

Acral Lentiginous Melanoma: A Case Presentation

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INTRODUCTION

Acral lentiginous melanoma (ALM) is a subtype of thin or cutaneous malignant melanoma that primarily affects the melanocytes of the palms, soles, and subungual areas of the digits. Accounting for less than 10% of the 4 major subtypes of primary cutaneous melanomas, it is the most frequent type of melanoma found in Asians and dark-skinned individuals. (1,2)

Initial metastasis occurs via lymphatic drainage. Histologic parameters are currently utilized to help predict the probability of sentinel lymph node involvement and prognosticate outcomes. Clark's level and Breslow's depth determine the degree of vertical penetration. Tumor invasiveness and likelihood of metastasis to regional lymph nodes may be predicted by the presence of ulceration, number of mitotic divisions, regression, tumor infiltrating lymphocytes, and degree of vascular, perineural, and lymphocytic invasion.

CASE REPORT

A 49-year-old African American man presented to the clinic with a chief complaint of pain and discoloration of the distal aspect of the right second toe. He was concerned it was infected because of a draining ulceration at the distal tip of the digit. The patient stated that 6 months previously, the nail fell off on its own, without any history of trauma. The patient also reported that the end of the toe had gradually turned black and the discoloration became larger. He was under the care of his primary physician and had been receiving treatment for Hepatitis C (HCV). It was thought the discoloration was secondary to his hepatitis C medication, which could not be identified at the time of the visit. The patient's medical history was significant for resolved papillary thyroid carcinoma and nontoxic multinodular goiter.

The podiatric examination showed sharply demarcated black discoloration at the distal aspect of the second digit of the right foot extending proximally to the proximal interphalangeal joint and measuring 5.0 x 3.4 cm. There was an area of granulation tissue measuring 0.4 x 0.3 cm where the nail bed should have been (Figure 1). Full-thickness skin breach at the distal aspect of the toe probed 0.2 cm

with serous drainage (Figure 2). Radiographs demonstrated focal erosion of the distal tuft of the terminal phalanx of the right second digit (Figure 3).

With patient consent, two excisional 3 mm punch biopsies were performed on the right second digit. Specimens were taken from the plantar margin of the pigmented lesion and from the lateral portion of the lesion where pigmentation was even and regular. A bacterial culture was also taken from the distal lesion and sent for culture and sensitivity.



Figure 1. Clinical view at initial visit.



Figure 2. Clinical view at initial visit. Biopsy was taken from the plantar margin and within the lesion laterally.



Figure 3. Focal erosion of distal tuft of the terminal phalanx of the right second toe present at the initial visit.

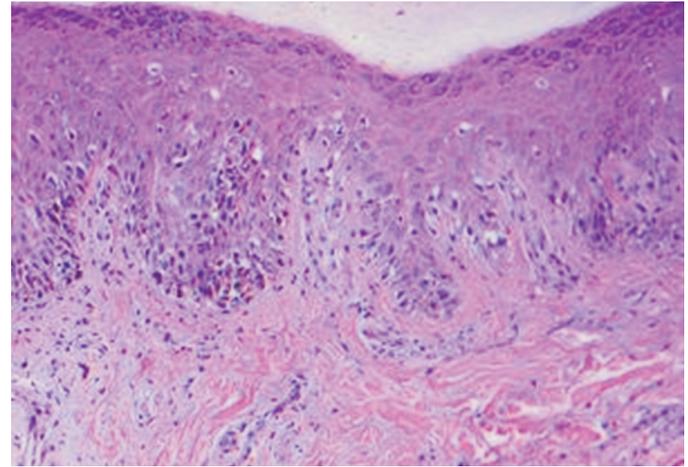


Figure 4. Malignant melanoma in situ. Proliferation of intra-epidermal melanocytes. There is confluence of melanocytes along the dermal-epidermal junction. The underlying dermis is uninvolved.

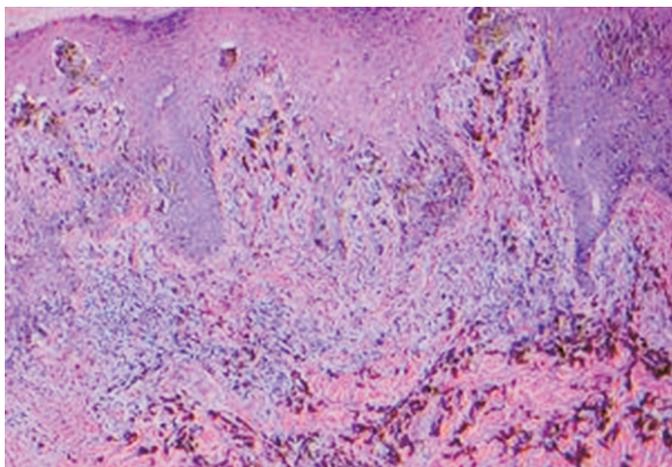


Figure 5. Acral lentiginous melanoma. Atypical melanocytic proliferation, which extends from the surface into the reticular dermis. Within the epidermis, melanocytes exhibit scatter above the basal layer and confluence along the dermal-epidermal junction. Within the dermis, melanocytes form nests with bizarre geometric shapes.

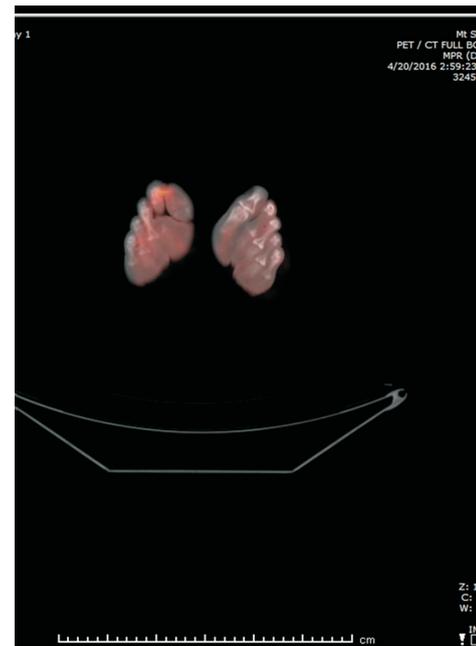


Figure 6. PET/CT scan demonstrating focal hypermetabolic uptake corresponding to the second digit of the right foot.

RESULTS

Histologic staining of the tissue from the plantar margin demonstrated a proliferation of intra-epidermal melanocytes with a confluence along the dermal-epidermal junction, which was characteristic of malignant melanoma in situ (Figure 4). Tissue taken laterally was evaluated for thickness and demonstrated an atypical melanocytic proliferation that extended from the surface into the reticular dermis. It was graded as a Clark's level II-III with Breslow's depth of 0.85 mm. The growth phase was vertical and tumor infiltrating lymphocytes brisk. The mitotic rate

was 0 (minimal intradermal component), with vertical growth phase, and partial lesion regression with peripheral margins involved. The findings were characteristic of acral lentiginous melanoma (Figure 5). Bacterial cultures taken from the draining ulceration were positive for heavy growth of oxacillin-sensitive *Staphylococcus aureus*, scant growth of *Pseudomonas aeruginosa* and light growth of Group B streptococcus.

The patient was referred to a surgical oncologist for further evaluation. A full body PET scan/computed tomography metabolic imaging study demonstrated focal hypermetabolic uptake corresponding to the second digit of

the right foot with no focal abnormal uptake in the popliteal region nor enlarged hypermetabolic inguinal or pelvic lymph nodes (Figure 6). Two months later, the patient had an amputation of the right second toe and a sentinel lymph node biopsy of the right groin was performed. Of the 3 lymph nodes removed, 2 of them showed high activity. Unfortunately, no other follow-up information is available.

DISCUSSION

ALM can present as brown to black macules and papules on the skin or nail with discolored, darkened longitudinal striae involving the nail bed as well. Cutaneous digital involvement may have the appearance of subdermal hemorrhage or an ischemic event with a potential myriad of etiologies, including a vasculitis-related drug reaction. Traditional guidelines for the recognition of melanoma, such as the ABCDEs of a pigmented lesion or the ugly duckling sign, may be helpful. This case considered a potential drug reaction as the etiologic factor. The presence of a distal, draining, digital ulceration could have had numerous potential etiologies (3).

In the case presented, changes in the appearance of the second toe were initially diagnosed as a reaction to previously prescribed HCV medication. HCV infection itself has been reported to cause dermatologic and muco-cutaneous manifestations as well as small vessel complications. Prescribed drug therapy has also been associated with adverse cutaneous reactions. Manifestations vary from patient to patient and according to the drug therapy prescribed (4). Skin reactions associated with this drug therapy may occur up to 6 months following completion of treatment, requiring evaluation during this period. Should a suspicious lesion occur after completely stopping HCV drug therapy, a biopsy of the lesion should be performed to accurately diagnose other skin pathologies.

Difficulties in diagnosing ALM have led to the creation of algorithms to help solve these challenges. Bristow (3) proposed the “CUBED” algorithm. This consists of color variation, uncertain diagnoses, bleeding lesions on the feet underneath the nail, enlargement or deterioration of a lesion or ulcer despite therapy, and delay in healing of any lesion beyond 2 months.

It is important in the evaluation and management of a patient with a lesion of uncertain etiology to take a biopsy sample. Ideally, one should excise the area of concern with adequate surgical margins, this is not always a possibility in the foot. When a biopsy report confirms ALM, a Breslow’s depth of greater than 1 mm and/or the presence of ulceration carry an increased probability of sentinel node involvement. When this occurs, sentinel lymph node biopsy

is recommended. The grade of sentinel node involvement is the most important predictive factor for survival rate and recurrence in non-metastatic melanoma (1,5). Predictors of sentinel node involvement determined histologically on the biopsy report include ulceration, mitotic rate, regression, and lymphocytic infiltration.

Ulceration is a significant independent predictor of 5-year survival rate. Ulceration can be measured either by diameter or as a percentage of the tumor’s width. Five-year survival rates in non-ulcerated versus ulcerated ALM lesions are 77.6% and 91.3%, respectively. Furthermore, the extent of ulceration is more important than its mere presence. It has been reported that minimally ulcerated lesions (<70% or <5 mm) have higher rates of survival than extensively ulcerated lesions (>70% or >5 mm) (6). Mitotic rate was zero in this patient. In thicker melanomas (1.01 to 2.0 mm), increased mitotic rate does correlate with greater probability of sentinel node involvement. However, this correlation is not apparent in melanomas less than 1.0 mm.

Regression occurs when the host immunological response is directed against the melanoma resulting in elimination of part or all of the lesion. Although regression is a good indicator of host defense, it can interfere with accurate measurement of the depth of a melanocytic lesion as it may appear thinner than it actually is. Therefore, regression is not a significant prognostic factor for patients with cutaneous melanoma. However, early signs of tumor regression are recognized by the presence of tumor infiltrating lymphocytes. The density and distribution of tumor infiltrating lymphocytes is associated with an improved prognosis. These lymphocytes infiltrate and disrupt nests of melanocytes. It has been reported that a “brisk” infiltration had a 5-year disease free survival rate of 91% in patients with cutaneous malignant melanoma measuring 1.0 mm or thicker, whereas a “non-brisk” infiltration carries a greater likelihood of tumor positive sentinel lymph node biopsy. In the case presented, application of these pathologic findings suggested that a sentinel node biopsy would be negative. Three sentinel nodes were resected, 2 were classified as highly active. There was a 2-month interval between diagnosis and node biopsy, perhaps this time interval enabled lymph node involvement.

In conclusion, this case highlights the importance of early recognition, the importance of skin biopsy, and the likelihood of sentinel node involvement based on clinical and histologic findings. ALM may mimic the appearance of numerous skin and vascular pathologies. Early recognition of ALM carries a more successful outcome. Sentinel node involvement and the probability of metastatic events may be predicted by specific cytological and clinical parameters.

Table 1. Pathology Report Predictors and Patient Results.

Breslow's Depth	0.85 mm
Clarks Level	II - III
Ulceration	Present
Mitotic Rate	0 (minimal intra-dermal component)
Growth Phase	Vertical
Regression	Partial
Tumor Infiltrating Lymphocytes	Brisk

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