Slow-growing melanoma: Report of five cases

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Abstract

Background: Epidemiologic data on melanoma reveal a considerable increase in incidence, especially of the early forms (melanoma in situ and early invasive melanoma), but the mortality rates are relatively stable. These data suggest the hypothesis of the existence of a melanoma with less aggressive biological behaviour. This hypothesis is, however, hard to be proven if the assumption is true that more and less aggressive melanomas very often exhibit overlapping clinical and histopathologic features. Digital dermoscopic imaging techniques permit today a detailed documentation of lesions over time and, therefore, represent an optimal tool to disclose the natural evolution of a given lesion. We present five case of slow-growing melanomas observed during a long-term period of follow-up.

Main observation: Five pigmented skin lesions from five patients with multiple atypical melanocytic nevi were examined at the baseline consultation and digital pictures were taken for monitoring purposes. The lesions have been followed-up for a long time because of the absence of significant changes over time. After a variable period of follow-up (1 to 10 years) all lesions were finally removed and subsequent histopathologic examination revealed early stage melanoma in all cases.

Conclusion: Dermoscopy and digital follow up might be the key factors to improve the knowledge about the natural evolution of nevi and melanoma and the spectrum of undefined melanocytic proliferations.

Introduction

Melanoma is one of the most aggressive tumors in humans. Usually melanoma grows first horizontally within the skin and, after a variable number of months or years, it may develop clones of cells that are able to grow vertically into the deep dermis and to metastasize. Among the four most common types of melanoma, nodular melanoma becomes thick faster due to its rapid vertical growth. In contrast, lentigo maligna represents the less aggressive form of melanoma thanks to its slow horizontal growth within the epidermis, which is on going over months or years, before starting with the vertical growth phase and reaching the potential to metastasize.¹ Current epidemiological data reveal a considerable increase in melanoma incidence, especially of the in situ and early invasive forms, whereas advanced disease and mortality rates remained relatively stable.² Due to these epidemiologic data, the question rose whether a new spectrum of melanomas characterized by a less-aggressive biological

behavior do exist.^{3,4} Proving the existence of biologically "indolent" melanoma is, however, difficult or even impossible because once melanoma is removed, its natural history will remain unclear, at least until metastases will eventually occur.⁵ The digital dermoscopic imaging technique (videodermoscopy) permits today a detailed documentation of lesions over time and, therefore, represent an optimal tool to disclose the natural evolution of a given lesion. We report 5 cases of melanoma characterized by a less-aggressive biological behavior as demonstrated by a long-term observation.

Case Reports

The first case originally reported by us⁶ refers to a 64-year-old man with a pigmented lesion located on the right upper arm, which has been followed up over a period of 10 years. At the baseline examination, in 1993, the lesion was an asymmetric brown-pigmented flat lesion with

a diameter of 8 x 5 mm, dermoscopically exhibiting a reticular pattern slightly prominent at the left border and multifocal areas of hypopigmentation. Despite the asymmetry and the slightly atypical network, the lesion lacked any other melanoma specific criteria, and a short-term follow-up was planned.^{7,8} However, the patient did not come back for the scheduled follow-up, but sought consultation again in 2003, 10 years after the first visit. At this time, the lesion showed a noticeable enlargement, together with the development of a more pronounced atypical pigment network and structural changes, such as regression structures in the central part of the lesion. Although the changes were not dramatic, they were relevant enough to prompt excision.⁹ Subsequent histopathological examination disclosed a large melanocytic neoplasm, mainly characterized by tightly packed melanocytes at the dermo-epidermal junction. A focal melanocytic spread within the upper layers of the epidermis was also noticed. In addition, a small, benign-appearing nevus cell component was detected in the dermis. A diagnosis of melanoma in situ over a small (possibly congenital) dermal nevus was made, mainly on the basis of the striking predominance of single melanocytes at the dermo-epidermal junction.

The second case refers to a 39-year-old man with a 9 mm, flat, pigmented lesion that was followed up for 2 years and a half. The patient had multiple atypical melanocytic nevi and did not recall any changes of his lesions

over time. At the first follow up consultation, performed 1 year later, all lesions remained basically unchanged. At the second follow up observation, performed 30 months after the baseline visit, only one lesion showed slight changes. The lesion was located on the back and exhibited slight enlargement that was only visible through side-by-side comparison with the baseline dermoscopic image. Dermoscopically, the pigment network and some regression structures were more pronounced with respect to the baseline image. Although the changes were only slight, complete excision was performed and subsequent histopathologic examination revealed a melanoma in situ.

Three additional melanomas were excised in our institution due to slight changes in size and dermoscopic features as observed over a follow up period of 1 year or more. They refer to two women and one man aged 55, 22, and 30 years, respectively. The lesions were located on the chest, leg, and back. Again, the follow up observation, performed after 1 year, did not reveal the striking changes in size and dermoscopic features as expected to be seen in a malignant proliferation. However, the lesions were excised due to the slight increase in size and in the amount of regression structures and irregular pigment network. Subsequent histopathologic examination revealed early stage melanoma in all cases (two early invasive melanomas of 0.7 mm and 0.4 mm of thickness and one melanoma in situ, respectively).

Figure 1

Clinical (left) and dermoscopic views (right) at baseline (A) and follow-up consultation (B) of a melanoma in situ located on the back of a 30-year-old man. The lesion was excised one year after the baseline consultation because of slight changes detected at the side-by-side comparison of dermoscopic images, but no increase in size is noted.

Discussion

The five examples of melanocytic proliferations we reported here, along with an additional documented case in the literature¹⁰, followed-up over one to ten years and finally diagnosed as melanoma in situ or early invasive melanoma, seem to underscore the existence of a peculiar group of melanomas with an unusual behavior. Instead of the expected significant structural changes and the eventual progression into nodular melanoma, just mild modifications were seen, characterized by a moderate to slight enlargement and an overall enhancement of the dermoscopic architectural irregularity. A possible explanation for this unusual behavior might be that these melanocytic proliferations were belonging to a spectrum of biologically "indolent" melanomas that would never progress into a metastatic disease. The existence of these melanomas is hard to be proven if the assumption is true that more and less aggressive melanomas very often exhibit overlapping clinical and histopathologic features. On the other hand the existence of an indolent type of this tumor could explain the rising incidence of early melanoma, whereas advanced disease and mortality rates remained relatively stable.⁵

Dermoscopy is a new noninvasive technique allowing the observation of structural changes over time, thus facilitating the comprehension of the biological behavior of melanoma. The technique consists in viewing pigmented skin lesions through a hand-held lens, a dermoscope or a digital video imaging system and is nowadays more and more used by dermatologists all over the world.¹¹ By using this technique a new morphologic dimension of pigmented skin lesions has been uncovered adding new criteria to the diagnostic armamentarium of clinicians for differentiating benign from malignant skin neoplasms.¹²

The use of digital follow up permits to identify an increased number of melanomas that do not show enough criteria for diagnosis at the baseline observation.¹³ It has been previously demonstrated that a lesion changing after an average time of 3 months has 11% probability being an early melanoma.⁸ After such short term follow up, changes seen in melanoma may be very subtle. By contrast, when a longer follow up documentation (6 to 12 months) is performed, melanoma exhibits striking changes in terms of size and usually develops clear cut atypical clinical and dermoscopic features allowing the correct diagnosis with increased confidence.^{14,15}

In the cases reported by us long-term follow up allowed us to discover a slow-growing type of melanoma, in which only subtle changes can be seen after prolonged observation. Further documentation of such cases is definitely required to clarify some of the questions related to melanoma epidemic and to the existence of a particular type of melanocytic proliferation typified by morphologic features of melanoma but never progressing into a metastatic disease. In this view, dermoscopy and digital follow-up might be the key factors to improve the knowledge about natural evolution of nevi and melanoma and the spectrum of undefined melanocytic proliferations.

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