vascular structures or black or grey dots, irregularly distributed on the periphery or on the entire surface of the lesion (four cases) (Figure 7, a–d).

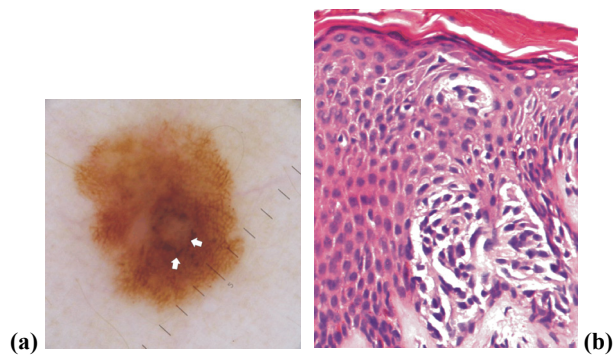


Figure 2 – In situ cutaneous melanoma: (a) Irregularly spread brown globules (white arrows); (b) Atypical melanocytic nests at the level of the epidermis and dermis (HE stain, ob. 20×).

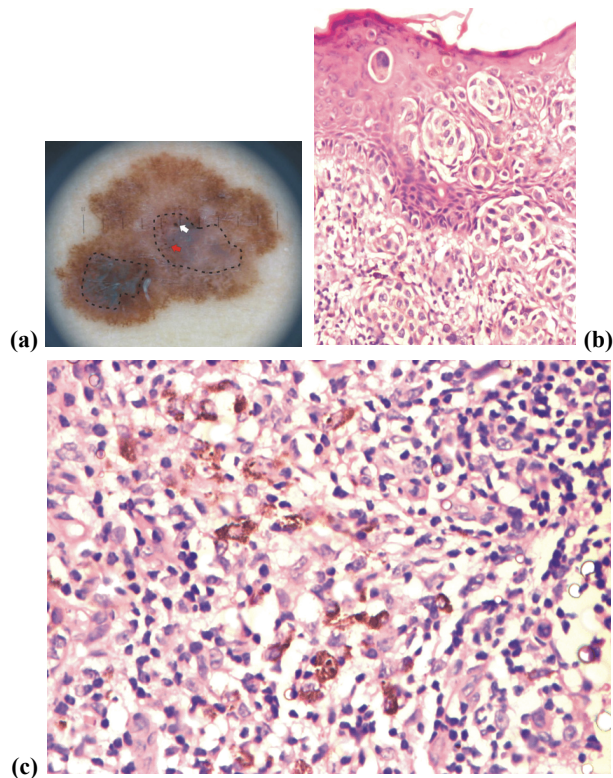


Figure 3 – In situ cutaneous melanoma: (a) Irregular brown globules (white arrow) and dots (red arrow), grey-blue network areas (highlighted area); (b) Atypical melanocytic nests corresponding to globules (HE stain, ob. 10×); (c) Lymphocytes and melanophages at the level of the dermis corresponding to grey-blue areas (HE stain, ob. 20×).

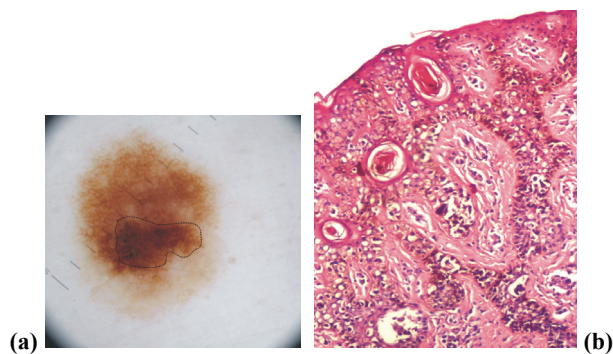


Figure 4 – Cutaneous melanoma, Breslow index <1 mm: (a) Atypical pigment network (highlighted area); (b) Crest elongation and melanin in the upper layers corresponding to the network (HE stain, ob. 10×).

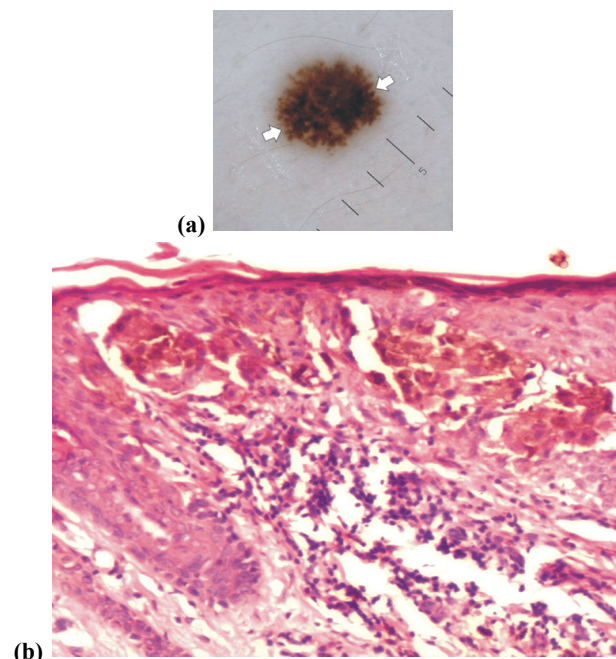


Figure 5 – In situ cutaneous melanoma: (a) Peripheral radial striae (white arrows); (b) Pagetoid extension of the atypical melanocytic cells at the periphery of the lesion (HE stain, ob. 10×).

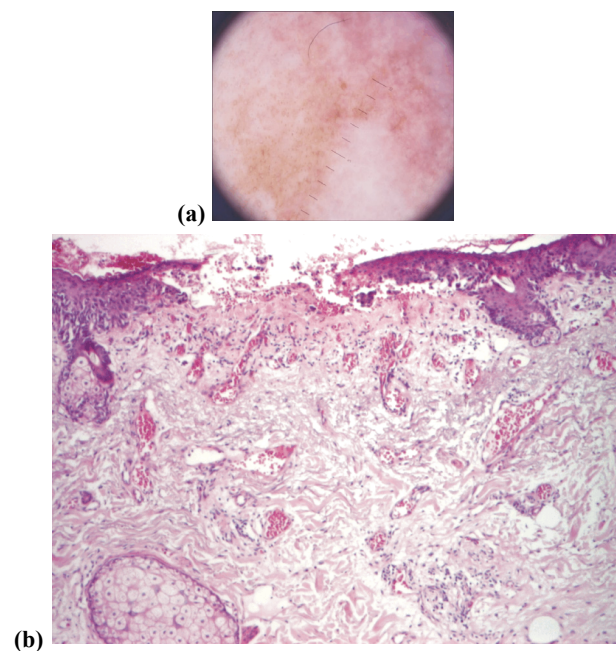


Figure 6 – Cutaneous melanoma, Breslow index 0.8 mm: (a) Polymorphous vascular pattern; (b) Pagetoid atypical cells, polymorphous vessels at the level of the dermis (HE stain, ob. 4×).

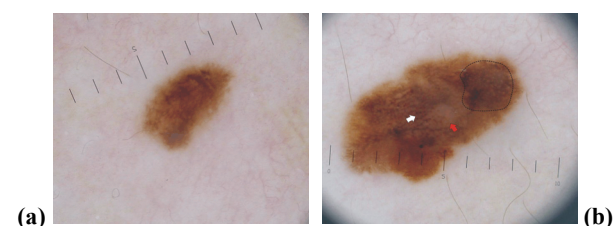


Figure 7 – In situ cutaneous melanoma: (a) and (b) Dermatoscopic change over a one-year period – shape modification, newly appeared atypical network (highlighted area) and grey-blue areas (red arrow), irregular black dots (white arrow).

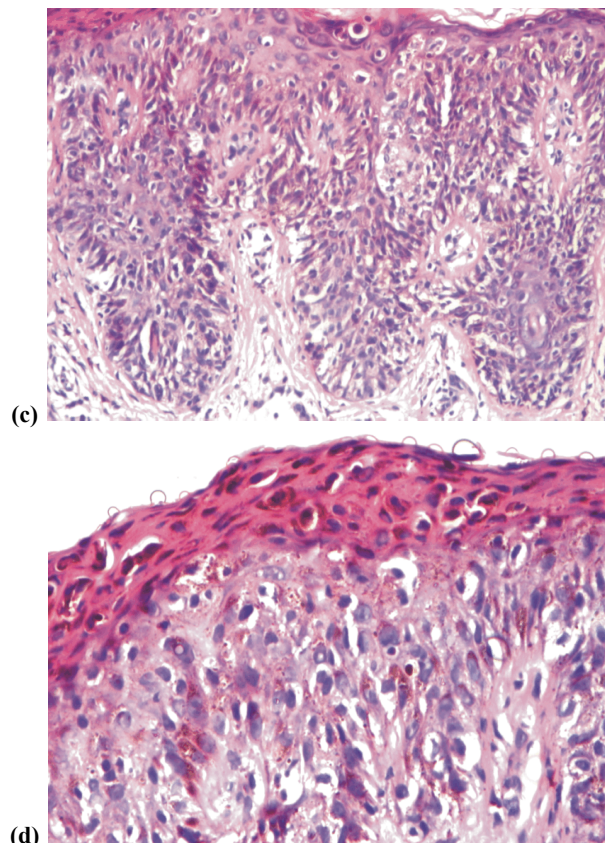


Figure 7 (continued) – *In situ* cutaneous melanoma:
(c) The proliferation of melanocytic cells at the junction level corresponding to the atypical network (HE stain, ob. 10×); (d) Isolated atypical cells and melanin in the stratum corneum corresponding to black dots (HE stain, ob. 20×).

Discussion

Early diagnosis of melanoma is crucial for the good prognosis of the patient [1]. Unfortunately, clinical criteria, such as the ABCD rule are not useful for thin melanomas [2]. This is particularly the case for the ‘diameter’ criteria, which suggests that melanomas are bigger than 6 mm. In fact, all melanomas start as lesions smaller than 6 mm, but in this stage they do not usually have irregular borders or color, as suggested by the ABCD rule [2].

Dermatoscopy improves the capacity of differentiating benign lesions from malignant ones, but the differential diagnosis between thin melanoma and dysplastic nevi is very difficult [8, 9]. However, dermoscopy identifies suspicious lesions, indicating the need of excision.

In our study, lesions that proved to be *in situ* or thin melanomas were associated with dermatoscopic structures, even if minimal, which raised the suspicion of malignant lesion, even if the clinical diagnosis was that of melanoma in only 12.5% of the cases. All the dermatoscopic structures that proved to be important for the diagnosis of thin melanoma were associated with histopathological changes characteristic for melanoma.

Pigmented globules are present both in benign lesions such as melanocytic nevi, especially in the papillomatous nevi, and in malignant lesions such as melanoma. Pigmented globules are regularly spread in benign lesions,

whereas melanoma is characterized by the presence of irregularly spread grey or black globules. Dots are dermatoscopic structures, smaller than globules, which can be also present in both benign and malignant lesions. Irregularly spread black or grey dots are characteristic for melanoma [12].

Our study demonstrates that pigmented globules or black or grey dots irregularly distributed at the level of the lesion, even in small number, are an indication for excision. Histopathologically, globules correspond to the presence of atypical melanocytic nests in the lower epidermis or in the papillary dermis, whereas black or grey dots indicate the existence of intensely pigmented macrophages in the dermis and single or small aggregates of melanoma cells in the epidermis. These two features characterize the radial growth phase of melanoma, including the microinvasive stage [11].

The presence of regularly distributed globules on the peripheral area of the melanocytic lesion indicates the fact that it is spreading. This is normal for common melanocytic nevi in young patients and does not indicate imminent or incipient malignity [12]. Our study shows that in patients over 40 years, lesion growth, even if symmetrical, with globules on the peripheral area, demands for excision, confirming the results reported by others [13]. Histopathologically, black or grey globules distributed on the peripheral area of the lesion are connected to the pagetoid spread of a thin melanoma.

Grey-blue areas or grey-blue veil have been described as expressing the regression of the melanocytic lesion. Classic dermatoscopy shows that regression mainly characterizes thick melanomas [4]. However, recent research has demonstrated that this is also present in thin melanomas, having a different morphological expression [14, 15]. Consequently, the frequency, extension and distribution of the regression depend on the thickness and the diameter of the melanoma. In invasive lesions, regression appears as structure-less areas associated with a white veil whereas in *in situ* melanoma it appears as a grey network with thick grey-blue lines and large holes. Moreover, blotting out the network or any other dermatoscopic structures in circumscribed areas of the lesion leads to structure-less light-brown areas [14, 15]. From a histopathological point of view, in thick melanomas grey-blue areas are determined by the presence of atypical, intensely pigmented melanocytes in the middle reticular dermis. On the contrary, in *in situ* melanomas, grey-blue areas indicate profound melanophagic infiltrate [14, 15].

The present study confirms the fact that small grey-blue areas characterize minimally invasive melanomas and represent an indication for melanocytic lesion excision, corresponding, from a histopathological point of view, to the presence of lymphocytes and melanophages in the dermis. This lymphohistiocytic infiltrate is usually present in the microinvasive stage of melanoma [11].

The pigment network is the result of the pigment layout at the level of the epidermis crests [12]. In benign lesions, the pigment network is regular, ‘as honeycomb’, whereas in melanoma, it is irregular, obvious and large

due to the atypical melanocytic hyperplasia along the dermo–epidermal junction [12]. Studies show that this dermatoscopic criterion is more frequent in the incipient stages of melanoma, but less frequent in thick melanomas, probably due to the loss of papillary crests associated with the progression of the tumor [7, 16]. *Radial streaming, pseudopods, irregular extensions* have different morphological aspects but a similar histopathological correspondent, represented by confluent melanocytic nests radial at junction level [12]. The present study demonstrates that these dermatoscopic structures, present even on small areas of the lesion, reflect suspicion of melanoma and, in our opinion, indicate the excision of the pigmented lesion. The histopathological examination of the lesion in areas correspondent to these dermatoscopic structures showed that the atypical network is correlated to the elongated epidermis crests and the proliferation of atypical melanocytes at the level of the dermo–epidermal junction. However, radial streaming, pseudopods and irregular extensions correspond to the pagetoid extension of the melanocytic nests at the periphery of the lesion. These histopathological features are all characteristics of thin melanomas [11].

As far as the *vascular aspect* is concerned, it is important in the diagnosis of incipient melanomas, especially the amelanotic or hypomelanotic forms. The most important aspects that may appear are: red dots, red-milky areas, winding irregular vessels or a combination of any of these – polymorphous vascularization [17]. Our study shows that an atypical vascular aspect, present even in small areas of the lesion raises the suspicion of melanoma. From a histopathological point of view, the dermatoscopically visible polymorphous vascular pattern was correlated in thin melanomas with pronounced vascularization, with vessels of different forms and sizes in the dermis.

Regarding lesions under dermatoscopic follow-up, several *patterns of change* in time, compatible with incipient melanomas could be observed. The following are among the changes that were observed in melanoma: focal growth associated with a shape modification and the presence of dermatoscopic structures characteristic for melanoma: irregularly spread black dots, pseudopods, irregular or prominent pigment network [12]. Our study demonstrates that the presence of new structures characteristic for melanoma or the presence of irregularly distributed peripheral globules demand for the excision of the lesion.

Considering the important role that the histopathological exam plays in the staging and prognosis of melanoma [18] and the correlation of dermoscopy with the histopathological structures, further studies are needed to investigate the possible prognostic value of the dermatoscopic structures.

✚ Conclusions

In spite of the fact that the sensitivity of dermatoscopy in detecting incipient melanoma is not very high, the presence of minimal dermatoscopic changes may raise

the suspicion of malignant lesion and determine its excision, assuring the removal of the melanoma in its early stages. In our study, all of the dermatoscopic features associated with thin melanoma were correlated with histopathological changes that are described in the microinvasive stage of melanoma. Dermoscopy can play an important role in early diagnosis of melanoma, by identifying suspicious lesions and inducing there excision.

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