Eruptive melanocytic nevi heralding the diagnosis of metastatic malignant melanoma: A case report

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INTRODUCTION

Eruptive melanocytic nevi (EMN) are an unusual phenomenon characterized by the rapid appearance of multiple melanocytic nevi. Whether atypical or benign, EMN are associated with various medications and diseases but not previously with melanoma.[1] EMN have been described in internal malignancy, such as prostate cancer, in which it is proposed as a paraneoplastic phenomenon, although the mechanism is unclear.[2]

One cutaneous phenomenon that arises from primary melanoma is epidermotropic metastatic malignant melanoma (EMMM), whereby malignant cells migrate from the dermal metastasis into the epidermis. Epidermotropic metastases are metachronous with the primary tumor or appear after resection or treatment of the primary disease, and melanoma is no exception.[3] Eruptive nevi may be clinically mistaken as EMMM; therefore, making the distinction is important.

We report a case of a patient who had 2 concurrent primary melanomas treated with wide local resection and in whom EMN developed, with no signs of EMMM, 8 weeks before diagnosis of widespread metastatic melanoma.

Abbreviations used:

EMN:	eruptive melanocytic nevi
EMMM:	epidermotropic metastatic malignant melanoma
ITM:	in-transit metastases

CASE REPORT

An 80-year-old man presented with a 3.2-cm × 2.6-cm pink-brown thin plaque with irregular borders and color variation on the vertex of the scalp. The lesion was present for 1 year. After referral to a dermatologist, a total body skin examination also revealed a 1.3-cm × 1.0-cm dark brown patch of unknown duration on the left ala. The patient denied any constitutional symptoms. His medical history was notable for significant cardiovascular disease, an arrhythmia, chronic renal insufficiency, and Barrett's esophagus, which was under periodic surveillance. Recently, he was hospitalized for methicillin-resistant staphylococcus aureus bacteremia and received a long course of intravenous antibiotics. Of note, results of his last screening colonoscopy were unremarkable, and he had no family history of melanoma.

Biopsy of the scalp lesion showed at least a 0.85-mm-thick melanoma, extending to the base (Clark's level III). Biopsy of the ala lesion showed a 1.6-mm-thick melanoma (Clark's level IV) (Fig 1). The patient underwent local resection of both tumors, but because of his medical comorbidities, a sentinel lymph node biopsy was not performed. Histology from the removed tissue on the scalp found a 2-mm-thick melanoma (Clark's level IV) with intravascular invasion and negative margins, with staging determined to be pT3a. The nasal ala tissue showed a 1.8-mm-thick melanoma (Clark's level IV) consistent with stage pT2a, however, with residual melanoma in situ at the surgical margins. After 3 months of treatment with topical imiquimod 5% cream and tazarotene 0.1% gel on the melanoma in situ lesion, 2 scouting biopsies of that area showed reactive changes and dermal fibrosis with no residual atypical melanocytes.

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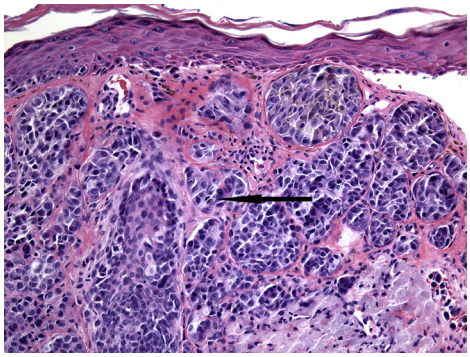

Fig 1. Histopathologic examination of the melanoma on the nose. There is irregular proliferation of melanocytes in the epidermis and in the dermis. The melanocytes are arranged in nests, which vary in size and shape. Single melanocytes are seen at the dermal epidermal junction and down a hair follicle. The melanocytes are pleomorphic. Some melanocytes display hyperchromatic nuclei, prominent nucleoli, and melanin pigment in their cytoplasm. A mitotic figure (*arrow*) is shown.

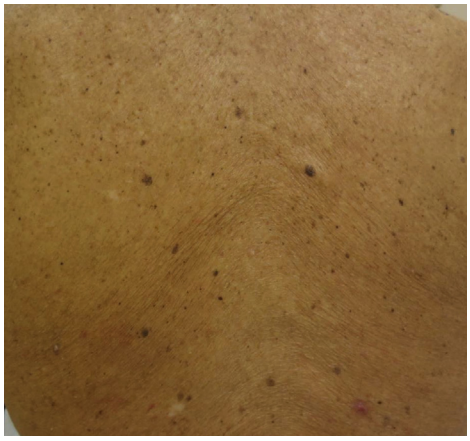

Fig 2. Eruptive nevi. At a follow-up visit 11 months after the initial diagnosis of melanoma, numerous monomorphic, 1- to 2-mm dark brown to black macules were noted scattered on the patient's back and posterior shoulders consistent with eruptive melanocytic nevi. On dermoscopic examination, these macules showed darker irregular centers. Because their appearance was concerning, histologic examination was indicated.

Eleven months after the initial diagnosis, a routine surveillance total body skin examination showed dozens of new, 1- to 2-mm monomorphic, dark brown to black macules scattered on the patient's back and posterior shoulders (Fig 2), some with darker, irregularly pigmented centers on dermoscopy. The lesions were consistent with new eruptive nevi, and histologic examination of a lesion on the left shoulder found a compound melanocytic nevus without histologic atypia (Fig 3). Importantly, genetic testing of 2 eruptive nevi and the resected scalp melanoma were BRAF and NRAS wild type.

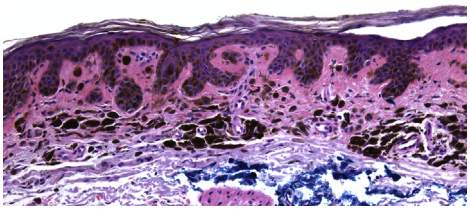

Fig 3. Histologic examination of an eruptive nevus. There is a compound melanocytic nevus composed of mostly single, small, and monomorphous melanocytes in the epidermis and in the papillary dermis. The melanocytes exhibit heavily pigmented cytoplasm. Numerous melanophages are seen in the papillary dermis at the base of the lesion.

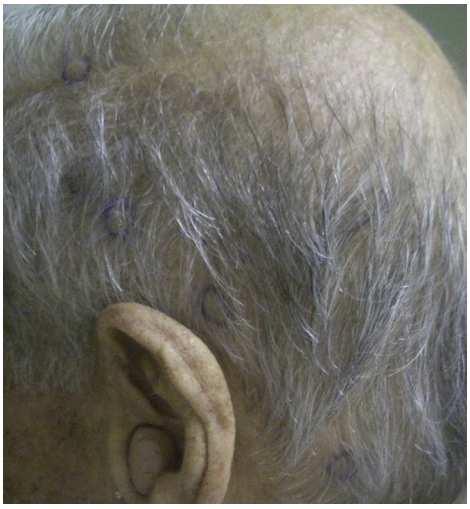

Fig 4. Development of ITM. More than 1 year after the initial diagnosis, the patient presented with five 5-mm firm nodules arranged in a linear pattern on the left parietal, left postauricular, and left mastoid scalp. Histologic examination found in-transit melanoma metastases.

Eight weeks later, the number of nevi had increased and now involved the patient's chest. He also had five 5-mm firm nodules, arranged in a linear pattern along the left scalp, concerning for in-transit metastases (ITM; Fig 4). Excision of one scalp nodule confirmed the diagnosis of ITM, consistent with T3b, N3, M0, or stage IIIC.

One week later, the patient had increased abdominal girth. Laboratory tests found worsening kidney and liver functions, and magnetic resonance imaging found multiple hepatic and peritoneal metastases. The patient refused further workup and died within 1 week, likely from hepatorenal syndrome.

DISCUSSION

This case highlights the curious development of EMN heralding the diagnosis of metastatic melanoma in a patient with a recent history of 2 deep primary

melanomas. The possibility of EMMM was considered as an explanation for the sudden appearance of the numerous pigmented macules. In our case, the histology of the eruptive nevi did not exhibit changes characteristic of EMMM, such as epidermal thinning or atypical melanocytes within the dermis and intradermal endothelial-lined spaces.[4]

Although the phenomenon of EMN remains unclear, at least 3 etiologies have been proposed. Some investigators argue that an immunocompromised state favors melanocytic proliferation.[5] This argument has been supported by multiple observations, including the emergence of dysplastic EMN in 7 AIDS patients concurrently with the increase in viral load and disease burden.[6] In our patient, chronic renal insufficiency and a recent long course of low-dose steroids may have contributed to a state of immunocompromise culminating in methicillin-resistant staphylococcus aureus bacteremia.

Survival and progrowth factors are also implicated in the etiology of EMN. For example, fibroblast growth factor, which is found to play a role in the pathogenesis of prostate cancer and bullous dermatoses, is also a key regulator of melanocytic proliferation.[2,7] Moreover, a synthetic analogue of α-melanocyte–stimulating hormone, an inducer of melanogenesis, is associated with darkening of dysplastic nevi and the emergence of EMN.[8] As such, melanocytic mitogens not only affect EMN but may predispose neoplastic lesions to acquire more aggressive features, which in our patient may have simultaneously spurred metastasis and EMN.

EMN may also result from the displacement of normal melanocytes by malignant melanoma cells into the lymphatic system.[9] This theory, known as the mechanical transport model, is supported by the fact that normal nevic melanocytes have been found in the lymph nodes of melanoma patients. Curiously, our patient did have obvious ITM shortly after the eruptive nevi were observed, suggesting that locoregional lymphatic spread may have been responsible for dissemination of both malignant and benign melanocytes.

Here we report a case of an 80-year-old white man with a history of 2 concurrent primary melanomas in whom EMN developed 11 months after his melanoma diagnoses and 8 weeks before presentation with ITM, followed shortly by terminal metastatic disease. This is a unique report of EMN presenting in the setting of in-transit and visceral metastatic melanoma.

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