Periungual Amelanocytic Malignant Melanoma with Osteocartilaginous Differentiation of the Right Hallux

A Case Report

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Malignant melanoma with osteocartilaginous differentiation is extremely rare. We report a case of periungual osteocartilaginous melanoma (OCM) on the right hallux. A 59-year-old man presented with a rapidly growing mass with drainage on his right great toe after treatment of ingrown toenail and infection 3 months earlier. Physical examination showed a 2.0×1.5×1.0-cm, malodorous, erythematous, dusky, granuloma-like mass along the fibular border of the right hallux. Pathologic evaluation of the excisional biopsy revealed diffuse epithelioid and chondroblastoma-like melanocytes with atypia and pleomorphism in the dermis with strong SOX10 immunostaining. The lesion was diagnosed as osteocartilaginous melanoma. The patient was referred to a surgical oncologist for further treatment. Osteocartilaginous melanoma is a rare variant of malignant melanoma that needs to be differentiated from chondroblastoma and other lesions. Immunostains for SOX10, H3K36M, and SATB2 are helpful for the differential diagnosis. (J Am Podiatr Med Assoc 113(1), 2023)

Osteocartilaginous melanoma (OCM), first described as a variant of melanoma in 1984,[1] is a rare entity. Fewer than 50 cases have been reported in the English literature.[2] Savant and colleagues[3] reviewed 17 cases of OCM and noted that the patients ranged in age from 32 to 83 years, with a mean age of 63 years. Men are more frequently affected than women, with a male-to-female ratio of 1:0.7.[3] The lesions are found predominantly in the subungual regions of either fingers or toes (58.8%).[3-7] Other locations, including retroauricular,[1] calf,[8] buttock,[8] back,[9-11] foot,[4,12-14] nasal cavity,[15-17] oral cavity,[18] esophagus,[19] and vaginal mucosa,[18,20] are also reported. Frequently, OCM presents as a pyogenic granuloma–like or ulcerated mass. Metastases to local lymph nodes or distant organs are observed in some patients.[4,16,21] Optimal treatments include wide local excision or amputation depending on the location of the tumor.[3] The outcome is similar to that of other melanoma types, with 47% of patients showing no signs of local recurrence at average follow-up of 51 months (range, 2–100 months).[3] However, local recurrences does happen in some patients at 6,[21] 20,[4] and 48[1] months.

Histologically, most OCMs are composed of spindle cell–like and osteocartilaginous melanocytes.[3] Desmoplastic or epithelioid cell components are less frequently observed.[14,18,21,22] Osteocartilaginous components can be purely cartilaginous,[6,7,23-25] osteoid,[2,5,13,14] or osteocartilaginous.[3,18,20,26] Therefore, OCM needs to be differentiated from chondroblastoma, osteosarcoma, and other benign lesions, including myoepithelioma, myositis ossificans, and fibro-osseous pseudotumor. Histologic evaluation and immunostain profiling of S-100, Melan-A, HMB-45, SOX10, and other biomarkers are useful for the differential diagnosis.

Several cases of OCM on different toes, including the first,[5,25,27] second,[13] and fifth[2] toes, have been reported. Herein we report a periungual melanoma with osteocartilaginous differentiation on the right hallux with the aim of shedding light on its clinical manifestations, pathologic features, and differential diagnosis.

Case Presentation

A 59-year-old man initially had an ingrown toenail with infection of the right first toenail that was

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treated 3 months earlier by permanent avulsion of the entire nail plate using blunt dissection. The patient recovered without infection or other complications. During the 3 weeks preceding the diagnostic visit, he noticed a rapidly growing mass with drainage along the fibular border of the right hallux. He also had constant pain in the right great toe, with a pain scale score of 6 of 10. The pain was not relieved by treatments with daily washing, topical antibiotics, and sterile dressing. Physical examination revealed a malodorous, 2.0×1.5×1.0-cm, dark-brown, ulcerated, granuloma-like mass along the distal end of the fibular border of the right hallux (Fig. 1A). The area was very tender to the touch. Anteroposterior, lateral, and lateral oblique radiographic views did not show erosion to the distal or proximal phalanges or signs of soft-tissue gas or foreign body in the right great toe. The granulomatous mass was completely removed and submitted to pathologic processing (Fig. 1B). Histopathologic observation showed an ulcerated neoplasia composed of a sheet of diffuse melanocytes with atypia and pleomorphism in the dermis (Fig. 2A). No melanin pigments were seen in the melanocytes. Large areas of the tumor had chondroblastoma-like morphologic features with more nuclear atypia and frequent mitotic figures (Fig. 2B). There were also admixed regions showing osseous differentiation (Fig. 2C). One of the tissue fragments with overlying epidermis showed single and small clusters of cytologically atypical epithelioid cells with somewhat amphophilic cytoplasm (Fig. 2D). Immunohistochemically, SOX10 showed diffuse nuclear positivity for both the epithelioid (Fig. 3A) and the chondroblastoma-like (Fig. 3B)

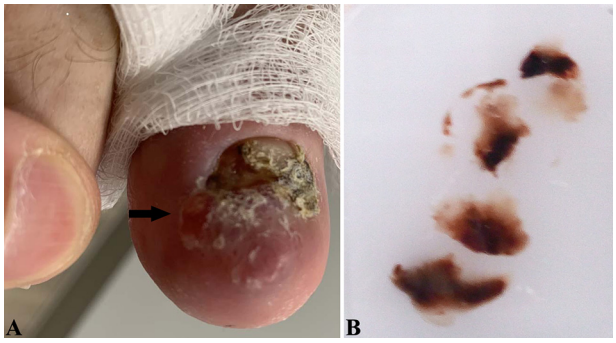

Figure 1. Clinical presentation of the periungual melanoma in the right great toe. A, The arrow indicates the scar where the mass was excised (note that the hallux nail had been previously avulsed, before the excisional biopsy visit). B, The dark-red, serially dissected, granuloma-like mass embedded in a paraffin block.

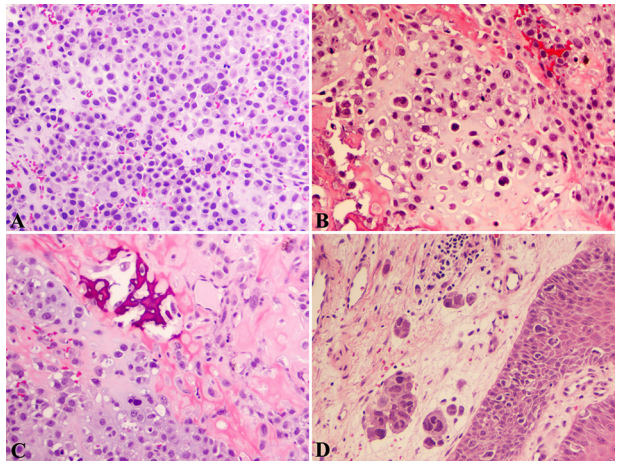

Figure 2. Histopathologic analysis of the melanoma in the right great toe. A, A sheet of round and ovoid epithelioid cells with atypia and pleomorphism but without melanin pigmentation (hematoxylin and eosin [H&E], ×100). B, Chondroblastoma-like cells embedded in the hyaline cartilage matrix (H&E, ×100). C, Osseous component in the mid-upper region (H&E, ×100). D, Multiple single and clustered epithelioid cells with atypia and pleomorphism in the epidermis and neoplastic melanocytes beneath the epidermis (H&E, ×100).

melanocytes. Only a small region of melanocytes in the superficial dermis and a few clusters of epithelioid cells in the epidermis showed strong immunoactivities for S-100 (Fig. 3C), Melan-A (Fig. 3D), and HMB-45 (Fig. 3E). More than 40% of melanocytes showed positivity for Ki-67 (Fig. 3F). The tumor cells were negative for CD31, CD34, CD68, and cytokeratin 5/6. H3K36M, a highly specific marker for chondroblastoma,[28] was negative, rejecting the diagnosis of chondroblastoma. However, SATB2, an osteoblastic transcription factor, exhibited extensive nuclear positivity (images not available). Immunostaining of H3K36M and SATB2 was conducted in the Department of Pathology, Brigham and Women's Hospital, Harvard University (Boston, Massachusetts). The histomorphology and immunostaining profiles pointed to the diagnosis of invasive malignant melanoma with prominent chondro-osseous differentiation (in consultation with Dr Christopher D.M. Fletcher, Harvard University). The patient was referred to a surgical oncologist for further evaluation and treatment.

Discussion

Divergent differentiation is a well-known phenomenon observed in different types of tumors, including

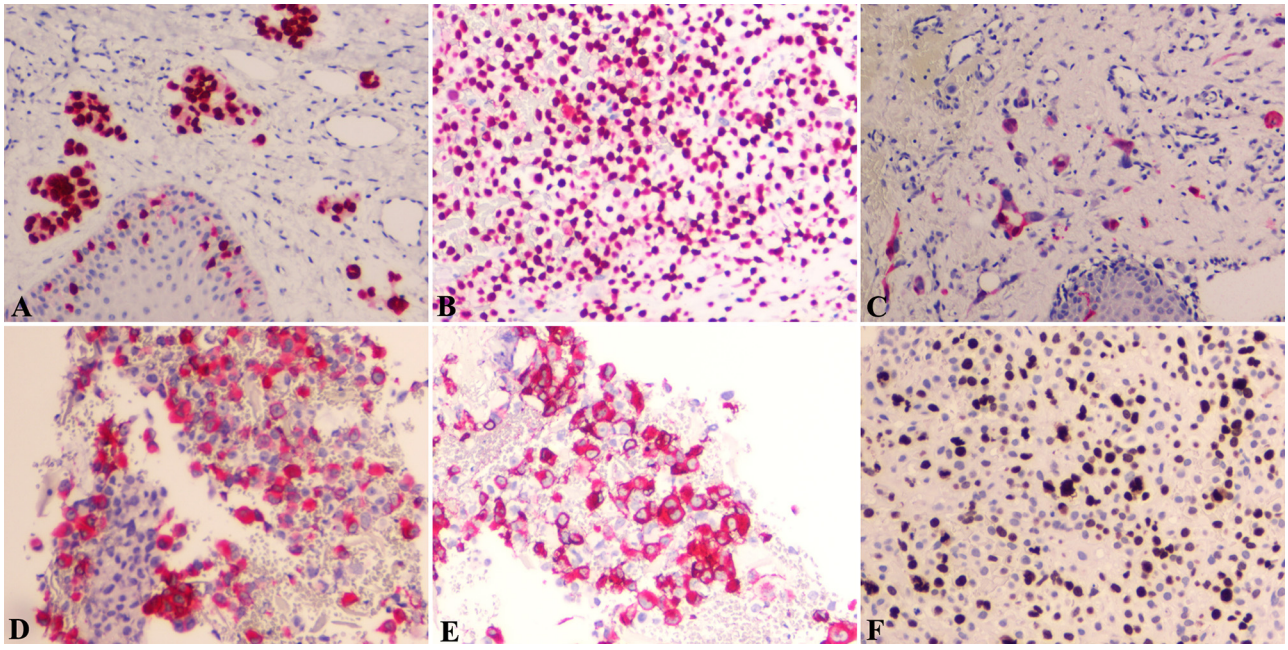

Figure 3. Immunostaining profiles of the melanoma in the right great toe. A, Strong nuclear expression of SOX10 in single and clustered epithelioid cells with atypia in the epidermis and tumor cells in the dermis (fast red, ×100). B, Strong nuclear expression of SOX10 in chondroblastoma-like melanoma cells (fast red, ×100). C, Cytoplasmic expression of S-100 in the epidermis and scattered tumor cells in the dermis (fast red, ×100). D, Cytoplasmic expression of Melan-A in a small region of melanoma cells in the dermis (fast red, ×100). E, Cytoplasmic expression of HMB-45 in a small region of melanoma cells in the dermis (fast red, ×100). F, Strong nuclear expression of Ki-67 in the chondroblastoma-like melanoma cells (3,3'-diaminobenzidine, ×100).

teratoma, blastoma, carcinosarcoma, phyllodes tumor, and synovial sarcoma. Several histologic components have been found in malignant melanoma, including fibroblastic/myofibroblastic, Schwannian and perineurial, smooth muscle, rhabdomyosarcomatous, osteocartilaginous, ganglionic and ganglioneuroblastic, neuroendocrine, and epithelial types. Osteocartilaginous differentiation is rare, with only limited cases reported. Although OCM occurs in any part of body, OCM seems frequently clustered in the subungual regions of either fingers or toes.

In the present case, the tumor was composed of both epithelioid and chondroblastoma-like melanocytes with areas of osseous differentiation, confirmed by extensive nuclear immunostaining of SATB2, an osteoblastic transcription factor. Most of the epithelioid and osteocartilaginous melanocytes were negative for melanocytic markers, including S-100, Melan-A, and HMB-45, suggesting that the tumor cells were dedifferentiated away from the nature of melanocytes. Interestingly, SOX10 showed diffuse strong nuclear expression in both epithelioid and osteocartilaginous components, which aids in the final diagnosis.[2] In addition, single and small clustered melanocytes with dysplasia in the epidermis were observed.

Conclusions

Osteocartilaginous melanoma is a rare histologic manifestation of malignant melanoma that needs to be differentiated from other benign and malignant lesions. Detailed histologic evaluation of both tumor cells in the dermis and dysplastic melanocytes in the epidermis and immunostain profiling with different biomarkers help to make a final diagnosis.

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Conflict of Interest: None reported.

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