Clinical Case Report

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A melanotic malignant melanoma presenting as a keloid

A case report

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Abstract

Rationale: Amelanotic malignant melanoma (AMM) is a rare subtype of malignant melanoma (MM) that manifests atypically and is easily misdiagnosed or missed altogether. The keloid type of AMM has rarely been reported. Herein, we provide information to improve the clinical diagnosis of AMM types and raise awareness to ensure early diagnosis and timely treatment.

Patient concerns: A 20-year old woman presented with a mass on her left shoulder of 1 year's duration that had been treated surgically. The lesion recurred 1 month before the present case, along with lymph node enlargement on the left supraclavicular fossa.

Diagnoses: Histopathology and immunohistochemistry findings suggested AMM.

Interventions: The original tumor recurred 1 month later after chemotherapy, and an extended resection and a second round of chemotherapy were performed. However, the patient exhibited suspected epileptic symptoms during chemotherapy and was required to return to the local hospital for treatment.

Outcomes: No tumor recurrence occurred within a 6-month follow-up period.

Lessons: Early AMM diagnosis has a very significant effect on prognosis. For some persistent and growing proliferative lesions, obliterative treatments should be avoided before a definitive histopathological diagnosis has been made.

Abbreviations: AMM = amelanotic malignant melanoma, CT = computed tomography, DCE-MRI = confocal scanning microscopy and dynamic contrast enhanced MRI, MM = malignant melanoma.

Keywords: amelanotic, biological therapy, keloid, malignancy, melanoma

1. Introduction

Malignant melanoma (MM), which occurs mainly in the skin, is a highly malignant tumor derived from melanocytes. Although MM accounts for only 3% to 5% of all skin malignancies, it is highly metastatic and accounts for nearly 75% of all skin tumor-related deaths. Accordingly, the early diagnosis of MM is very important. Amelanotic MM (AMM) is a rare subtype, with an incidence of approximately 8%. AMMs lack melanin and exhibit diverse, nonspecific clinical manifestations, leading to diagnostic difficulties.[1] Few reports have described the keloid type of AMM, which is even more rare, and these lesions are easily misdiagnosed or missed in the absence of a histopathological examination.[2] Here, we report a case of AMM manifesting as a keloid.

2. Patient information

A 20-year-old woman presented with a mass on the left shoulder. One year earlier, she had inadvertently identified a cherry-sized, asymptomatic brown mass on her left shoulder and visited a local hospital for surgical resection. At that time, the lesion was diagnosed as a benign tumor. One month before the current presentation, an irregular, skin-colored mass relapse without ulceration, pruritus, or tenderness appeared gradually at the original site. The patient was normally healthy, with no changes in body weight, and her relatives were healthy with no similar diseases. She had a history of allergies to penicillin, ginger, and pollen.

3. Clinical findings

A physical examination revealed stable vital signs and palpably enlarged lymph nodes in her left clavicle. No involvement of the superficial lymph nodes, liver, and spleen was observed, and a systematic examination revealed no evident abnormalities. A dermatological examination revealed a crab-like scar on the left shoulder and an irregular, skin-colored nodule measuring 2 cm × 3 cm distributed along the scar. This nodule was tough in texture, with little mobility and no tenderness (Fig. 1).

4. Diagnostic assessment

An auxiliary color Doppler ultrasound examination revealed a hypoechoic nodule in the left supraclavicular fossa, which was

Editor: N /A.

The authors have no conflicts of interest to disclose.

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Medicine (2017) 96:49(e9047)

Received: 1 November 2017 / Received in final form: 10 November 2017 / Accepted: 13 November 2017

http://dx.doi.org/10.1097/MD.0000000000009047

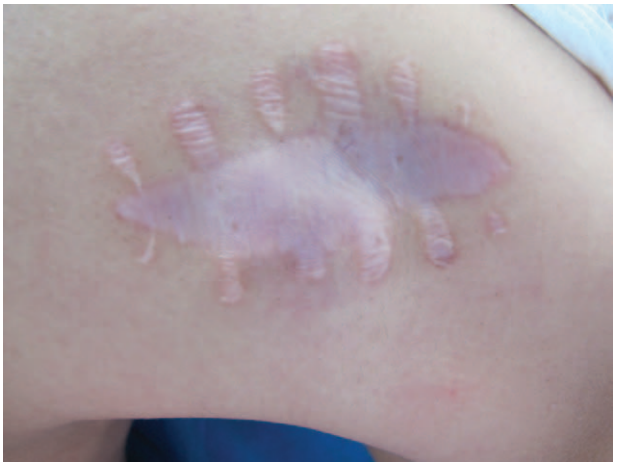

Figure 1. Clinical manifestations of the left shoulder.

considered an enlarged lymph node. Chest and abdominal computed tomography (CT) revealed multiple nodules in the right middle lobe of the lung. A histopathologic examination of the left shoulder tumor and left supraclavicular lymph nodes revealed normal epidermis. However, nests of monomorphic tumor cells had infiltrated the lower dermis and subcutaneous fat layer; some cells had large atypia and deeply stained nuclei with active mitotic figures, but no obvious melanin (Fig. 2). Immunohistochemistry revealed the following: S100 (+++), HMB45 (+), cytokeratin (CK) (−) CK7 (−), CK20 (−), CD34 (−), epithelial membrane antigen (EMA) (−), and Ki67 > 70% (−) (Fig. 3). A diagnosis of AMM was made.

5. Therapeutic intervention

The patient was subsequently transferred to the Department of Oncology, where a chemotherapy regimen comprising temozolomide at 200 mg on days 1 to 5, cisplatin at 60 mg on day 1 and 50 mg on day 2, and bevacizumab at 200 mg on d 1. One month later, another recurrence was observed. B-ultrasound revealed enlargement of the left cervical lymph nodes and subcutaneous hypoechoic lesions under the left shoulder scar. An extended resection (>1 cm beyond the primary site) and complete resection of the left supraclavicular lymph node were performed, and the skin was sutured using a Z-shaped flap technique.

Postoperatively, a second chemotherapy regimen comprising gemcitabine at 1400 mg on days 1 and 8, and tegafur–gimeracil–oteracil at 100 mg on days 1–14 was initiated. On day 9 of chemotherapy, the patient suddenly experienced chest tightness and dyspnea accompanied by numbness and convulsions, indicative of allergic shock. Her symptoms were gradually alleviated following an injection of 80 mg of methylprednisolone.

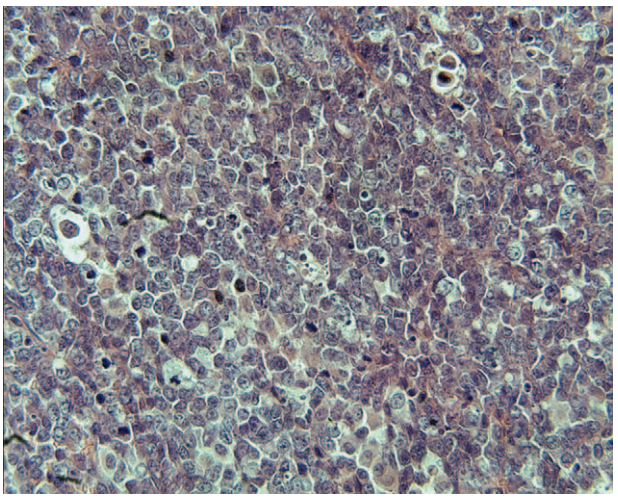

Figure 2. Pathological examination. Hematoxylin-eosin staining showed nests of monomorphic tumor cells with big, atypia, deep stained nucleus, and active mitotic figures but no obvious melanin (magnification 400×).

6. Follow-up and outcomes

A brain CT scan revealed no obvious abnormalities. However, an ambulatory electroencephalogram was abnormal, with a large number of single, middle- and high-amplitude, repeated bursts, spikes, and slow waves at each wake-up stage. After consulting the Department of Encephalopathy, we could not exclude a diagnosis of epilepsy. Although the suspension of chemotherapy and administration of molecular target treatment (i.e., BRAF inhibitors) were recommended, the patient and her families refused and insisted upon receiving further treatment at the local hospital. At a 6-month follow-up, the patient reported using oral Chinese medicine of an undetermined type and had not relapsed.

7. Discussion

The pathogenesis of MM remains somewhat unclear, although some tumors are known to derive from benign nevi, likely in response to adverse external stimuli that induces the malignant transformation. Such transformations often occur in areas targeted by laser surgery or frictional palmoplantar areas. MMs can usually be divided into 4 common types—acral lentiginous melanoma, lentigo maligna melanoma, nodular melanoma, and superficial spreading melanoma—and are generally easily diagnosed from the medical history, color (e.g., melanin), morphology, and histopathological features.[3,4]

The rare subtype AMM is considered a degenerative development from MM and comprises cells derived from melanocytes, but not fully formed melanin granules. AMMs do not manifest typically and usually appear as red or pink macules or papules with unclear boundaries, uniform color, and slight pigmentation at the edge. These tumors often occur in the nail bed, forehead, trunk, extremities, periorbital region, female genitalia, or other parts of the body. These tumors exhibit similar growth and infiltration patterns as other MMs, and can later form red plaques, granulomatous nodules, or ulcers.[5–7]

Similar to MM, AMM exhibited the histological characteristics of subepidermal and (or) intradermal nests of anomalous cells containing large, deeply stained nuclei, and mitosis. However, AMMs do not exhibit melanin granules when stained with ordinary hematoxylin and eosin (HE) staining. Electron microscopy to detect melanin granules is the gold standard for diagnosis, and dermatoscopy, confocal scanning microscopy, and dynamic contrast-enhanced MRI (DCE-MRI) can facilitate a diagnosis.[8] Additionally, melanin can be detected using silver staining, dopa, and tyrosinase reactions. Immunohistochemistry is also used to improve the sensitivity of a MM diagnosis. However, S100, one of the most common markers, is highly sensitive but poorly specific because it is also expressed by schwannomas, gliomas, osteosarcoma, and Langerhans cells. By contrast, HMB-45 yields better specificity with poorer

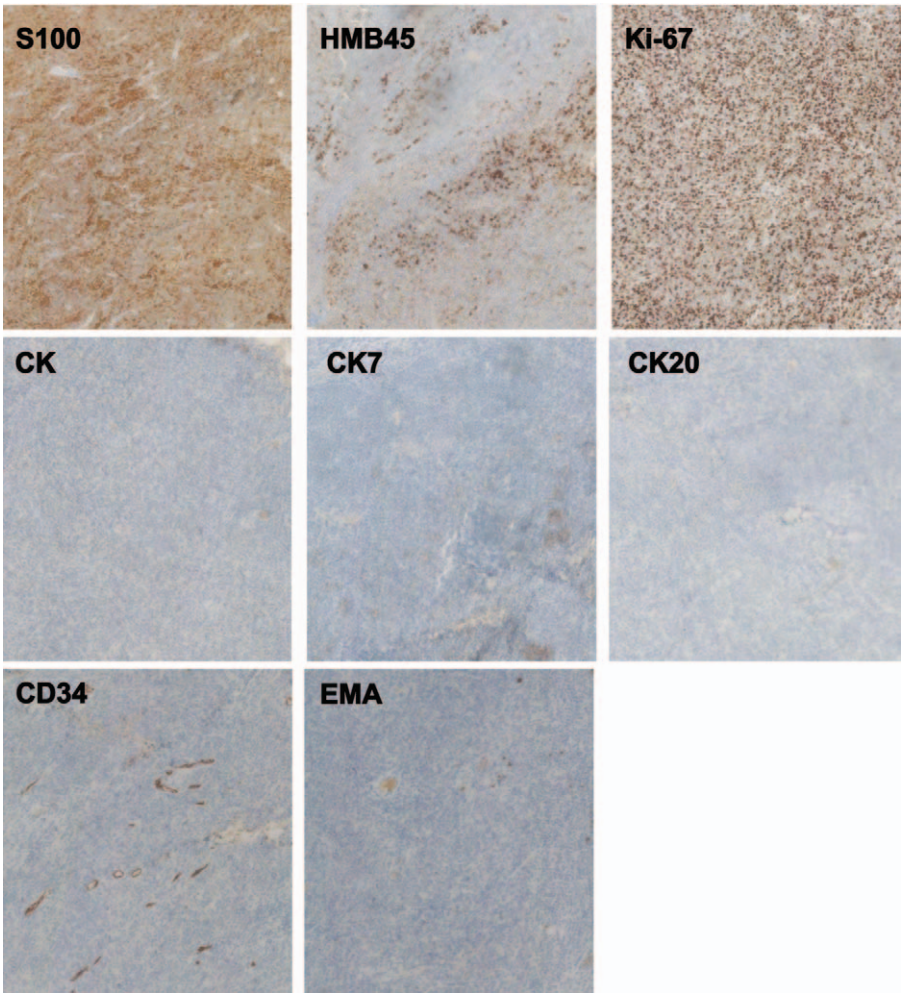

Figure 3. Immunohistochemical staining shows S100 (+++), HMB45 (+), CK (−) CK7 (−), CK20 (−), CD34 (−), EMA (−), Ki67 more than 70% (+) (magnification 100×).

sensitivity.[9] Other MM-associated antigens, such as Melan-A, tyrosinase (T311), and NKIC3, are also diagnostically useful.[10] AMM is frequently misdiagnosed because of the absence of specific clinical features. Clinically, AMM should be differentiated from other benign tumors such as eczema, nevus, seborrheic keratosis, verruca vulgaris, pyogenic granuloma, scar, and hemangioma, as well as malignant tumors such as basal cell carcinoma, squamous cell carcinoma, and Paget's disease. Histologically, AMM should be differentiated from hyperplastic benign melanocytic nevus, Spitz nevus, Paget's disease, malignant fibrous histiocytoma, and spindle cell squamous cell carcinoma.[11]

Currently, no ideal treatment for MM has been identified, and complete surgical resection at an early stage remains the preferred method. The extent of resection is usually determined according to the pathological stage: a 5-mm excision margin for melanoma in situ (restricted to the epidermis), 1-cm margin for a melanoma <1.0 mm thick, 1 to 2-cm margin for a melanoma 1.0–4.0 mm thick, and a ≥2-cm margin for a melanoma >4 mm thick.[3] Although MM is generally considered insensitive to radiotherapy,[12] chemotherapy can be used as a palliative treatment (i.e., survival prolongation and symptom relief) for patients with advanced, metastatic disease. Currently, MMs are generally treated with combination chemotherapy regimens,[13] although increased interest has been given to biological agents such as targeted therapies (BRAF inhibitors dabrafenib and vemurafenib, MEK inhibitors trametinib and cobimetinib, anti-CTLA-4 monoclonal antibodies ipilimumab and tremelimumab, anti-PD-1 monoclonal antibodies nivolumab and pembrolizumab, and anti-VEGF monoclonal antibody bevacizumab), cytokines (interferons and interleukins), and tumor vaccines.[14] However, most of these agents are still being tested, and the overall prognosis of MM remains poor.

The absence of specific clinical features often leads to a delayed diagnosis of AMM at an advanced stage. Given the importance of early diagnosis in terms of prognosis, we stress the importance of remaining vigilant about early stage lesions. For some persistently growing and proliferating lesions, conventional treatment is largely ineffective and is followed by rapid relapse. Accordingly, these lesions should be subjected to pathologic and immunohistochemical examinations. Given the link between adverse stimuli and MM, patients with atypical clinical manifestations should avoid destructive treatments such as cryotherapy, electrocautery, and laser therapy before receiving a definitive histopathological diagnosis.

The young female patient in the present case presented with a brown nodule on her left shoulder that rapidly relapsed as a hyperplastic keloid after surgical resection. Reports of the keloid form of AMM are extremely rare; Brandt et al[2] reported a case

involving a tumor in a cesarean scar, wherein the patient did not receive timely treatment and died 1 year later. These lesions are likely to be diagnosed as keloids if the clinician is not fully informed about the medical history. In this case, the patient received an early diagnosis of a benign lesion at a local hospital, and the extent of the initial resection surgery was not sufficient; in fact, it may have been an important stimulant of the left supraclavicular fossa lymph node metastasis.

In summary, earlier histopathological and immunohistochemical examinations and surgery with an appropriate margin could have allowed the patient in the current case to avoid a late metastasis of AMM and systemic chemotherapy, which led to suspected epilepsy and chemotherapy and targeted therapy cessation. Despite the lack of recurrence during a 6-month period, this patient should be followed closely to detect any recurrence or metastasis at an early stage.

Acknowledgments

This work was supported by the Second Affiliated Hospital of Xi'an Jiaotong University and approved by the ethic committee of the Second Affiliated Hospital of Xi'an Jiaotong University, and informed consent was obtained from the patient.

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