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Neurotropic Melanoma Invading the Median Nerve

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Abstract

We report a case of acral lentiginous melanoma of the right thumbnail bed which demonstrated characteristic intraneural invasion and extension along the median nerve. Four years after amputation of the involved thumb, a melanotic tumor recurred on the right thenar. Radiation therapy was given. The tumor invaded the median nerve, however, causing progressive pain and paralysis of the right hand. Despite right arm amputation, the tumor extensively metastasized, and the patient died three years later.

Histopathologically, the tumors were characterized by extensive proliferation of spindle-shaped cells forming neuroid fascicles especially prominent in the metastatic region. Tumor cells were positive immunohistochemically with S-100 protein antisera.

Key words: neurotropism; neuroid fascicles; acral lentiginous melanoma; neurotropic melanoma

Introduction

Neurotropism of malignant melanoma is an important feature indicating that melanocytes derive from neural creast. We report a case of acral lentiginous melanoma of the fingernail bed invading the median nerve and provide supportive evidence for the diagnosis of neurotropic melanoma (NTM).

Case Reports

In July of 1983, a 50-year-old woman noticed that her right thumbnail was cracked, and half of it had fallen off. The patient consulted a clinic where the nail was avulsed without further treatment. Two months later, a black macule appeared in the same nail bed. The black macule gradually enlarged and she consulted a dermatologist, who referred her to our clinic in July of 1984. The nail was missing, and the nail bed was black and eroded. A small nodule in the eroded bed and the surrounding area were slightly erythematous and swollen (Fig. 1). The clinical diagnosis was acral lentiginous melanoma. The right thumb was amputated at the level of 5 mm proximal to the interphalangeal joint. Extensive work-up revealed no evidence of metastasis, and she refused further surgery and chemotherapy. She was treated with immunotherapy consisting of Bacillus Calmette-Guerin (BCG), and Picibanil was performed at this time. In October of 1987, the patient presented with palpable bilateral axillary lymphadenopathy. Histopathological examination of dissected lymph nodes

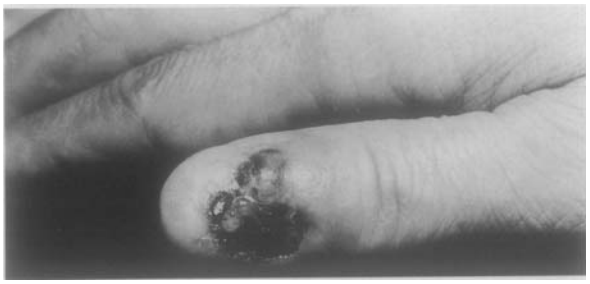

Fig. 1. Clinical features of the primary lesion. The nail bed is black and eroded without nail.

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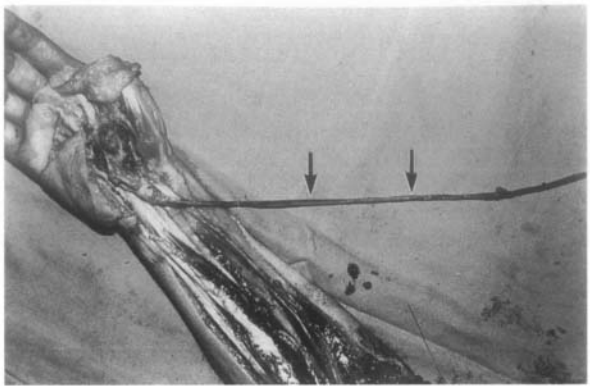

Fig. 2. Operative findings of amputation. The median nerve (arrows) is discolored black at the level of the middle upper arm.

did not reveal metastasis. Immunotherapy with interferon β was performed as a prophylactic measure. In December of 1987, an indurated area was palpated in the surgical scar extending over the thumb. Because the patient refused amputation of the right arm, a localized excision of the mass was performed. Soon thereafter, apparent local recurrence was seen. She received a total of 500 cGy of radiotherapy, following which the mass disappeared. In December of 1988, the patient complained of pain in the right arm with swelling and paralysis of the right hand, and the right forearm was amputated at the level of the proximal side of the elbow joint. In operative findings, no metastasis of the skin or soft tissue of the right arm was detected. However, the median nerve was discolored black at the level of the middle upper arm (Fig. 2). In June of 1990, metastatic nodules were seen on the chest X-ray, and two months later, positive metastases were detected in the thyroid, for which subtotal thyroidectomy was performed. The residual tumor gradually enlarged and pressed the trachea. Tracheotomy was performed in April of 1991. The patient was treated with irradiation of the thyroid region, as well as the brain and back after detection of brain and skin metastasis. Her condition deteriorated progressively, and she died in September of 1991.

Histopathology

In the primary lesion, a broad and asymmetric melanocytic proliferation was seen. Atypical melanocytes extended from the basal layer of

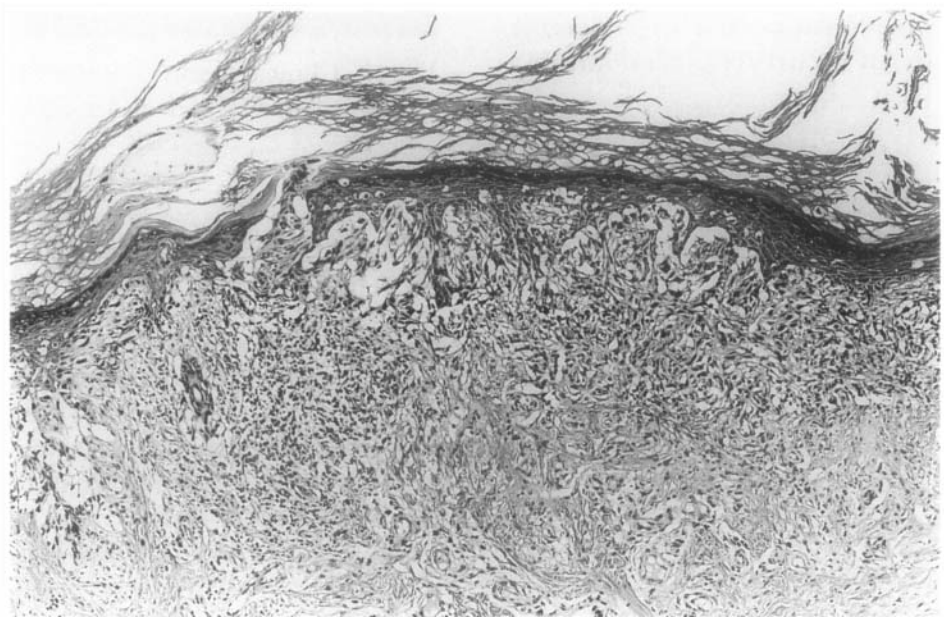

Fig. 3. Histological features of the primary lesion. A bulky tumor nodule in the lower part of the dermis and junctional complex with downward extension from the epidermal basal layer into the dermis. (H-E stain, ×40)

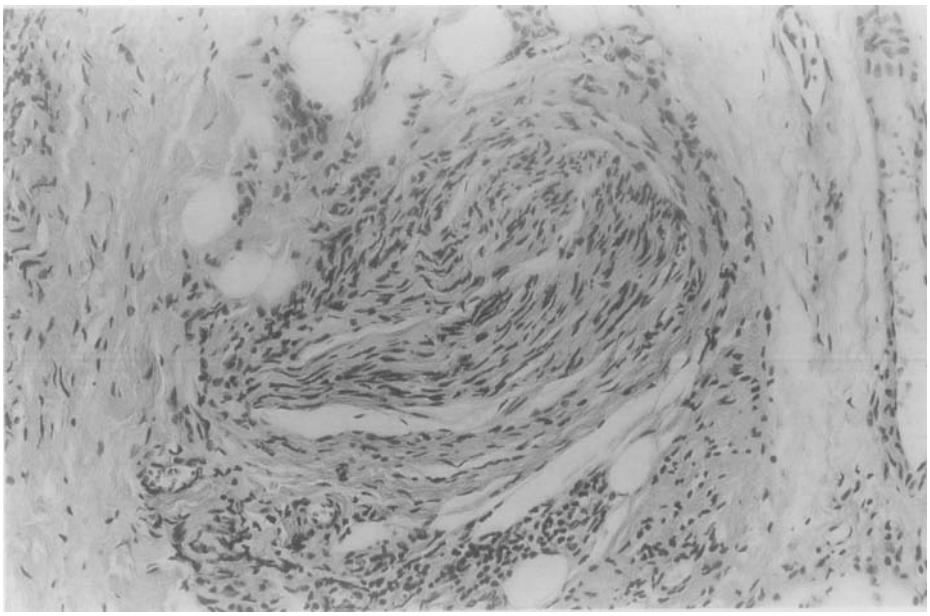

Fig. 4. Histological features of the peripheral portion of the primary lesion. Spindle-shaped cells that show various-sized nuclei with melanin are arranged in fascicular pattern. (H-E stain, ×400)

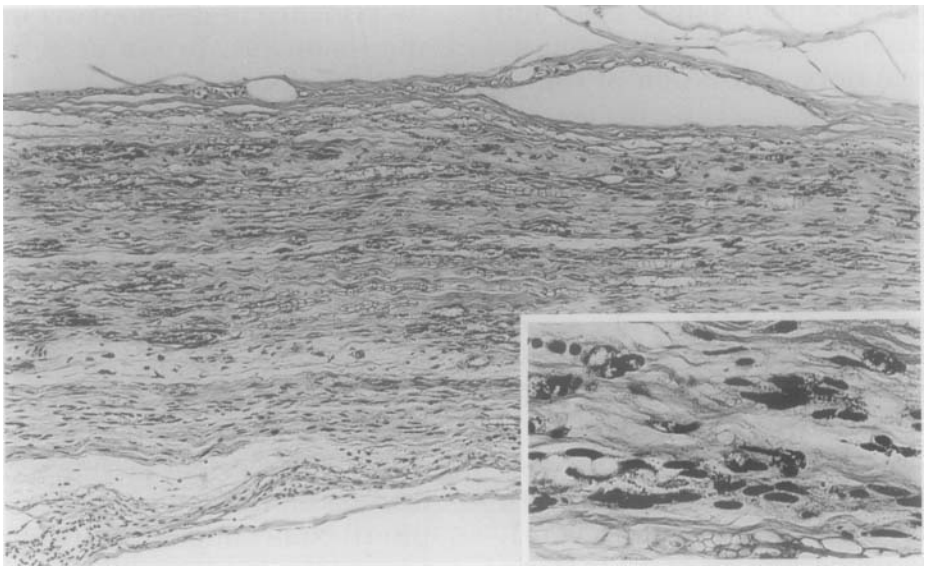

Fig. 5. Histological features of the median nerve. The median nerve is infiltrated by spindle-shaped cells containing abundant melanin. (H-E stain, ×40)

the epidermis and invaded the dermis. There was a bulky tumor nodule in the lower part of the dermis and a junctional activity with downward extension from the basal layer of the epidermis into the dermis (Fig. 3). Spindle-shaped cells possessed atypical nuclei, and some of

those cells contained melanin. In the peripheral portion, the melanin contained spindle-shaped cells that were arranged in fascicular pattern (Fig. 4). Desmoplasia was not dominant. The tumor cells invaded the periosteum (Clark level V). The tumor cells were sparsely positive for S-100 protein antisera, but negative for neuron-specific enolase (NSE).

In the right arm, the median nerve was infiltrated by spindle-shaped cells containing melanin (Fig. 5).

Discussion

In 1979, Reed and Leonard reported 22 patients with neuroid cutaneous tumors associated with, or preceded by, a melanocytic dysplasia (1). They believed that these represented a variant of desmoplastic melanoma, which was termed neurotropic melanoma (NTM). They noted that NTM had distinctive histopathologic features. The pattern is characterized by the following: 1) fasciculation: the dysplastic spindle cells invade the dermis in the form of fascicles of elongated slender spindle cells, and 2) neurotropism: the spindle cells permeate the peripheral nerves. Invasion of tumor cells into adjacent structures occurs *via* perineural and intraneural extension (1). Because melanocytes with spindle cell morphology often cease melanogenesis, neuroid properties may develop in NTM; these are indicative of Schwann cell differentiation of melanocytes (2). NTM may be associated with a desmoplastic component (1, 3). However, the recurrent lesion may lack a desmoplastic pattern (1). The clinical course is characterized by local recurrence (17 of 22 patients) (1). The neuroid pattern usually develops in recurrent lesions (1). Clinically, the primary lesion of NTM shows no distinctive characteristics separating it from other types of malignant melanoma (1).

Histopathologically, neurotropism is most often observed in the vertical growth phase of melanoma, specifically of lentigo maligna melanoma, acral lentiginous melanoma, and mucosal lentiginous melanoma (1, 4, 5). Elder and Murphy, in a survey of lentiginous melanoma, noted nerve involvement in approximately 20% of their patients, and they considered that this phenomenon is not as rare as has been supposed (5). However, most of these cases are contiguous neurotropism, in which the involved nerves are intermingled within the tumor and widely clear of the margins. Non-contiguous neurotropism in which the neoplastic cells may extend considerable distances from the primary tumors is less common (5). Neurotropic melanoma invades mainly the cranial nerves, most commonly the fifth and seventh cranial nerves according to recent publications (6–8). Our patient showed acral lentiginous melanoma with neurotropism and repeated local recurrence. Recurrent lesions were composed of spindle cells with neuroid fascicles and apparent invasion of spindle cells with prominent melanization into the median nerve. Barnhill et al. reported neurotropic melanoma with prominent melanization (9). There was no evidence of desmoplasia in any part of the lesion (9). Brujin et al. thought that neurotropism may develop in the setting of lentigo maligna or acral-lentiginous melanoma with little or no associated desmoplasia (2). Elder and Murphy noted an association primarily with dysplastic melanoma and asserted that desmoplasia is not essential for the diagnosis of neurotropic melanoma (5). Our patient would be considered to have neurotropic melanoma.

The prognosis of neurotropic melanoma is poor, especially after local recurrences. Neural involvement may be seen within the margins of the tumor (contiguous neurotropism). Noncontiguous spread may be seen beyond the borders of the tumor; the latter is more severe because it may extend to the margins of the specimen. When one observes neurotropism in a biopsy specimen, excision with wide surgical margins and identification of the cutaneous nerve at the margin is required (4).

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