Red Nodule in a Post-surgical Scar: A Quiz

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A 79-year-old Caucasian woman (Fitzpatrick 1 phototype) was referred to our dermatosurgery unit for diagnosis and treatment of a nodular lesion on her right shin. The patient reported that the lesion had appeared 2 months before the visit. The lesion was located in a post-surgical scar. Three years earlier (in January 2017) a suspicious looking mole had been excised from her right shin, which, after a pathophysiological examination, was found be a naevus marginals. The current nodule was not painful nor pruritic. The woman did not report any comorbidities, and was generally in good health. In 2016 she underwent excision of a lentigo maligna (50 × 30 mm) located on her back. The woman reported excessive ultraviolet (UV) exposure with occasional burning, mostly on her back and extremities.

On admission, physical examination revealed an asymmetrical, solid, ulcerated red nodular lesion 1.5 cm in diameter (Fig. 1A), located on the right shin, in the scar from the naevus excision. There was an accumulation of brown pigment in the upper part of the lesion. Dermoscopy revealed white lines, milky-red areas and scarring (Fig. 1B). A decision was taken to excise the lesion and perform histological examination (Fig. 1C).

What is your diagnosis? See next page for answer.

Fig. 1. (A) Red nodular lesion before surgery. (B) Dermoscopic image of the lesion. (C) Histopathological image of the excised lesion (Hematoxylin and eosin stain ×100).
Red Nodule in a Post-surgical Scar: A Commentary

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Diagnosis: Nodular amelanotic melanoma

Melanoma is the most aggressive skin and mucous malignant tumour (1). It usually develops in healthy-looking skin; however, it may also arise from epidermal pigmented naevus and lentigo maligna (LM). There are 4 major subtypes of melanoma: superficial spreading (SSPM), nodular malignant (NMM), lentigo maligna (LMM), and acral lentiginous (ALM) (2). In addition, authors also describe unusual clinical manifestations, such as amelanotic melanoma (AM) (3).

AM represents approximately 8% of all melanomas (4, 5). However, the amount of “true” AMs is estimated to be less than 2% (5). AM is defined in 2 different ways. Some authors describe it as a melanoma with complete lack of pigment, whereas others describe it as a lesion without macroscopic pigmentation. Due to those differences the actual prevalence varies significantly (5, 6). Any histological subtype of primary cutaneous melanoma may be amelanotic. AM usually affects Caucasian patients over 50 years of age, more often patients with type I skin (Fitzpatrick scoring rate) (7). Nonetheless, AMs are also observed in the paediatric population. According to the study by Cordoro et al. (8) AMs may constitute up to 77% of melanomas in children younger than 10 years old. In addition, the paediatric additional ABCD criteria include “amelanotic” features (8). Association of AM with sex is controversial, with reports of predominance in males, females or neither sex (5, 6).

Authors recognize 3 main clinical forms of AM. The most common is papulonodular form, which may be manifested as an ulcerated nodule or a vascular lesion. The other forms are an erythematous macule, AMs may be skin-coloured, reddish (nearly 70% of AMs), pink or erythematous. Sometimes a slurred rim of the peripherally distributed pigment is a subtle clue to the proper diagnosis of hypomelanotic melanomas (6, 9, 10). AMs are often ulcerated, friable and bleed readily. Most of the lesions tend to develop rapidly (weeks–months), however, AMs in acral sites change slower and therefore are often ignored (4). In the current case the growth was steady, and it took almost 2 years to start to worry the patient. AMs appear on all parts of the body. The most common localization varies among different races and sexes with a predilection for trunks in males and limbs in females (6, 11). According to the study by Pampena et al. (9) the mean diameter of AM at the time of diagnosis is usually approximately 10.9 mm (2.0–25 mm) and the mean Breslow thickness is 1.4 mm (0–11.0 mm). AM appears both as primary and metastatic melanoma. In the letter, AM manifests as a single or multiple lesion, even when the primary neoplasm was pigmented (6).

The diagnosis of AM consists of clinical and histopathological examination. The clinical examination includes examination with naked eye, dermoscopy and non-invasive imaging techniques, such as reflectance confocal microscopy (RCM) (6). Dermoscopic diagnosis of AMs depends mainly on vascular features, especially when lesions are completely amelanotic. Polymorphous vascular patterns, including milky-red areas, hairpin vessels, dotted vessels, and linear irregular vessels, are characteristic for AM (3, 6).

The gold standard for AM diagnosis is histology with immunohistochemistry. It is recommended to take a complete full-thickness excisional biopsy with 1–3 mm margin of normal skin (6). The histopathological diagnosis is based on a combination of architectural, cytological, and host response features. The commonly used markers include S100, MelanA, HMB-45, tyrosinase, MITF and Ki-67. Although HMB-45 is very specific and its intensity correlates well with melanin, some true AMs can be negative for it. The Fontana-Masson stain may be useful to identify deposits of melanin, which are undetectable with conventional haematoxylin-eosin stain. Moreover, electron microscopy is useful in searching for melanosomes in difficult cases (6).

Clinical misdiagnosis of AM is extremely frequent and its rate has been reported to be up to 89% (5). The differential diagnosis should include both benign (e.g. keloid, intradermal naevus, seborrhoeic keratosis or pyogenic granuloma) and malignant (e.g. basal cell carcinoma, keratoacanthoma, Bowen’s disease or Merkel cell carcinoma) lesions (4, 12). Due to frequent misdiagnoses at the time of diagnosis both Breslow thickness and Clark’s level are significantly higher than in pigmented lesions, which correlates with greater risk of death and recurrence (6, 12). In our case, due to the localization, the differential diagnosis with hypertrophic scar and keloid had to be performed. In addition, the prevalence of AM in post-surgical scar is extremely rare, with only 2 cases described in the literature (13, 14).

The treatment of AM is similar to other types of melanoma; however, due to delayed diagnosis the cases are usually advanced, and the prognosis is much poorer. The gold standard is surgical removal of the lesion with margins depending on the neoplasm staging. Mohs surgery could be used in patients with non-invasive in situ melanoma (15).

Amelanotic melanoma is a rare clinical variant of malignant melanoma. The diagnosis is very difficult, and the rate of misdiagnoses is extremely high. Therefore, at the time of diagnosis, the tumour is frequently advanced and metastatic. The current case is an infrequent example of amelanotic melanoma in a post-surgical scar. Even though the woman regularly visited her physician for a follow-up and was thoroughly examined, at the time of diagnosis the melanoma was Clark level III and had Breslow thickness of 3 mm.

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