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CASE REPORT

Epidermotropic Metastatic Melanoma Clinically Resembling Agminated Spitz Nevi

Hee Joo Kim, Byoung Joon So, Min Gun You, Il-Hwan Kim

Department of Dermatology, Korea University Ansan Hospital, Ansan, Korea

Herein, we report a 36-year-old Asian male patient who presented with grouped multiple erythematous waxy papules and nodules on his right medial thigh. He had undergone amputation of the right second toe because of a stage IIa malignant melanoma, 3 years previously. At the time of surgery for the primary tumor, right inguinal lymph node dissection revealed no nodal involvement. Three years after the diagnosis of the primary tumor, crops of multiple erythematous papules and nodules developed. Initial histopathologic evaluation of the papules showed nests of small epithelioid cells similar to compound nevi. However, cytologic features, including high mitotic figures, lack of maturation, and some hyperchromatic nuclei suggested metastatic melanoma. In addition to the pathologic findings, the tumors were on the right thigh, which was the same side as the primary malignant melanoma. The patient underwent wide excision of the tumor and split-thickness skin grafting.
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-Keywords-
Epidermotropic metastatic malignant melanoma

INTRODUCTION

Metastatic melanoma of the skin might sometimes mimic clinically and histologically primary melanoma or other benign and malignant neoplasms[1]. In most cases, the distinction between metastatic melanoma from primary benign to malignant melanocytic lesions is straightforward. However, in some instances in which the lesions have an unusual appearance, a thorough search for clues of malignancy and clinicopathologic associations are needed. Epidermotropic metastatic malignant melanoma (EMMM) is one such disease that is difficult to identify. Cutaneous metastatic melanoma usually involves the dermis and/or subcutaneous fat; however, atypical melanocytes might be observed more superficially, within the epidermis and upper part of the dermis[2].

This report describes a patient who presented with intransit EMMM clinically resembling agminated Spitz nevi.

CASE REPORT

A 36-year-old Asian male patient presented with grouped multiple erythematous waxy papules and nodules on the right medial thigh (Fig. 1). He had no symptoms including pruritus or tenderness; however, careful physical examination showed mild ulceration on the surface of the nodules. He had a history of malignant melanoma on the dorsal aspect of his right metatarsophalangeal joint. His right second toe was amputated and the right inguinal lymph node dissection revealed no lymph node involvement at the time of the surgery. After 1 year of interferon therapy, he was periodically followed-up in the Departments of Dermatology, Orthopedics, and Oncology. Two years later, he presented with multiple grouped erythematous papules and nodules on his right medial thigh. Positron emission tomography scanning at this time showed no signs of recurrence or metastasis.

One of the nodules was excised for histopathologic evaluation. Scanning view revealed a well-circumscribed symmetric dome-shaped nodule surrounded by an epidermal

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Corresponding author: Il-Hwan Kim, Department of Dermatology, Korea University Ansan Hospital, 123 Jeokgeum-ro, Danwon-gu, Ansan 425-707, Korea. Tel: 82-31-412-5180, Fax: 82-31-412-5985, E-mail: kumcihk@korea.ac.kr

collarette (Fig. 2A). Partial epidermal ulceration and epidermal thinning with various-sized nests of tumor cells were present. Single or nested tumor cells were visible in the epidermis and dermal epidermal junction. Epidermal components did not extend beyond the dermal portion, and they were mostly focused around the area of epidermal ulceration (Fig. 2B). Tumor cells focally involved the deep dermis, including areas around sweat glands and subcutaneous fat. Higher-power magnification showed that the tumor cells had an epithelioid morphology with monotonous and hyperchromatic nuclei and loss of maturation (Fig. 2C). In addition, multiple atypical mitoses were evident (Fig. 2D, E). Some angiotropism was noted (Fig. 2F). The entire lesion lacked melanin.

On immunohistochemical staining, the Ki-67 index was $<5\%$, while p53, HMB-45, and Cyclin D1 were focally positive on the superficial dermis. P16 was only sparsely positive throughout the lesion. Melan-A, and Bcl-2 were diffusely positive in the lesion (Fig. 3).

The patient had a history of malignant melanoma on the dorsum of the right foot, which was on the same side as the current crops of papules on the right thigh, as well as findings resembling agminated Spitz nevi. Histopathologic examination revealed a symmetric well-circumscribed lesion with some characteristics similar to those of small compound type melanocytic nevi; however, the examination still showed findings suggesting malignancy, such as epidermal ulceration, hyperchromatism, increased atypical mitoses, nests of atypical melanocytes, loss of maturation, and melanization. The immunohistochemistry findings of negative p16 staining with positive p53 and Bcl-2 staining were consistent with melanoma. Angiotropism without lymph node invasion implied in-transit metastasis. On the basis of these findings, the patient was diagnosed with in-transit epidermotropic metastatic mela-

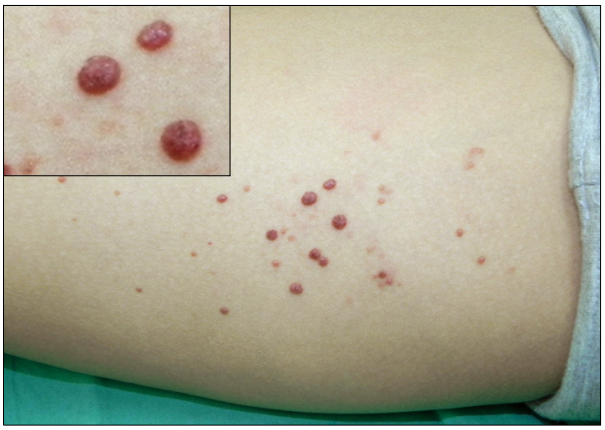

Fig. 1. Multiple erythematous waxy papules and nodules on the right medial thigh (insert: close-up view).

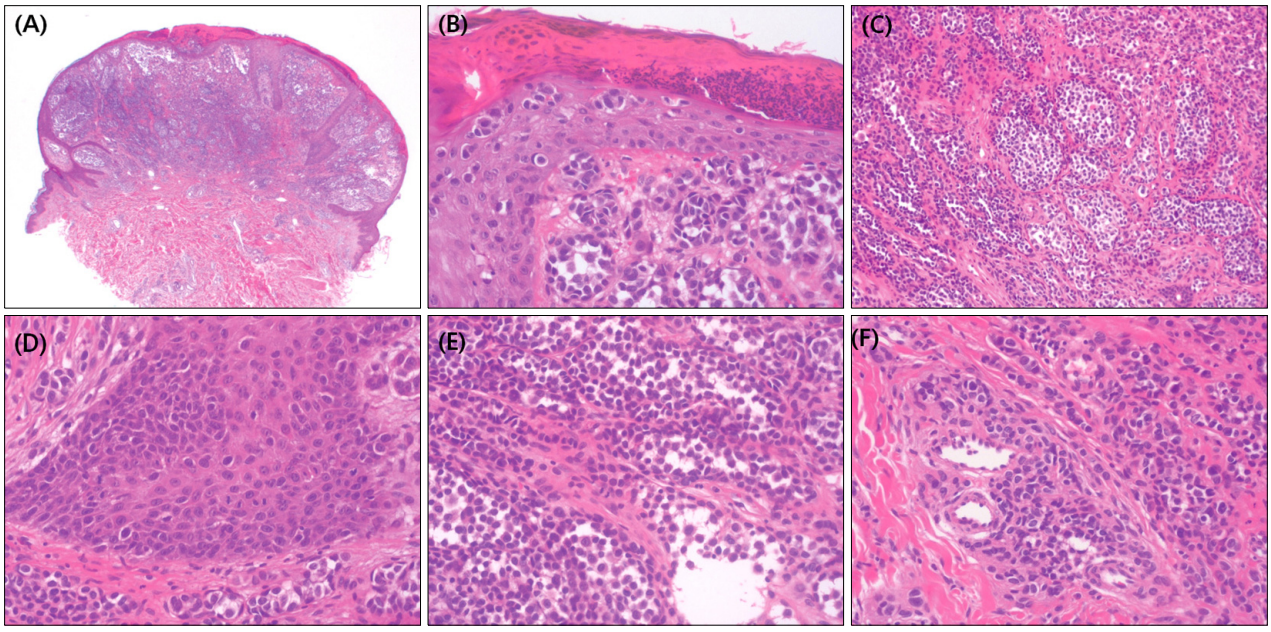

Fig. 2. (A) Scanning view showing a well-circumscribed symmetric dome-shaped nodule comprising various-sized nests of tumor cells (H&E, ×12). (B) Epidermal tumor nests and single cell exhibiting pagetoid spread throughout the epidermis (H&E, ×40). (C) Tumor cells exhibiting epithelioid morphology, with monotonous and hyperchromatic nuclei, and loss of maturation (H&E, ×100). (D) Atypical mitoses in the epidermis (H&E, x200). (E) Atypical mitoses in the dermis (H&E, ×200). (F) Atypical tumor cell nests and individual cells around blood vessels and inside vessel lumens, indicating angiotropism (H&E, ×200).

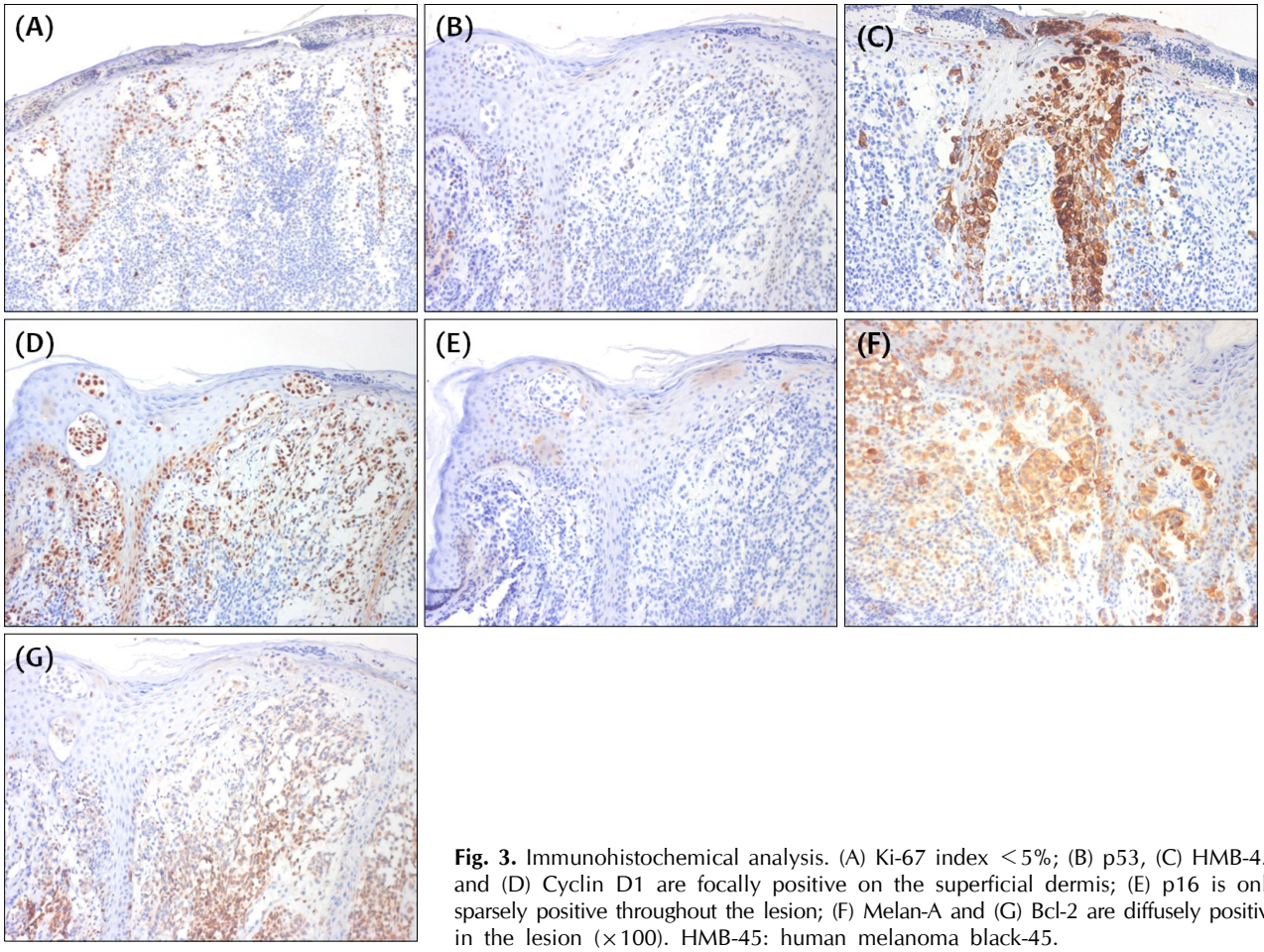

Fig. 3. Immunohistochemical analysis. (A) Ki-67 index <5%; (B) p53, (C) HMB-45, and (D) Cyclin D1 are focally positive on the superficial dermis; (E) p16 is only sparsely positive throughout the lesion; (F) Melan-A and (G) Bcl-2 are diffusely positive in the lesion (×100). HMB-45: human melanoma black-45.

noma, and he underwent wide excision of the entire lesion and split-thickness skin grafting.

DISCUSSION

Histopathologic findings for distinguishing primary cutaneous melanoma from cutaneous metastasis include inconspicuous epidermal components and junctional activity and tumors located in the dermis or subcutaneous in metastatic lesions, while some epidermotropic metastasis have an intra-epidermal component. Metastatic tumors are usually smaller than primary lesions and have more epidermal collarettes, and rather monotonous cells with angiolymphoid invasion. Moreover, inflammatory cell infiltrates are less copious than primary lesions[1,3].

The diagnosis of EMMM has great prognostic significance, because the American Joint Committee on Cancer guidelines consider localized metastatic diseases such as satellitosis and in-transit metastasis in the nodal category of N2C or stage IIIB disease[4]. Kornberg et al[5]. report the following distinguishing features of EMMM: epidermal thinning owing to aggregates of atypical melanocytes, widening of dermal papilla, elongation and inward bending of the rete ridges at the periphery (i.e. epidermal collarette), a population of atypical melanocytes within the dermis equal to or greater than the intra-epidermal component, and atypical melanocytes in the vascular lumina. After several cases of EMMM that did not follow any of the aforementioned criteria were reported[6,7], some helpful features for recognizing EMMM including EMMM localized to the epidermis were identified, such as small size, symmetry, extensive pagetoid scattering, and adnexal epithelial involvement, among others[8]. Angiotropism, absence of the "shoulder" phenomenon, and fibrotic dermal stroma might be particularly helpful when the differential diagnosis of metastatic melanoma with an epidermal component from the second or third primary melanoma is challenging[1,9].

In the present case, the dermal component of the atypical tumor cell nests without maturation was encircled by elongated and inwardly bending peripheral rete ridges,

and exhibited features of angiotropism. Although the dermal component was obvious, epidermal thinning with focal ulceration, epidermal tumor nests, and pagetoid tumor cell spread throughout the epidermis suggested epidermotropic metastatic melanoma.

Immunohistochemical analyses are helpful ancillary studies. Bcl-2 is frequently negative or only weakly positive in benign melanocytic lesions, whereas the majority of tumors are strongly positive for melanoma. Cyclin D1 is overexpressed in melanoma throughout the tumor. p53 is typically positive in many nodular melanomas. Furthermore, decreased nuclear immunoreactivity for p16 in the dermal melanocytic component is present in melanoma[10,11].

Kornberg et al.[5] consider lymphatic channel invasion as a primary sign of epidermotropic metastasis, although this is not supported by additional evidence. Melanoma may spread via lymphatic channels, by direct extravascular migratory spread, or hematogenously. Nevertheless, the mechanisms of melanoma metastasis require further study. Lymph nodes are the most common sites of metastasis[3,12-14]. Lymphatic drainage of acral melanoma runs along the thigh. According to Plaza et al.[1], 7.8% of metastatic melanoma patients present with multiple regional metastases. Nearly 50% of patients with metastatic melanoma develop skin metastases, which may occur in the area of locoregional lymphatic drainage or at a remote location. Therefore, it may be concluded that during the development of metastases of acral melanoma via lymphatic vessels, multiple metastatic papules or nodules can develop on the thigh.

The most common clinical presentation of metastatic melanoma of the skin is papules or nodules in patients previously diagnosed with primary melanoma[1]. Plaza et al.[1] report that most of the 192 cases studied were clinically described as pigmented nodules, with a minority of benign lesions such as dermatofibroma and nevi, among others. In the present case, grouped erythematous nonpigmented papules were clinically reminiscent of agminated Spitz nevi. However, histologic evaluation suggested malignancy. Furthermore, angiotropism without lymph node invasion implied in-transit metastasis. To our knowledge, this is the first report of EMMM clinically resembling agminated Spitz nevi.

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