Cutaneous Metastatic Melanoma Masquerading as a Pigmented Rash: A Case Presentation and Discussion

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Abstract
Cutaneous melanoma has a high metastatic potential. Spontaneous eruption of darkly pigmented papules is a rare manifestation of cutaneous metastatic melanoma. Herein, we describe a case of a 79-year-old male with a history of superficial spreading malignant melanoma, status post lymphadenectomy, who presented with rapidly progressing, asymptomatic, hyperpigmented papules. Biopsy revealed metastatic melanoma. We report this case to highlight the unique presentation of cutaneous metastatic melanoma to increase detection of this deadly disease. Timely diagnosis is essential for staging, prognosis, and therapeutic options and may maximize disease-free survival.

Introduction
Cutaneous melanoma is an aggressive disease arising from melanocytes. Melanocytes are a type of dendritic cell that provide melanin to keratinocytes and can be found in most organ viscera. Melanosomes within melanocytes of melanoma have been shown to carry microRNA into primary fibroblasts and serve to increase proliferation, migration, and pro-inflammatory gene expression. Although melanoma represents less than 5% of all skin cancers, it has a high potential for widespread metastasis and is subsequently associated with high mortality. The incidence of melanoma is growing faster than any other potentially preventable cancer in the United States, with an approximate 1.9% annual growth rate between 2000 and 2009. Globally, 132,000 new cases of melanoma were predicted to arise in 2017, with 48,000 deaths per year.

Metastasis involves dissemination of neoplastic cells to different anatomic sites and the adaption of these cells into a foreign-tissue microenvironment. The interplay between metastatic tumor cells, host factors, and homeostatic mechanisms determines the process. The interaction between neoplastic cells and non-neoplastic stromal cells are important in the progression of the invasion-metastasis cascade. The skin and subcutaneous tissue represent a common site of metastasis in melanoma. The most common presentation of cutaneous metastatic melanoma is of single or multiple papules and nodules that are brown-to-black or skin-colored. Various other morphologic patterns of cutaneous metastasis from malignant melanoma have been reported, including erythematous patches and plaques and inflammatory cellulitis-like lesions. Presentations such as diffuse sclerodermiform induration of the skin, zosteriform vesiculobullous lesions and even alopecia areata of the scalp have been documented as presentations of malignant melanoma.

Case Report
A 79-year-old Caucasian male presented to the outpatient office setting with a six-month history of progressive, asymptomatic, brown-to-black pigmented papules, plaques, and nodules of the right shoulder, axilla, chest, upper abdomen and lateral trunk (Figures 1, 2). Two months prior to this skin eruption, the patient underwent primary resection of a right mid-back malignant melanoma. The melanoma was histologically classified as superficial spreading and nodular type with a Breslow’s depth of 1.4 mm and Clark’s level IV, with no ulceration, lymphovascular invasion, or satellitosis (January 2016). Sentinel node biopsy showed extension to the right axillary lymph nodes, prompting axillary lymphadenectomy (February 2016).

Past medical history included multiple non-melanoma skin cancers, treated with wide excision on the left upper back (2006) and Mohs micrographic surgery on the right upper occipital scalp (2010), and lymphoma treated with chemotherapy and radiation three years prior. His family history was significant for lung cancer in both parents and breast cancer in his brother and sister, respectively. The patient denied systemic complaints, pain, pruritis, and discomfort.

On physical examination, the excision scar at the right mid-back had signs of hypertrophic scarring but no evidence of pigmentation or recurrence of melanocytic features (Figure 3). More than 100 non-tender, smooth, firm, 3-mm, dark purple-black papules were localized to the right shoulder, axilla, chest and upper abdomen.

Figure 1. Multiple (> 100) hyperpigmented, purple/brown/black papules with mild erythema and variable size coalescing into plaques and nodules localized to the right shoulder, axilla, chest, and upper abdomen.

Figure 2. Palpation revealed smooth, firm, and soft surface texture without sensitivity, pain, or blanching to pressure.

Figure 3. Lesions were in a remote location from the excision scar at the right mid-back representing resection of primary melanoma in January 2016.
Histopathologic evaluation of two isolated lesions at the right chest wall via two 5-mm punch biopsies revealed extensive involvement of the papillary dermis demonstrating confluenct of heavily pigmented pleomorphic melanocytic nests with absence of maturation (Figure 6). Additional microscopic features included: epidermal and adnexal sparing, thinning of the epidermis around melanocytes, flattening of rete ridges, prominent nucleoli with increased mitoses, and increased nuclear-to-cytoplasmic ratio (Figure 7). Interestingly, a focal area of intravascular invasion was noted in the dermis, representing angioinvasion (Figures 8, 9). Immunostaining was positive for pan-melanoma stain (HMB45/MART-1/tyrosinase). CD31 positivity was noted as well, confirming the intravascular focus of melanoma cells. Genetic testing failed to detect mutations in BRAF V600, EGFR, or NRAS.

Discussion

Cutaneous melanoma has the potential to metastasize hematogenously, via the lymphatic system, or both ways.2 The progression of primary cutaneous melanoma has been explained by three models. The stepwise-spread model suggests that melanoma spreads initially toward regional lymph nodes via the lymphatic system, and systemic dissemination occurs subsequently.17,18 This model argues in favor of sentinel lymph node biopsy, as lymphatic spread occurs prior to systemic metastasis.19 The second predominant model is the simultaneous-spread model, which maintains that hematogenous and lymphatic spread of cutaneous melanoma can occur simultaneously.20 This model, lymph node involvement is a marker of systemic disease.21 The final, differential-spread model proposes multiple independent dissemination pathways to explain the progression of cutaneous melanoma.17,18,22 Some cutaneous melanomas do not have the biological potential to metastasize. Others metastasize only to regional lymph nodes, only hematogenously, or in both modes.17,22

Cases of skin metastasis can be divided into different categories based on distance from the primary melanoma: 1) satellite metastasis (within 2 cm of the primary tumor); 2) in-transit metastasis (within the dermal and subdermal lymphatics in the drainage area before the first regional lymph node basin); 3) intralymphatic metastasis (both satellite and in-transit metastasis); and 4) distant metastasis (beyond regional lymph nodes, frequently involving visceral sites).23,24 Satellite metastasis, in-transit metastasis, and lymph node metastasis represent loco-regional metastases, which occasionally can occur distal to the primary tumor in the limbs. Studies have found that two-thirds of patients who develop metastases initially present with loco-regional metastases, and one-third presents with distant metastases.23,25-27 This is consistent with our patient, who did not demonstrate distant metastases.

Meier et al. found that the time course to the development of metastases in patients with primary cutaneous melanoma differed significantly between the different routes of metastasis. The median time course to the development of distant metastases as first tumor recurrence was 25 months; it was 16 months for regional lymph node metastases and 17 months for satellite or in-transit metastases.23 The clinical outcome is reported to be less favorable when the site of metastatic skin involvement is distant to the primary melanoma. One trial reported cutaneous-to-visceral progression of metastasis at a median of 17.8 months for patients with distant metastasis and stage IV disease, compared to 62.5 months for those with local recurrence and stage III B disease.28 The short time period of six months in our patient is unique for in-transit metastasis and emphasizes the rapidly progressive and destructive course.

Clinically, the differential diagnosis for dark purple-black papules coalescing into plaques and nodules is broad. It may include: cutaneous metastasis, angiosarcoma, Kaposi's sarcoma, leukemia cutis, cutaneous B-cell lymphoma, lymphangiomatosis, lymphomatoid papulosis, cutaneous tuberculosis, coccidioidomycosis, bacillary angiomatosis, and secondary syphilis.29 Histologically, metastatic melanoma generally invades the dermis and subcutis without invasion of the epidermis. While at low power, this may
resemble a benign intradermal nevus, on high power one can appreciate the nuclear atypia with mitoses and lack of maturation. At times, the metastatic melanoma can invade the epidermis and closely mimic a primary melanoma. Rarely, melanoma that has metastasized to the dermis may closely resemble a blue nevus. Histopathologic evaluation in our patient revealed not only striking pleomorphic melanocytic nests located predominantly within the papillary dermis but also notable angioinvasion. Periendothelial migration of melanoma cells from angiocentric spread can serve as an additional indicator for metastatic disease.35

Treatment of melanoma skin metastasis is extremely difficult, with primary focus on decreasing disease progression to prolong survival. When surgical resection is not reasonable, case reports have shown some success with use of topical imiquimod, regional chemotherapy with drugs such as melphalan through hyperthermic isolated limb perfusion (ILP) or isolated limb infusion (ILI), immunotherapy with systemic agents or intralesional immunotherapy, and electrochemotherapy.34-36 However, aggressive treatments may lead to unwanted toxicity. With multiple new targeted therapies on the horizon, accurate staging and close surveillance of high-risk patients is of utmost importance.

Conclusion
Melanoma undergoes rapid growth, causes extensive damage, and leads to high morbidity and mortality. The spontaneous eruption of extensive, coalescing, purple-black pigmented papulonodular lesions as a presentation of metastatic melanoma is uncommonly reported. We have presented this case to address the need for prompt workup with a potential diagnosis of metastasis, especially in patients with a known history of cutaneous melanoma, and initiation of aggressive treatment to prolong survival. Physicians must maintain a high index of suspicion for cutaneous metastasis in rare eruptive presentations in patients with a previous history of malignant melanoma, as it may be the result of an underlying life-threatening event. Immunotherapy advancements over the past six years have had a profound impact on how clinicians approach metastatic melanoma treatment, and we hope this case study helps physicians in all specialties understand the complexity of presentation for this deadly disease.

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References
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