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Professional paper

Dermoscopy and Early Melanoma

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ABSTRACT

The lack of effective therapies for patients with advanced melanoma establishes an early recognition as the aim of clinical and dermoscopic examination, which is the most important factor for improving patient survival and decreases the treatment and management costs. Melanoma in situ is the earliest stage of melanoma. The features of early melanomas, especially in those lesions smaller than 3mm, can be very subtle clinically, dermoscopically and pathohistologically, and it is often impossible to discriminate between a melanoma and nevus. Clinically, de novo melanomas are small brown to black macula with an irregular outline. In melanomas developing in a nevus, there is an asymmetry of the lesion with marked change in color and/or shape of the pre-existing nevus. Dermoscopically, early stages of melanoma show the same global features as thicker melanomas, but in a more subtle way. Asymmetry is the most important parameter; multiple colors are rare. Significant local melanoma-specific criteria, especially when present at the periphery, are irregular pigment network, irregular streaks, and irregular dots/globules, while blue-white structures are rarely found.

Key words: *melanoma, early melanoma, dermoscopy*

Introduction

The incidence of melanoma of the skin is rising more rapidly than any other cancer[1]. Due to the fact that melanoma is an aggressive skin tumor with high mortality rate, the main goal of clinical and dermoscopic examination is the early detection of melanoma, in fact, the recognition of thin melanoma, especially melanoma in situ, which is at the present time still very challenging. Early recognition and excision of melanoma is the most important factor for improving patient survival[2]. In contrast, melanoma in the advanced stages is usually recognizable by the naked eye, and is not curable as invasion thickness increases[3].

Melanoma in situ is the earliest stage of melanoma. About 75% of melanomas develop de novo and only 25% are associated with a nevus[4]. Clinically, de novo melanomas are small brown to black macula with an irregular outline, whose diameter varies from 2mm to several centimeters, and the period of this lateral growth may last for years. Often the patient recognizes that the lesion is growing and digitate extensions can be noticed during the period of radial growth, when the melanoma cells are confined to the epidermis[5].

Furthermore, small diameter melanomas represent a distinct clinicopathological entity that do not have to have enough clinical, dermoscopical and histopathological criteria to differentiate from atypical nevi. Reported frequency of small diameter melanomas is 11.4–38.2%[6]. Only a few case reports of in situ melanomas with a diameter of less than 2 mm were reported[6–8]. The smallest reported melanoma with dermoscopic features which evoked suspicion to malignancy had a diameter of 1.6 mm[7,9].

Morever, superficial atypical melanocytic proliferations of uncertain significance (SAMPUS) is confined to the epidermis and papillary dermis, without evidence of tumorigenic proliferation or mitotic activity. These lesions are clinically, dermoscopically and pathologically challenging as differential diagnosis of melanoma in situ is difficult or impossible to rule out (Figure 1)[10].

Moreover, featureless melanoma are melanoma without clinical and dermoscopic characteristics of melanoma but digital dermoscopy monitoring and total body photography are used to identify it only based on the criteria of the change over time[11,12].

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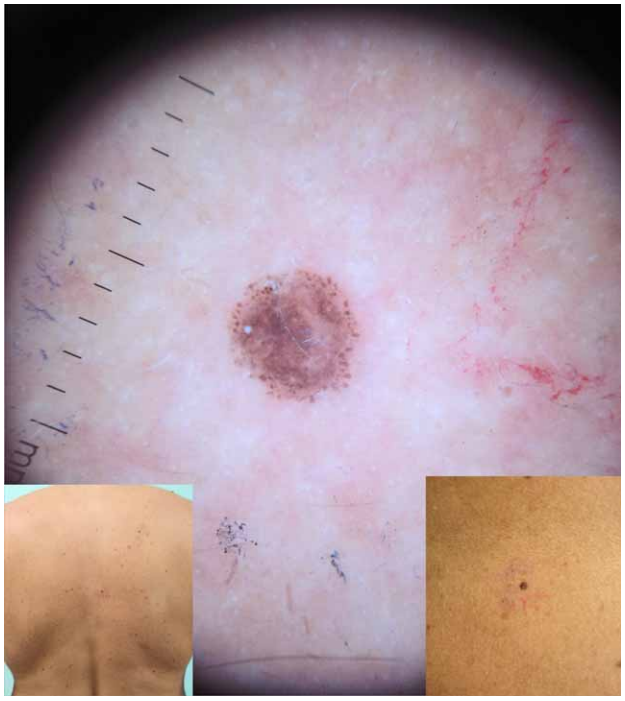

Fig. 1. Dermoscopic image: combination of globular, reticular and nonspecific global structure, asymmetry of the structure with irregular globules at periphery, atypical network and blotch centrally; inserted clinical images of a brown pigmeted lesion of 4mm on the upper back of the 44-year-old man with negative family history for melanoma and syndroma nevi dysplastici, and without history of change of nevi; clinical examination revealed more than 50 nevi with mainly reticular global structure; patohistology diagnosis is Superficial atypical melanocytic proliferations of uncertain significance.

Over the last two decades sensitive diagnostic techniques have been developing in order to improve detection of both early and featureless melanomas[12].

Dermoscopy is a noninvasive technique that allows in vivo observation by magnification and illumination of the skin structures, from the epidermis to the papillary dermis, that are not seen with the naked eye[13]. Dermoscopy is a diagnostic tool in clinical examination of pigmented and non-pigmented skin lesions that improves melanoma detection and decreases unnecessary excision rate of benign lesions and this have been proved in numerous studies, including three meta-analyses[2,14–18].

Early Melanoma, Melanoma *in situ*, thin Invasive Lesions ≤1 mm, Featureless Melanoma, small Diameter Melanoma and Melanoma Developing in Nevus

Early melanoma includes melanoma in situ and thin invasive melanomas less than or equal to 1 mm in depth[13–19]. The latter have 85–90% chance of a 10 year-survival after surgical excision with a 1 cm margin[13].

In general, dermoscopic characteristics for melanoma are asymetry in two axes, atypical dots/globules, atypical network, streaks, pseudopods, blotches, blue-white veil, structureless area, atypical vessels, milky red area, dermoscopic island, peppering, white like scar area[4,20–21].

However, the features of early melanomas, especially in those lesions smaller than 3mm, can be very subtle clinically, dermoscopically and pathohistologically, and it is often impossible to discriminate between a melanoma and nevus.

Thin melanomas dermoscopically show asymmetry in two axes, three or more colors, atypical dots and globules and atypical network or streaks[13]. Melanoma in situ mainly tends to have 2 colors, blue-whitish veil, grey-blue areas, black dots and irregular extensions and branched streaks. Less frequently there are brown globules, irregular pigmented network, pseudopods, and depigmentation[19]. Thin invasive melanomas are associated with white scar-like area and linear and/or dotted vessels[19]. Therefore, dermoscopic criteria for melanoma in situ and invansive melanoma are similar[19].

According to Silva VPM et al. atypical network is more frequently found in thin invasive melanoma than in melanoma in situ[13]. The regression interferes with the assesment of the level of invasion in melanoma and carries great histopathologic controversy, as well as can be a confounding feature for histopathologic differentiation between melanoma and nevus[22]. According to Seidenari S et al. regression variables are blue areas (structureless, reticular and globular), peppering, white areas, blue-whitish veil, pink areas, light brown areas and regression of dermoscopic structures. Regression and the number of regression parameter are more frequent and extensive in invasive melanomas than in melanoma in situ[22].

Dissapearance of the network or of the dermoscopic structures in circumscribed regions of the lesion form the areas of light brown pigmentation withouht structures[22]. Therefore, melanoma in situ have mainly light brown areas (Figure 2) and regression of dermoscopic structures and less blue areas and pink areas, otherwise characteristic for invasive melanoma. Among blue areas the reticular type is characteristic for melanoma in situ, although structureless type can also be present[22]. Light brown structureless areas are statistically significant discriminator and one of the most reliable predictors for thin melanomas[23]. Dermoscopic islands have been associated with thin melanomas arising from a nevus but in previously described study islands were less frequent[4]. Also, the same study showed that regression is not the only characteristic and that is not more frequent for invasive melanomas, but that is also present in in-situ melanomas as light brown structureless pigmentation, while in invasive melanomas it presents as white scare-like area and peppering. Invasive melanomas also tend to have multiple colors (three or more) and atypical network or streaks, especially appearing at the periphery. Since there is no definitive diferentiating criteria between the atypical nevus and melanoma in situ in many clinical cases, other different morphologic features have been described in order to determine more

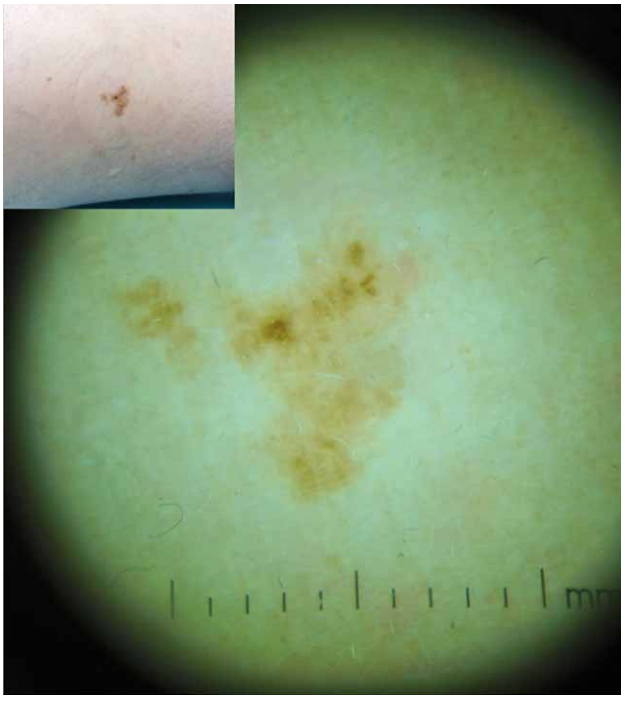

Fig. 2. Dermoscopic image: light brown pigmentation and asymetrically pigmented follicular oppenings; inserted clinical image of newly developed otherwise asymptomatic lesion on the anterior part of the lower leg of a 40-year-old woman with few nevi on the body with mainly reticular global structure; patohistology diagnosis is Melanoma in situ.

specific potential descriptor. One of them is so-called »mistletoe sign«, which appears in the inflammatory stage of the melanocytic nevus and in melanoma in situ, and is an indication for the excision of suspicious lesions. It implies multiple, well circumscribed areas, consisting of non uniform, at times pseudo-dichotomously brunched structures, resembling pseudopods, which are not reticular, arising from an overall reticular and homogenous pattern[24].

Pizzichetta MA et al. also showed that asymmetric pigmentation, multicomponent pattern in the combination with irregular distribution, and peripheral location of negative pigmented network are helpful as additional features in distinguishing melanoma lesions from other control lesions[25]. They reported high specificity 77.4%, but low sensitivity 34.6% of negative pigmented network for the diagnosis of melanoma[25].

When morphology of early or featureless melanoma is unrecognizable, Lallas et al. suggested that clinicians should use seven management rules, which might help in improving early and correct diagnosis of melanomas that do not meet the standard morphologic features. Following these seven specific simple and practical rules should integrate clinical and dermoscopical examination: 1) look basically at all lesions, 2) undress high risk patients, 3) use the 10 seconds rule in single lesion, 4) compare and monitor multiple moles, 5) excise doubtful nodular lesions, 6) combine clinical and dermoscopic criteria, 7) combine clinical and histopathological criteria[26].

Small Diameter Melanoma

Dermoscopically, small diameter melanoma present with atipycal pigmented network or irregular globules and streaks, multiple colors, blue-white veil or regression and De Giorgi et al. expressed that these features should arouse suspicion of melanoma even in small lesions[27].

Melanoma Developing in a Nevus

In melanomas developing from a nevus, there is an evident marked change in color and/or shape of pre-existing nevus, leading to an asymmetric appearance of the entire lesion[11].

Sequential Dermoscopy Imaging

Recognition of early and featureless melanoma can be improved by follow up with digital dermoscopy, revealing morphologic changes by sequentional monitoring thus offering better management of pigmented lesions in everyday practice. Dermoscopic follow up of melanocytic lesions allows observation of dermoscopic alterations over time, and thus, detection of melanomas in early stages, while reducing the excision rate, which especially refers to multiple nevi patients. With digital follow up melanomas that at baseline lacked dermoscopic features can be recognized[1,28,29]. According to Kittler et al. with longer folllow-up, melanomas tend to enlarge asymetrically with architectural and color change, and nevi tended to enlarge symetrically without architectural and color change[11]. When follow-up was shorter than 4.5 months the observed changes or dermoscopy features of melanomas and changing nevi could not have been differentiated[11].

The decision for surgical intervention should be made after follow up with digital dermoscopy[28,30].

When using digital dermoscopy follow up, the proportion of thin melanomas and in situ melanomas is higher than expected in general population[30]. Assessment of individual lesions is followed up in short term interval, while medium/long term follow up refers to patients with multiple nevi with or without personal and/or familial history of melanoma, as well patients with atypical mole syndrome[28]. Since there is an increasing trend of thin melanomas in the population, high risk patients should be followed up regularly through follow up programs in specified centers and institutions, which allow early recognition and good prognosis, even when both clinical and dermoscopic features of melanoma are lacking. Follow up includes comparison of clinical images e.g. total body photography as well in order to detect newly developed lesions, that could be de novo melanoma and therefore an early melanoma.

Limitations of Dermoscopy

Although dermoscopy helps to achieve diagnostic accuracy for melanoma, since dermoscopic criteria of melanoma appear earlier than the clinical characteristics, histopathological examination is indispensable and is still considered as a gold diagnostic standard, having decisive contribution to the definitive diagnosis of melanoma. Since featureless and early melanomas may present with uncharacteristic dermoscopic appearance, and may lack some specific dermoscopic features, because morphologic features of melanoma have not yet been fully developed, as well as they can be clinically and dermoscopically indistinguishable from benign lesions, dermoscopy is found to be limited, and melanoma may be overlooked[30]. These cases of melanoma that are difficult to diagnose are reported with the prevalence of 5–10%[14]. Despite available algorithms and methods for classifying the lesions sometimes it is very difficult to distinguish among them, and even experienced clinicians have diganostic accuracy below 85%, especially when differentiating early melanomas from melanocytic nevi[30]. It is also shown that 3-color test, another in a series of algorithms, reevaluated by Blum et al., is not sensitive enough to detect early melanoma, due to the fact that only one or two colors may be present in early melanoma, depending on the thickness of the lesion[14].

Conclusion

Melanoma is still a major public health problem worldwide. It can be prevented by early recognition of the earliest stages of melanoma. Dermoscopy is a part of clinical examination of nevi and in general of pigmented and nonpigmented skin lesions as a complete skin examination, and sequential dermoscopy imaging can detect an early melanoma.

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DERMATOSKOPIJA I RANI MELANOM

S A Ž E T A K

Obzirom na nedostatak učinkovite terapije za uznapredovali melanomom, rano prepoznavanje melanoma je osnovni cilj kliničkog i dermoskopskog pregleda, jer je to najvažniji čimbenik za unapređenje preživljavanja pacijenata s melanomom. Melanom *in situ* je najranija faza melanoma. Značajke ranog melanoma, posebno u promjenama manjima od 3 mm, mogu biti vrlo suptilne klinički, dermoskopski i patohistološki, a često je nemoguće izdiferencirati melanom od nevusa. Klinički, *de novo* melanomi su male smeđe do crne makule s nepravilnim rubovima. U melanomima koji se razvijaju iz nevusa postoji asimetrija promjene sa značajnom promjenom u boji i/ili obliku već postojećeg nevusa. Dermoskopski, rane faze melanoma pokazuju iste, ali diskretnije globalne/osnovne karkateristike kao deblji/uznapredovali melanomi. Asimetrija je najvažniji parametar; više boja je rijetkost. Značajni lokalno-specifični kriteriji melanoma, posebno kada su prisutni na periferiji, su nepravilna pigmentna mreža, nepravilni pigmentni izdanci i nepravilne točkaste strukture, a plavo-bijele strukture se rijetko nalaze.