

Primary acral amelanotic melanoma: A rare case report

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Abstract. The aim of the present study was to present a rare case of primary acral amelanotic malignant melanoma (AMM). A 61-year-old man developed an aggressive tumor in the front part of the sole of his left foot, which continued to increase in size for >1 year. The biopsy results revealed epidermis loss, ulcer formation, and the presence of abundant allotropic tumor cells throughout the dermis, with deeply stained nuclei, light reddish cytoplasm and visible multinucleated giant cells with heterogeneous nuclear division. The tumor cells exhibited partial formation of nests and bundled distribution, and there were no observed pigment particles. The diagnosis was confirmed as AMM based on the findings of the histopathological examination and immunohistochemical staining for Ki67 (+++), Melan-A (+++), human melanoma black 45 (+), CD20 (-), cytokeratin (CK)7 (-) and CK5/6 (-).

Introduction

Malignant melanoma (MM) is a cutaneous and/or extra-cutaneous tumor that arises from the embryological remnants of neural crest cells/melanocytes, melanoma can happen in eyes and internal organs but rare (1). The number of recorded new cases in 2018 was 2,87,723, whereas the number of deaths in 2018 in both sexes and across all ages was 60,712 (Globocan 2018, International Agency for Research on Cancer, World Health Organization; [https://gco.](https://gco.iarc.fr/today/data/factsheets/cancers/16-Melanoma-of-skin-fact-sheet.pdf)

[iarc.fr/today/data/factsheets/cancers/16-Melanoma-of-skin-fact-sheet.pdf](https://gco.iarc.fr/today/data/factsheets/cancers/16-Melanoma-of-skin-fact-sheet.pdf)). According to the National Cancer Institute, the incidence of melanoma has increased sharply over the last 30 years, and ~7,230 deaths were caused by melanoma in 2019 (2). Cancer Research UK estimated that the incidence rate of melanoma is 3.1/10,000, with a mortality rate of 0.8/10,000 worldwide (3). Despite the advances in the treatment of metastatic melanoma, the 5-year survival rate of melanoma with distant metastasis remains low at ~16% (4,5). Due to the high propensity for metastasis and poor prognosis of MM, early diagnosis and timely treatment are crucial. Amelanotic MM (AMM) is a rare clinical type of melanoma that comprises 2-8% of all MM cases (6,7). AMM is a clinically diverse entity and its clinical characteristics are non-specific; hence, the diagnosis of AMM is difficult, and it can easily be misdiagnosed as other cutaneous diseases and/or tumors, such as benign ulcerations or squamous cell carcinoma (8,9). The aim of the present study was to report a rare case of primary acral AMM that was initially misdiagnosed as cutaneous squamous cell carcinoma.

Case report

On 1 January 2019, a 61-year-old man presented to the Dermatology Clinic at the Affiliated Hospital of Guangdong Medical University with a painful pinkish tumor on the sole of his left foot that had been enlarging over the last 3 months. Approximately 1 year before the patient presented at the Dermatology Clinic of the Affiliated Hospital of Guangdong Medical University, he observed an ulcerated mass with exudate in the sole of the left foot, sized ~2x3 cm, that developed after an injury. The ulcerated wound was treated with local povidone iodine and oral cefuroxime axetil for 2 months at a local clinic, but without obvious improvement. After 3 months, the mass in the left foot gradually increased in size to 7x6x5 cm (Fig. 1). Macroscopically, the mass was cauliflower-like, with a pinkish color and no pigmentation. The mass appeared to be locally infiltrative with poorly defined boundaries, and was adherent to the subcutaneous tissue with poor mobility (Fig. 1). The findings of the chest X-ray, electrocardiogram and abdominal B-ultrasound were normal. A biopsy was performed in the previous hospital and the lesion was originally diagnosed as squamous cell carcinoma. The mass was surgically resected, and histopathological

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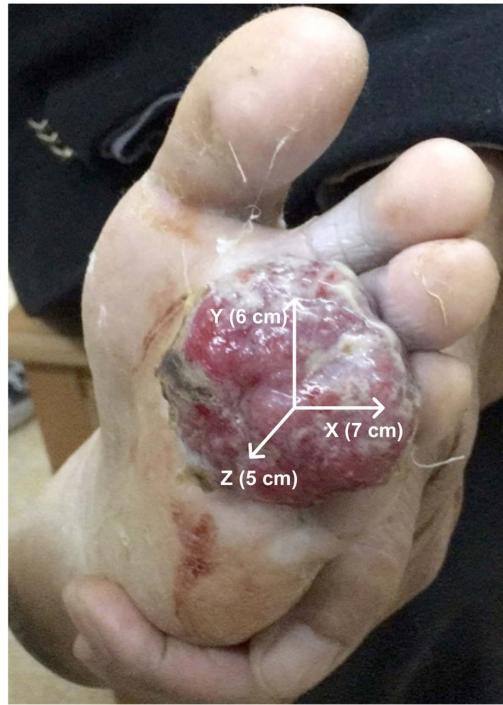


Figure 1. The dimensions of the mass were 7x6x5 cm. Macroscopically, the mass was cauliflower-like, with a pinkish color and no pigmentation. The mass appeared to be locally infiltrative with poorly defined boundaries, and was adherent to the subcutaneous tissue with poor mobility.

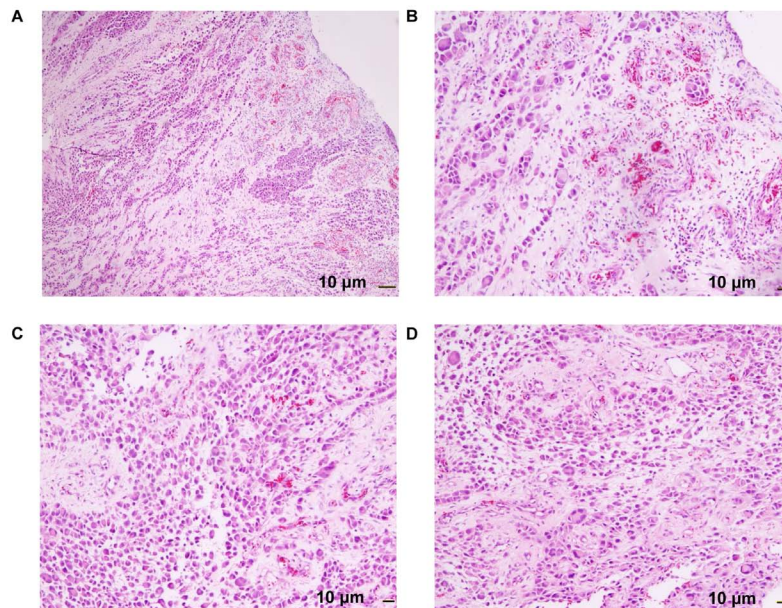


Figure 2. The findings on histopathological examination were as follows: (A) Loss of epidermis with ulcer formation, (B) with abundant tumor cells in the whole dermis, (C) heterogeneous nuclear division, (D) partial nest formation and bundled distribution, without pigment particles. Hematoxylin and eosin staining; all magnifications, x10.

examination revealed loss of epidermis with ulcer formation, abundant tumor cells throughout the whole thickness of the dermis (characterized by deeply stained nuclei, reddish cytoplasm and visible multinucleated giant cells), heterogeneous nuclear division, partial formation of nests and bundled distribution, and lack of pigment particles (Fig. 2). The results of immunohistochemical examination were as follows: Ki67 (+++), Melan-A (+++), human melanoma black (HMB)45 (+), CD20 (-), cytokeratin (CK)7 (-) and CK5/6 (-)

(Fig. 3). The evidence mentioned above was consistent with the diagnosis of AMM. The patient was subjected to partial amputation of the left foot and plastic reconstructive surgery on January 4, 2019, and the pathological examination of the surgical specimen further confirmed the diagnosis of AMM (Fig. 4). The patient is currently followed up and awaiting positron emission tomography-computed tomography (PET-CT) examination to determine the presence of metastatic disease. The last follow-up was on January 23, 2019.

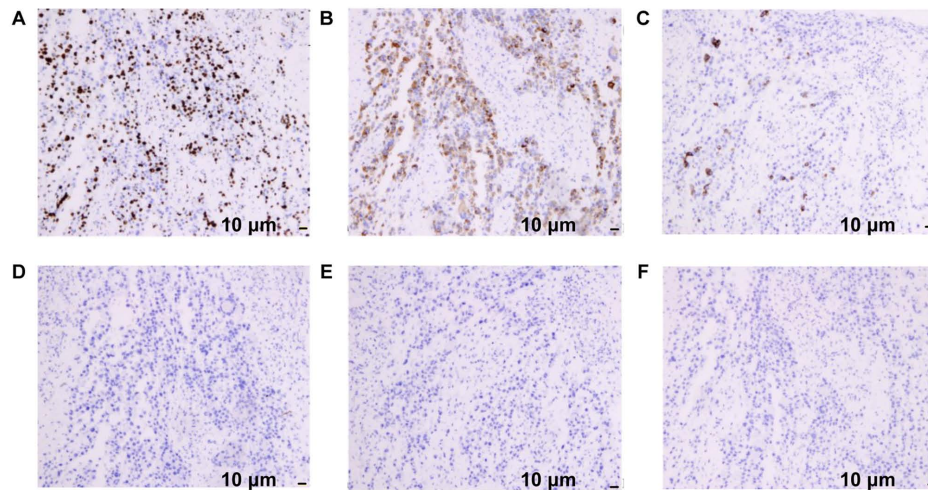


Figure 3. The results of the immunohistochemistry examination were as follows: (A) Ki67 (+++), (B) Melan-A (+++), (C) human melanoma black 45 (+), (D) CD20 (-), (E) CK7 (-), (F) CK5/6 (-). CK, cytokeratin; all magnifications, x20.



Figure 4. The patient was subjected to partial amputation of the left foot and plastic reconstructive surgery.

Discussion

MM is a highly malignant tumor, accounting for 6.8-20% (third in incidence) of cutaneous malignant tumors, that mostly occurs in the skin, although rare cases of non-cutaneous melanoma may be encountered in the eyes and internal organs (10). Primary acral AMM is an aggressive rare neoplasm, with only few cases reported to date. AMM does not produce melanin, therefore it may easily be misdiagnosed as benign ulcer or/and squamous cell carcinoma (8,9). When the patient was first referred to our hospital, he had stage T4b disease. A PET-CT scan was suggested; however, there were no readily identifiable metastases around the MM lesions, and the patient refused. Without a PET-CT scan, the presence or absence of visceral metastases could not be confirmed. The etiology of AMM remains unclear, although it was previously hypothesized that decreased tyrosinase activity and/or melanin transport disorders may constitute possible reasons (11). AMM has been reported in the skin and the mucosa of the digestive and/or genitourinary tracts (1,10). AMM is a clinically diverse entity without specific characteristics; early lesions are atypical and

usually appear as pinkish papules, either as a single lesion or in clusters (10,12). Invasive growth during the later stages may manifest as red plaques with granulomatous nodules or ulcers; therefore, it is important to be aware of the diagnostic difficulties of primary acral AMM. In the present case, the diagnosis of AMM was confirmed by histopathology and immunohistochemistry. The immunohistochemistry staining may help diagnose AMM using common immunological markers, including HMB-45, Melan-A, S-100 and Ki-67 (13). Ohnishi *et al* (13) have reported that Melan-A is the most precise marker in terms of sensitivity and specificity; in the present case, the immunohistochemical results revealed that the tumor was positive for HMB-45, Melan-A and Ki-67, while it was negative for CD20, CK7 and CK5/6.

The characteristics of AMM occurring in the limbs and body differ from those of other tumors, such as squamous cell carcinoma (13), basal cell carcinoma and lymphoma. AMMs are characterized by a higher proportion of nodular and acral lentiginous melanoma subtypes compared with pigmented melanomas. AMMs are also characterized by a greater Breslow thickness, higher mitotic rate, more frequent ulceration, higher tumor stage at diagnosis, and lower survival rates compared with pigmented melanomas (14). Early surgical resection is the first choice of curative treatment and chemotherapy is the most commonly used palliative treatment. Although there have been advances in MM immunotherapy for patients with late-stage disease and metastasis, such as PD-1/CTLA-4 antibodies and IL-2 targeted therapy, due to the prognosis, early detection and treatment remain crucial for prolonging survival.

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Availability of data and materials

The datasets generated and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JZ and RC were responsible for writing the manuscript. HY, JL and FZ performed data collection. JZ and JL performed analysis. JZ was responsible for arranging the figures. JS and RC were responsible for critically reviewing and editing the manuscript. JZ, JS and RC were responsible for case design. All the authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The patient provided written informed consent prior to treatment.

Patient consent for publication

The patient provided written informed consent to the publication of the case details and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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