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A rare case of circumferential osteoinvasive subungual melanoma: A case report

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Abstract

Subungual melanoma is a rarer form of melanoma encountered in clinical practice that often has a poor prognosis because it presents with advanced disease. We report a case of a 46-year-old male with a circumferential osteoinvasive melanoma that invaded the superior and lateral aspects of the periosteum of the distal phalanx. We discuss pathologic findings and common physical exam findings to facilitate earlier diagnosis of subungual melanoma.

Keywords

Skin cancer, subungual melanoma, osteoinvasive, dermatopathology, tumor

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Introduction

Subungual melanoma (SUM) is a clinical term that refers to cutaneous malignant melanoma that arises in the nail unit, independent of its histological subtype. The overall prevalence of SUM in the general population is 1.9%.[1] The nail apparatus represents <1% of the total body surface area, perhaps suggesting that melanomas are overrepresented in the nail apparatus.[2] Nevertheless, the rate of misdiagnosis for SUM is >20%.[3]

SUM is often diagnosed at advanced disease stages due to misdiagnoses, late presentation, insufficient biopsy material, co-existing pathologies that mask signs of melanoma, and concealment with nail lacquer perhaps contributing to a poor prognosis[4] with an estimated 5-year survival rate of 77%.[1] The standard treatment for SUM is surgical resection and/or digit amputation.

We present an aggressive case of a circumferential osteoinvasive SUM on the right hallux to emphasize the importance of making a timely diagnosis in cases of melanoma, due to its ability to rapidly metastasize into regional lymph nodes and have extensive local spread. The patient provided verbal consent for the reporting of this case.

Case report

A 46-year-old male patient presented with an atraumatic, non-healing ulcer for 6 months duration on the dorsal surface of the distal phalanx of the right great toe (hallux) following unsuccessful treatment with antibiotic and antifungal agents by an outside hospital. The patient reported a history of a black discolored nail bed and a dystrophic nail which progressively detached, leading to the development of an ulcer. On exam, the ulcer was full thickness with a friable base, irregular edges, and black discoloration at left edge of the nail matrix (Figure 1(a)).

Radiographic assessment of the affected hallux was unremarkable. A tissue biopsy from the ulcer margin was obtained and revealed melanoma with ulceration (Figure 1(b))—the tumor was positive for Melan-A (Figure 1(c)), S100, and Sox10, and negative pancytokeratin AE1/AE3 immunohistochemical stains. The depth of invasion on biopsy was at least 4.2 mm, with 2 mitoses per mm^2. Genetic testing was negative for a BRAF mutation.

The patient's findings were discussed at the hospital Tumor Board with a recommendation for a partial right hallux amputation and sentinel lymph node biopsy. The hallux amputation revealed melanoma with Breslow thickness 13 mm, Clark level ⩾ V, with extension to deep dorsal soft

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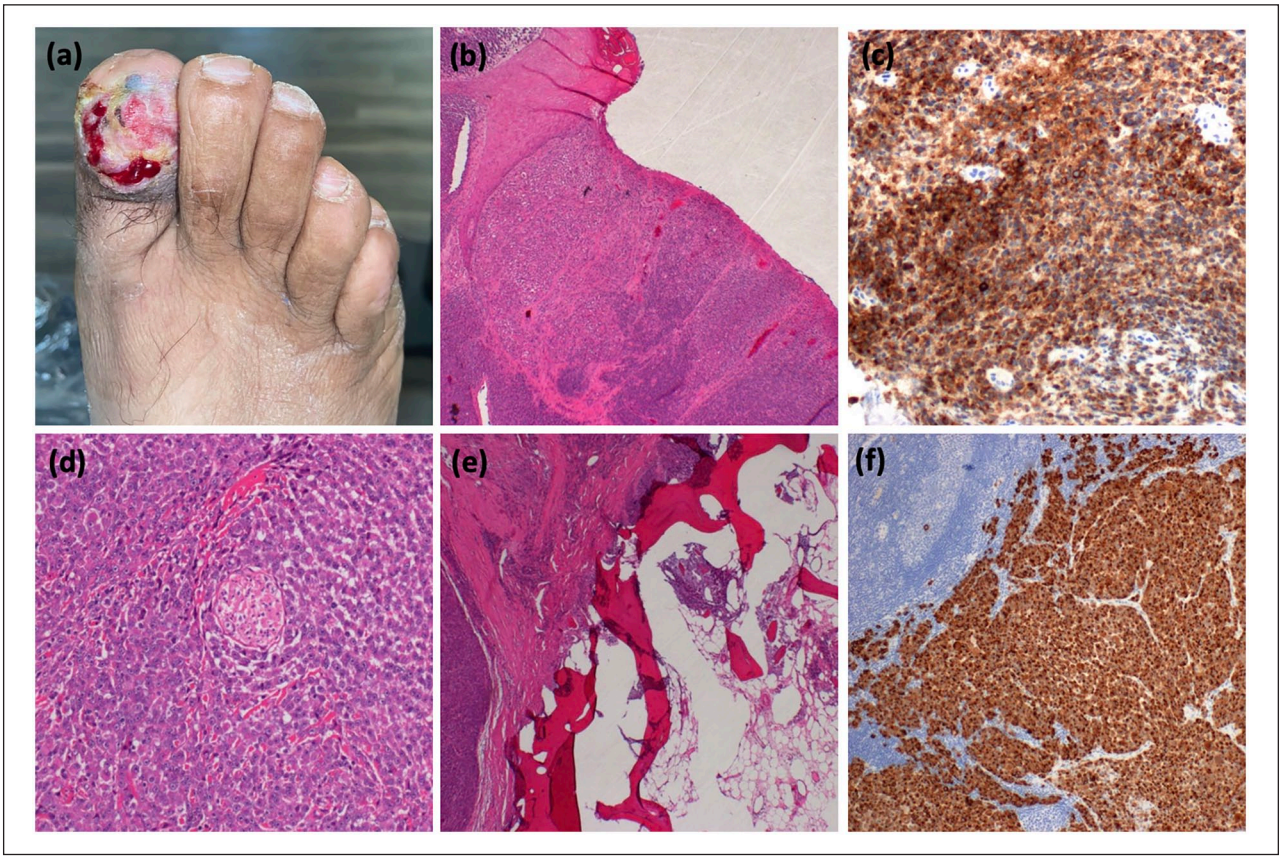

Figure 1. (a) Clinical photo of right distal hallux prior to partial amputation. (b) H&E stain of ulcerated nail bed, 2× magnification. (c) MelanA stain of nail bed, 10× magnification. (d) H&E stain demonstrating perineural invasion of melanoma, 10× magnification. (e) H&E stain demonstrating melanoma invasion into periosteum and focally into a marrow space 2× magnification. (f) MelanA stain of inguinal lymph node demonstrating metastasis, 4× magnification.

tissue, perineural invasion (Figure 1(d)), and focal invasion of underlying bone (Figure 1(e)). The extent of ulceration was up to 8 mm in width, with a mitotic rate of 20 mitoses per mm^2. Immunohistochemical stain Melan-A was positive in one right inguinal lymph node, supporting lymph node involvement by melanoma (Figure 1(f)). The pathologic staging was pT4b, N1 (melanoma >4.0 mm in thickness, with ulceration; one lymph node involved by tumor).

An MRI of the brain was completed 6 months after presentation to the emergency room and showed a 9 mm parietal lobe lesion—unknown if benign or malignant. The patient was started on pembrolizumab 200 mg every 3 weeks for 1 year.

Discussion

This case is a rapidly metastasizing SUM that demonstrates circumferential invasion through periosteum into the distal phalanx of the great toe, highlighting the importance of prompt biopsy for early recognition and diagnosis, due to the aggressive nature of the tumor. As the matrix produces the nail plate, atypical melanocytes that proliferate in the nail matrix are propelled forward across the nail bed. It is hypothesized that atypical melanocytes can be seen in the hyponychium at early stages with progression to subepithelial invasion below the nail matrix, nail bed, and hyponychium.[5] As the atypical melanocytes proliferate, the likelihood of bone attachment or invasion increases when tumor thickness exceeds 4 mm.[6]

The overall survival rate for foot melanoma is 70.6%.[7] It is unclear if subungual anatomic site is a poor prognostic factor among the acral lentiginous melanoma histologic subtype.[7–9] A 2016 retrospective chart review of 211 patients over 10 years showed that SUM was statistically significant to be associated with poorer survival and advanced disease compared to non-subungual toe melanoma.[7] Conversely, a retrospective cohort analysis of 627 primary acral melanomas showed a non-significant difference in the 1-, 5-, 10-year overall survival rates at 81%, 40%, and 28%, respectively, for SUM and 94%, 59%, and 38%, respectively for SUM.[8] Poor prognostic factors for overall survival include lesion duration (⩽2.5 years), high mitotic rate (>6 mm^{-2}), presence of vascular invasion, older age, ulceration, Breslow thickness, and sentinel lymph node positivity.[8,9]

It is hypothesized that most cases of SUM present due to concern for the appearance of the affected digit rather than

Table 1. Acronyms that can be used to guide the physical exam of suspected melanomas. (a) The "CUBED" acronym for foot melanoma.[11] (b) The "ABCDEF" criteria for subungal melanoma.[15]

(a) CUBED for foot melanoma
Colored lesions: where any part is not skin color
Uncertain diagnosis: any lesion that does not have a definite diagnosis
Bleeding lesions: direct bleeding or oozing of fluid as seen in granulation tissue
Enlargement: enlargement or deterioration of a lesion or ulcer despite therapy
Delay in healing beyond 2 months: delay in healing of any lesion beyond 2 months
(b) ABCDEFs of SUM
Age: Range 20–90 y, peak 5th–7th decades of life in *A*frican-Americans, Native *A*mericans, and *A*sians
Band (nail band): Pigment (*B*rown-*B*lack), *B*readth (⩾3 mm), *B*order (irregular/blurred)
Change or lack of *C*hange: Rapid increase in size/growth rate of nail band; failure of nail dystrophy to improve despite adequate treatment
Digit involved or *D*ominant hand: Thumb > hallux > index finger > single digit > multiple digits
Extension: extension of pigment to involve proximal or lateral nail fold (Hutchinson's sign) or free edge of nail plate
Family or personal history: of previous melanoma or dysplastic nevus syndrome

pain, highlighting the importance of timely diagnosis and management. The poor prognosis of melanoma is often contributed to delayed presentation at an advanced disease state. The SUM may appear as a superficial lesion but can present as a deeply invasive and aggressive tumor by the time of diagnosis. The differential diagnosis for SUM includes subungual hematoma, subungual hemorrhage, paronychia, pyogenic granuloma, onychomycosis, warts, callus, glomus tumor, benign nevus, poroma, subungual fibroma, keratoacanthoma, Bowen's disease, and subungual squamous cell carcinoma.[2,10,11] The case presented here highlights the importance of a prompt biopsy of clinically suspicious lesions due to the quick and aggressive nature of melanoma.

A detailed physical examination is important in identifying clinical features of early melanomas and can be remembered by the "ABCDE" mnemonic: Asymmetry, Border irregularity, Color variegation, Diameter >6 mm, and Evolution. Physical examination should focus on the width, pattern, and homogeneity of nail pigmentation, boundaries of the lesion, presence of nail deformity, extension of brown-black pigment from the nail bed, matrix, and nail plate onto the adjacent cuticle and/or proximal/lateral nail fold, known as Hutchinson's sign.[12] When paired with the ulceration of the nail bed or obliteration of the nail plate, Hutchinson's sign is pathognomonic for SUM.[12]

Not all melanomas present with the typical physical exam findings such as the dark pigmentation of the nail bed or adjacent cuticle. Black et al.[13] describe a case of osteoinvasive amelanotic melanoma of the nail bed that was difficult to diagnose due to lack of pigmentation on physical exam. Kleinerman et al. describe a case of osteoinvasive SUM with direct invasion through the periosteum, cortex, and marrow cavity of the distal phalanx with a negative Hutchinson's sign.[14] Nevertheless, there should be a low threshold for biopsy when suspicious of SUM.

Melanomas beneath the nail are often diagnosed later than melanomas located elsewhere due to frequent misdiagnosis as other more common foot disorders. The acronym "CUBED" can be used as an alternative acronym to highlight potential melanoma on the foot (Table 1(a)).[11] Another framework that can be used to clinically assess and identify features of early malignant melanomas on nail examination is the "ABCDEF" criteria proposed by Levit et al.[15] (Table 1(b)).

Despite the controversial opinions about the nature of SUM in the literature, this case proves the aggressive nature of this tumor and importance of the early diagnosis and management.

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Patient consent

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