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Review

A Case Report of an Unrecognized Nevoid Melanoma in a Young Woman – Clinicopathological Diagnostic Challenge

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A B S T R A C T

Nevoid melanoma is a rare form of melanoma histologically resembling benign melanocytic nevi and may be overlooked in routine histological sections. Authors are presenting a case of a 31-year-old woman who presented with bizarre pigmented skin lesions in the area of the postoperative scar on the back where, 6 years earlier, a »nevus pigmentosus epidermo-dermalis« was excised and hystologically confirmed in outer institution. The lesions were surgically removed and histopathological findings were characteristic for nevoid melanoma. Additionally, specimen of primary removed lesion was reexamined and primary nevoid melanoma was then recognized, therefore indicating that the lesions our patient presented with are nevoid melanoma recidivisms. Extensive diagnostic procedures showed no signs of melanoma dissemination. Three months later, the patient returned for consultation and presented with two new brownish-pigmented papules n the area of the new postoperative scar. The lesions were excised and new nevoid melanoma recidivism was confirmed. The patient remained under the regular follow up and, almost 9 years after the removal of primary nevoid melanoma, followed by two cutaneous recidivisms, remains disease-free. This case aims to highlight the problematic area in the analysis of pigmented skin lesions where nevoid melanoma represents one of the clinical and pathological diagnostic challenges.

Key words: *nevoid melanoma, melanoma, problematic melanocytic lesions*

Introduction

Nevoid melanoma (NM) is a rare form of melanoma, comprising approximately 1% of melanomas[1,2]. Histopathologically, nevoid melanoma is specific because it may mimic architectural features of a common or intradermal nevus when composed of small melanoma cells, or Alen-Spitz nevus when composed of medium-sized or large melanoma cells[3]. However, these lesions involve dermal portion of the skin and have metastatic potential, therefore are classified as malignant tumours.

Case report

A 31-year-old woman presented with darkly pigmented, papular, linearly distributed, nevoid skin lesions in the area of the postoperative scar on the back where, 6 years before, a »nevus pigmentosus epidermo-dermalis« was excised and hystologically confirmed in outer institution (Figure 1a). Immediate excision was recommended but, due to patient's personal obligations, was performed not until 6 months later, elsewhere. The histopathological analysis reported an old cicatrix and four brownish ragged lesions nearby. The smallest one was histologically diagnosed as an »intradermal nevus«. The remaining three lesions, on low-power examination showed sharp lateral circumscription (Figure 1b). They were consisted of clusters and sheets of medium to large sized nevus cells which focally showed atypia and few mitotic figures (Figure 1c). In some areas nevus cells showed maturation in the deeper portion of the lesions (Figure 1d). None of the lesions showed intraepidermal spread (pagetoid growth). The lesions were 0.75–1.5 mm thick,

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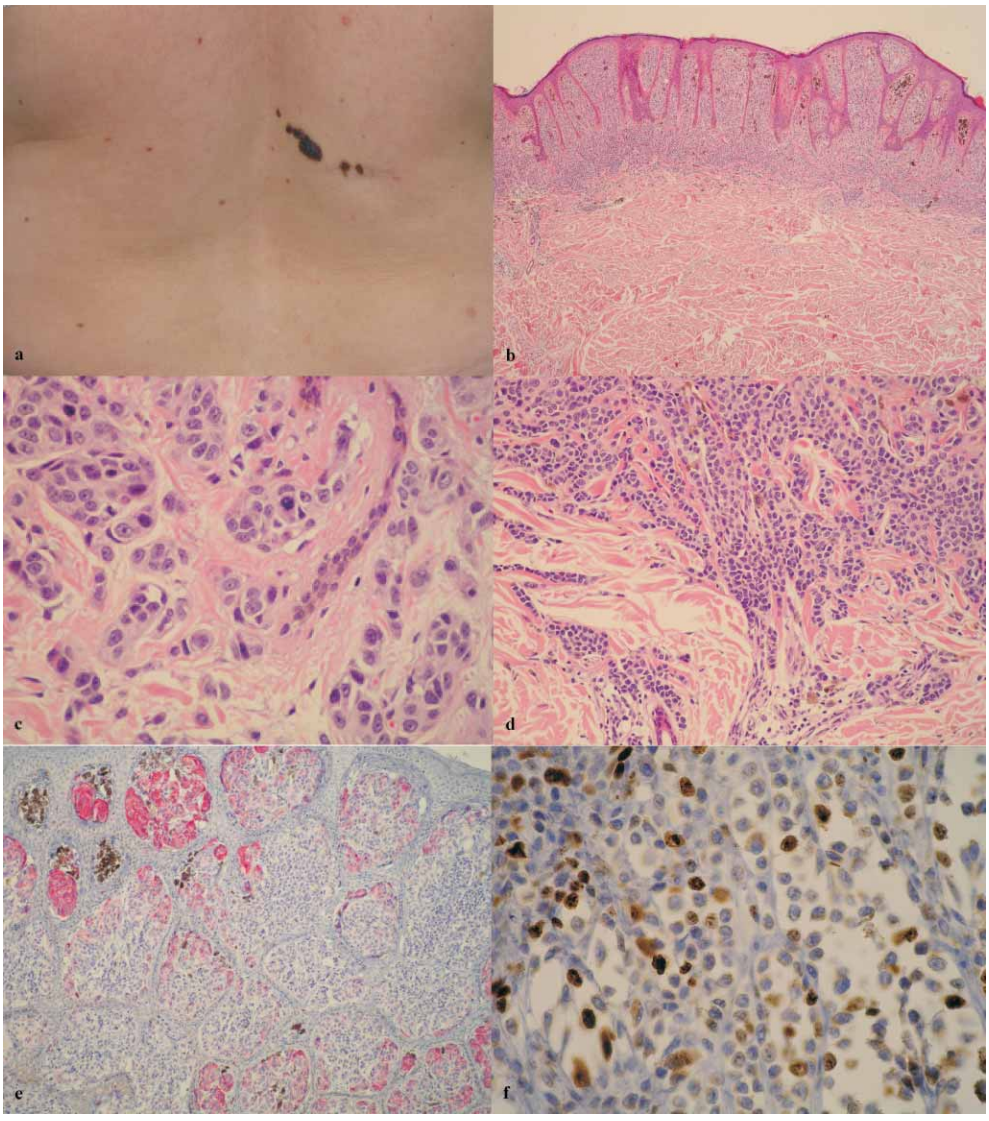

Fig. 1. a) Darkly pigmented, papular, linearly distributed, nevoid skin lesions in the area of the postoperative scar on the back, b) Histological examination showed nevoid lesion with sharp lateral border expanding into papillary dermis and reaching reticular dermis with sparse lymphocytic infiltrate at the base (40x, HE), c) Nevoid lesions were consisted of clusters and sheets of medium to large sized nevus cells which focally showed atypia and few mitotic figures (400x, HE), d) In some areas nevus cells showed maturation in the deeper portions of the lesions (200x, HE), e) Tumour cells showed partial positivity for HMB 45 (100x), f) Cellular proliferation measured immunohistochemically by Ki-67 expression was high in dermal component of tumour (400x).

expanding into papillary dermis and reaching reticular dermis with sparse lymphocytic infiltrate at the base. Tumour cells showed partial positivity for HMB 45 and, cell proliferation measured by Ki-67 was high (Figures 1e and 1f). Histological and immunohistochemical findings indicated NM. Additionally, specimen of primary removed lesion was reexamined and the analysis revealed that the primary lesion was histologically consisted of the same atypical, mitotically active nevus cells, similar to described before. Primary NM was then recognized, hence indicating that the lesions our patient presented with were nevoid melanoma recidivism. Subsequently, wider excision was performed and histopathological analysis showed only scar and no tumour cells. Regular diagnostic procedures (laboratory tests, chest X-ray, abdominal and peripheral lymph node sonogram, skeletal scintigraphy, head, chest and abdomen CT scans) showed no signs of NM dissemination. Three months later, the patient returned for consultation and presented with two new brownish-pigmented papules sized 3 mm in the area of the new postoperative scar. The lesions were excised and new nevoid melanoma recidivism was histologically confirmed. Therefore, new reexcision of the scar was performed and histopathological analysis again showed only scar and no tumour cells. The patient remained under the regular follow up and, almost nine years after the removal of primary NM, followed by two local cutaneous recidivisms, is disease-free.

Discussion

Pigmented skin lesions belong to the group of the most common skin lesions. A majority of them are histopathologically easily diagnosed, however, a small part of the cases are difficult to discern with certainty because they may share features with benign counterparts or have subtle morphologic features and have the potential for error with catastrophic consequences for patients[4–6]. One of such potential diagnostic pitfalls in the histological assessment of melanocytic lesions is the inability to recognize unusual melanoma variants, such as nevoid melanoma (NM)[1].

The term »nevoid melanoma« was first proposed by Schmoeckel et al[3] to describe a heterogeneous group of unusual melanomas in their study group of 33 patients of whom 15 had developed metastases and 8 had died of disseminated melanoma. These tumors were called »nevoid« because of their histological features closely resembling benign nevus. The tumours were showing two types of growth; symmetrical, verrucoid (dome-shaped) and papillomatous shape, as well as the apparent maturation of cells with descent in the dermis[3,7,8–12]. NM can mimic ordinary compound or intradermal melanocytic nevus when the melanoma cells are small or Alen-Spitz's nevus when the cells are large[3].

Demographic profiles of NM are still not well established due to its low incidence, small series studied and variations in the definition of the lesion made by different authors. NM can occur at any age, but is mostly reported in young to middle-aged adults. In the series analyzed by Wong et al[8] the average age at presentation was 40 years and, in the series reported by McNutt et al[2] the average age was 43 years.

Just like in the histopathological analysis, NM may also clinically resemble benign nevi[1]. The lesions are generally small (5–10 mm) papular, nodular or verrucoid. The colour may be uniform or irregular, tan to dark brown and the borders are usually sharp. The lesions appear mostly on trunk or proximal limbs in a young adult, slightly more often in women[1]. Usually, the lesions are solitary and are excised for cosmetic reason or due to recent growth.

Low-power architectural examination of NM can show either a verrucoid or a dome-shaped pattern[1,3]. The lesions usually have sharp lateral circumscription[2,8]. When the melanoma cells are small, NM may mimic ordinary compound or intradermal melanocytic nevus and, when the cells are large, it may resemble Alen-Spitz's nevus[3]. Features that enable the recognition of the lesion as a melanoma, such as a pushing border, high mitotic activity, and striking pleomorphism, are usually absent or subtle, which compounds the risk of misdiagnosis of such lesions as benign dermal nevi[1]. Overall, the lesions are symmetrical, with sharp borders, have minimal proliferation in the epidermis, and often have dispersion of cells at the base. Inflammatory reaction is usually slight or even absent. It has been asserted that ordinary melanomas arise in the epidermis and extend in a disorderly and asymmetrical manner within the epidermis as individual cells and nests along the dermal-epidermal junction, down adnexa, and upward in a pagetoid manner[13,14]. However, NM lacks prominent intraepidermal growth (pagetoid infiltration), forms rather discrete nests of cells in the dermis as well as confluent sheets of cells, and often appears symmetrical in outline[7]. Junctional activity is uncommon but can be observed in some cases of verrucoid forms of NM. The dermal component typically extends into the superficial reticular dermis[12]. The superficial dermal component is composed of nests of epithelioid-appearing melanocytes; a discernible spindle-cell component is not identified. In the verrucoid variant, the superficial nests can be quite large and confluating. There may be a gradual diminution in cell size toward the base, however the base is not well demarcated[2,12]. Although the cells at the base are smaller, they show atypical features including conspicuous nucleolation, nuclear membrane irregularity, hyperchromasia, increased nuclear-to-cytoplasmic ratios, and mitotic activity, all of which are unusual in the banal common acquired nevus. McNutt et al[3] suggest that NM represents an early stage in the evolution of nodular melanomas in which the melanoma cells have developed the ability to grow within the dermis but have not fully transformed and have not lost all of their ability to form the architecture of a nevus. Often in large nodular melanomas, there are regions with different morphologies of the melanoma cells that suggest an evolution in the dermis toward a more malignant cell type[15].

As it was mentioned above, NM can contain either small nevoid cells or larger cells that resemble those in Spitz's nevi. The lesions with small nevoid cells are particularly difficult to distinguish from common intradermal or compound melanocytic nevi. Additional staining for a proliferation marker, such as Ki-67, can help further in distinguishing NM from a Spitz's nevus. Reactivity of the intradermal component for HMB-45 antigen, without antigen retrieval, or for Ki-67 antigen can show that the dermal cells have an immature phenotype and, in combination with histological criteria, support a diagnosis of NM[3]. Melanomas show high nuclear staining for Ki-67 throughout the lesion, whereas Spitz's nevi have more staining at the top of the lesion than at the bottom. The patterns of HMB-45 and Ki-67 staining can be applied together with standard histological criteria for recognition of NM, based on the detection of lack of true tumour cells maturation with progressive descent in the dermis. The differential superficial expression of HMB-45 and Ki-67 which characterizes benign melanocytic proliferations is characteristically lost in NM[1]. HMB-45 may be positive or negative and, when positive, aberrant patterns of reactivity can be seen. Ki-67 reactivity is positive in both, upper and lower portions of the lesion.

Certain unusual types of nevi are difficult to differentiate from NM, including cellular blue nevus, combined nevi, deep penetrating nevus, »atypical dermal melanocytic lesions with differentiation along Schwannian lines« and dermal melanocytic tumors of uncertain poten-

tial[16–19,20,21]. An important problem is that the cytological criteria in routine sections are not always easy to evaluate, such as those regarding maturation of cells with progressive descent in the dermis[3]. Occasionally, nevi may lack good evidence of maturation; for example, nevi with architectural disorder and cytological atypia of melanocytes (dysplastic nevi) may have disordered maturation in the dermis[15,19]. On the other hand, when a melanoma is composed of small epithelioid cells, the evidence of maturation can be deceptive, particularly with dispersion of cells at the base of the lesion. However, dispersion can occur in NM, which makes it even more difficult to recognize[3]. Also, in some case of metastatic melanoma, the correlation between clinical and histopathological aspects is crucial to distinguish them from primary NM[3].

Nevoid melanoma behaves like invasive melanoma in the context of local recurrence and metastatic disease[7,8]. Histopathologically, lymphatic invasion can be observed and may be a sign of more aggressive behavior[12]. In the previously mentioned study by Schmoeckel et al[7], a series of 33 cases of unusual melanomas were analyzed and, 15 patients developed metastatic disease and eight died of disseminated melanoma. In a series of 20 patients with NM studied by Zembowicz et al[22], the mortality and metastasis rate at 3 years was 37.5%. In the series of 15 NM patients reported by McNutt et al[2], recurrent disease was observed in three patients.

Some authors suggest that NM and ordinary melanomas have similar prognosis, with the depth of invasion into the dermis being the most important prognostic factor[3,7]. However, there are studies that suggest that patients with nevoid melanomas have a better prognosis than those with classical type of melanoma[8,23–25].

Conclusion

NM is a rare form of malignant melanoma that may escape detection in routine histological sections because of the lack of a prominent intraepidermal component, sharp lateral circumscription, and evidence of partial maturation with descent in the dermis. When analyzing melanocytic lesions, scanning power examination only is insufficient to avoid the potential diagnostic pitfalls. Every melanocytic lesion should be carefully examined in at least several high-power fields, with special emphasis on cytological atypia and mitotic activity. For the recognition of NM, it is important to see the entire lesion to determine important histologic features, such as borders (lateral circumscription), maturation, and deep mitotic activity. Immunohistochemical analysis may be useful, but it cannot replace careful examination of H&E-stained sections with both, low and high magnification. More patients need to be studied and followed to see the prognosis of NM. In this case, a young woman with initially unrecognized primary NM, after 6 years developed cutaneous recidivisms twice, but in the 9-year period after the excision of the primary NM, she has not developed any metastases and remained disease-free. However, some patients with nevoid melanoma develop metastases and die from it. Therefore, the recognition of NM is extremely important in order to provide the appropriate treatment for the patients with this tumour. This case report aims to highlight the problematic area and diagnostic pitfalls in melanocytic lesions with emphasis on NM that might be underdiagnosed.

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PRIKAZ SLUČAJA NEPREPOZNATOG NEVOIDNOG MELANOMA U MLADE ŽENE – KLINIČKO-PATOLOŠKI IZAZOVI U DIJAGNOSTICI

S A Ž E T A K

Nevoidni melanom je rijedak oblik melanoma koji histološki izrazito nalikuje dobroćudnom melanocitnom nevusu zbog čega ponekad ostane neprepoznat u rutinskoj patohistološkoj analizi. Autori iznose slučaj neprepoznatog nevoidnog melanoma u 31-godišnje žene koja se javila na dermatološki pregled zbog tamno pigmentiranih, linearno razmještenih nevoidnih promjena u području postoperativnog ožiljka na leđima, gdje je, 6 godina ranije, u vanjskoj ustanovi kirurški odstranjen i histološki dijagnosticiran »nevus pigmentosus epidermo-dermalis«. Opisane tvorbe su ekscidirane, a patohistološki nalaz bio je u skladu s dijagnozom nevoidnog melanoma. Potom je primarno odstranjena tvorba primljena radi ponovne analize te je tada prepoznat primarni nevoidni melanom. Stoga su promjene s kojima se bolesnica prezentirala dijagnosticirane kao recidiv nevoidnog melanoma. Učinjena je opsežna dijagnostička obrada kojom nije nađeno znakova diseminacije melanoma. Tri mjeseca kasnije, na redovitoj kontrolnoj obradi, uočene su dvije novonastale pigmentirane promjene u blizini novog ožiljka na leđima, te je patohistološki ponovno potvrđen recidiv nevoidnog melanoma. Bolesnica je pod redovitom kontrolom i trenutno je, gotovo 9 godina nakon odstranjenja primarnog nevoidnog melanoma, praćenog kožnim recidivima, bez znakova novog recidiva ili diseminacije osnovne bolesti. Ovaj prikaz slučaja neprepoznatog nevoidnog melanoma u mlade žene naglašava problematično područje melanocitnih lezija gdje nevoidni melanom predstavlja klinički i patohistološki izazov u dijagnostici.