CHAPTER **41**

RECOGNITION AND BIOPSY OF MALIGNANT MELANOMA OF THE LOWER EXTREMITIES

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IMPORTANCE OF EARLY IDENTIFICATION OF MELANOMA

Malignant melanoma accounts for only about 3% of all cases of skin neoplasm. However, it is documented as the cause of death in 65% of fatalities attributed to skin cancer.[1] It is, therefore, a potentially lethal skin tumor, and malignant melanoma affecting the sole or periungual region of the foot is generally understood to be particularly aggressive. Because of the aggressive nature of this form of skin cancer, it is important for the podiatric physician to maintain a high index of suspicion whenever a questionable lesion, whether pigmented or not, is encountered.

Early recognition and proper therapeutic management are crucial if the patient is to have an optimal chance of survival. Early identification and proper excision of a suspected lesion can be curative, and it is the purpose of this discussion to review the various types of malignant melanoma that affect the foot and leg. The proper biopsy technique for those lesions suspected of being melanoma will be described.

CLASSIFICATION

Malignant melanoma develops when the melanocytes in the basal layer of the epidermis uncontrollably expand locally, causing surrounding tissue destruction, and ultimately systemic involvement via metastases. The melanocytes are of neural crest origin, and migrate to the epidermal germ cells at about ten weeks intrauterine. Thereafter, the number of melanocytes stays constant in the normal state.

Melanocytes are responsible for the production of melanin, a brown-colored pigment responsible for the absorption of ultraviolet radiation. The pigment is contained in the dendritic processes of the melanocyte, which fan out through the epidermis from their origin in the basal layer (Fig. 1). The underlying living cells of the epidermal basal layer and the dermis are thereby protected from the potentially mutagenic effects of ultraviolet radiation.

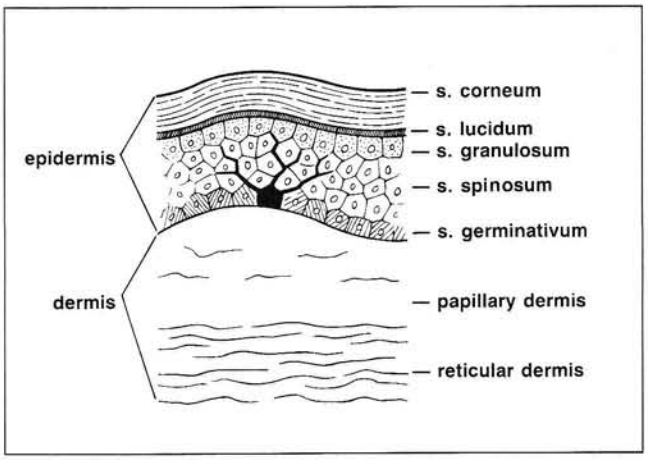

Figure 1. Melanocyte in the basal layer of the epidermis, with dendritic processes containing melanin pigment.

Other than the relationship with exposure to ultraviolet radiation, the etiology of malignant melanoma is not known. There is a statistically significant difference between the number of melanoma cases in the "sun-belt" regions of the world, as compared to other regions. Light-skinned individuals with melanoma tend to develop the tumor on sun-exposed surfaces of the body. Individuals with naturally more darkly-pigmented skin, who develop melanoma, more commonly display the lesions on the less pigmented skin surfaces such as the palms or soles.

There is ongoing speculation as to whether or not certain forms of trauma, (particularly in regard to lesions on the sole of the foot), environmental carcinogens, and an oncogenic RNA virus, are associated with the development of malignant melanoma. Recently, there has a been a greater focus on genetics as a major determinant in the development of malignant melanoma.

Once established, a melanoma displays two different phases of growth: radial growth and vertical growth. Radial growth results from lateral expansion of the melanoma, and is clinically represented by an increase in the size or change in the

shape of a pigmented skin lesion. This leads to the development of border irregularity, lesion asymmetry, and heterogenous coloration often involving various shades of tan, brown, and black. Lesions in the radial phase of growth are macular and have very little potential for metastasis. Vertical growth results from invasion of the deeper skin layers by the melanoma. Clinically, this process is represented by the conversion of a macular lesion to one that is papular or nodular. Furthermore, such lesions convey a much higher likelihood of metastasizing. Histopathologic classification of malignant melanoma is based on the depth of skin penetration by the tumor. Clark's level (Fig. 2) and Breslow's thickness (Fig. 3) are the primary histological classification schemes for staging malignant melanoma of the skin.

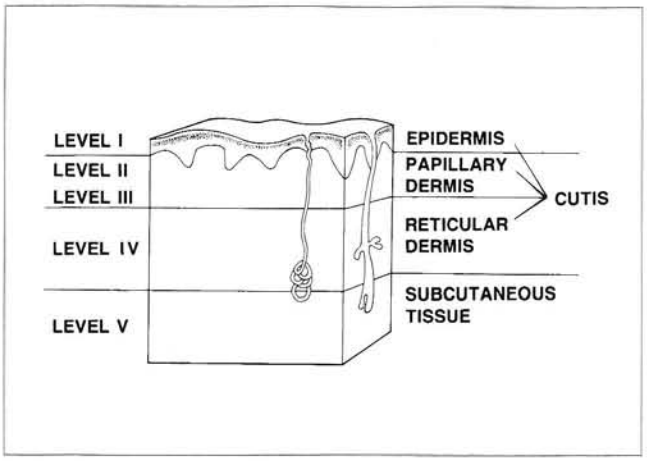

Figure 2. Clark's levels of melanoma penetration.

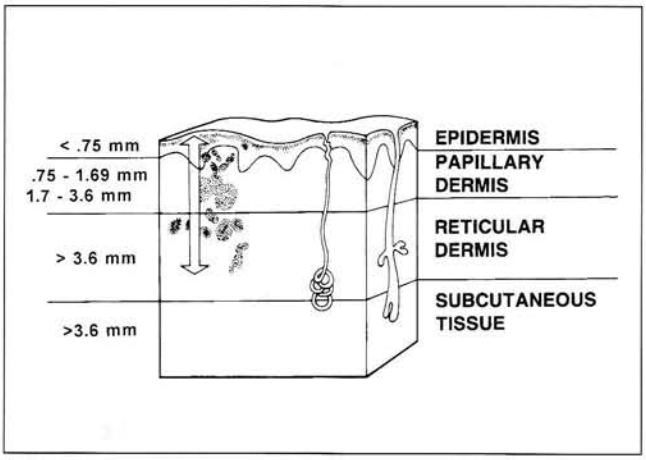

Figure 3. Breslow's thickness for staging of melanoma penetration.

There are four basic types of malignant melanoma that affect the lower extremities. These include lentigo maligna, superficial spreading melanoma, nodular melanoma, and acral lentiginous melanoma.

Lentigo maligna accounts for about 10-15% of malignant melanoma cases. It is most commonly seen in elderly individuals, and is localized to sun exposed skin surfaces. In the lower extremity, it typically involves the legs above the sock-line, and tends to be minimally aggressive because it exists for long periods of time in the radial growth phase. Lentigo maligna is, therefore, rather curable with proper excision.

Superficial spreading melanoma accounts for about 70% of all melanoma cases and is of moderate aggressiveness (as it displays a combination of radial and vertical growth). It is more commonly seen on the torso in men, and the proximal portions of the extremities in women. Color variegation and an asymmetrical contour are typical. In some instances, rapid growth of melanocytes is associated with cessation of melanin production, and areas of the melanoma may appear white or depigmented (amelanotic).

Nodular melanoma accounts for about 12% of melanoma cases, and displays very aggressive and highly lethal behavior. It microscopically demonstrates essentially only vertical growth. These lesions, as the name depicts, are nodular, and are associated with a high rate of metastasis. They can be found on any skin surface and may metastasize to other areas of the body, including mucous membranes, the choroid of the eye, internal organ parenchyma, and other skin surfaces.

Acral lentiginous melanoma is of moderate to severe aggressiveness. It is found on the sole of the foot or in periungual areas, and accounts for about 7-8% of cases of malignant melanoma. Chronic, non-healing lesions of the foot, such as a persistent plantar ulceration, chronic pyogenic granuloma, or a recurrent plantar verruca with an open wound, should always bring to mind the possibility of malignant melanoma or some other form of skin cancer. Lesions such as these, that do not heal with seemingly appropriate therapy in a reasonable period of time, should be considered for biopsy and pathological identification.

Clinical staging of malignant melanoma statistically correlates strongly with prognosis. Clinical stage I lesions include the primary melanoma, satellite lesions within 5 cm of the primary tumor, recurrence at the site of previous excision of a primary lesion, and metastases in-transit to the regional lymph nodes. Pedal lymphatics drain primarily to the ipsilateral inguinal lymph nodes,

while only the distal-lateral aspect of the dorsum of the foot drains to the popliteal lymph nodes. Clinical stage II malignant melanoma displays palpable involvement of the ipsilateral regional lymph nodes. Clinical stage III malignant melanoma displays distant metastasis.

Prognosis is based on both the histopathological depth of primary lesion invasion, and the clinical stage of the disease. Clinical stage I lesions with penetration less than 0.76 mm from the basal layer of the epidermis (Breslow's thickness), or Clark's level I or II, are highly curable with early recognition and proper excision.

APPROPRIATE BIOPSY TECHNIQUE FOR SUSPECTED MELANOMA

Malignant melanoma should be considered in the differential diagnosis of a variety of benign pigmented lesions, as well as several malignant neoplasms of the skin. These include common benign nevi (junctional, compound, and intradermal), seborrheic keratosis, hematoma, Kaposi's sarcoma, basal cell carcinoma, hemangioma, dermatofibroma, pyogenic granuloma, and Spitz nevus.

General recommendations for biopsy of pigmented skin lesions located on the foot include any or all of the following findings: a lesion of recent onset in an adult; a lesion measuring greater than 5 mm in diameter; a lesion localized to the sole or digit; or any pigmented lesion showing color variegation or border irregularity. It is critical that the biopsy specimen include a section of full thickness skin, as well as tissue from the most representative section of the lesion (Fig. 4).

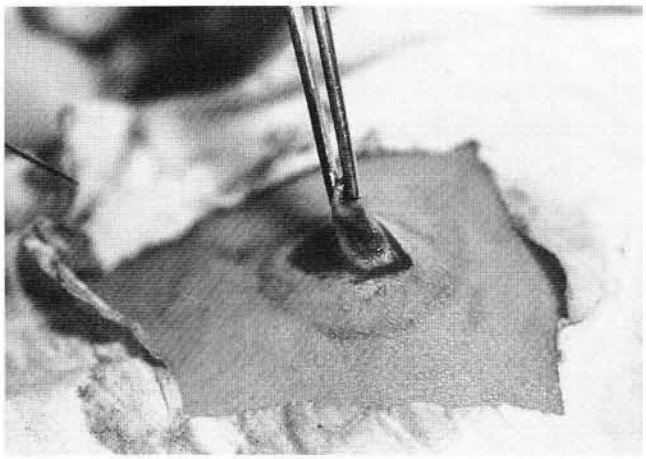

Figure 4. Full-thickness excisional biopsy of suspected malignant melanoma.

The depth of the biopsy specimen must be to the level of the subcutaneous fat. Ideally, the entire lesion should be excised in toto, however this is not always possible when dealing with a large lesion of unknown etiology. An incisional technique or punch biopsy (4 mm or larger) utilized to obtain a representative portion of a large cutaneous melanoma is appropriate, as long as proper follow-up management is maintained based on the histopathological diagnosis (Fig. 5). It is necessary to use separate instruments for each lesion, and attention must be paid to accurately labeling the location of each lesion biopsied.

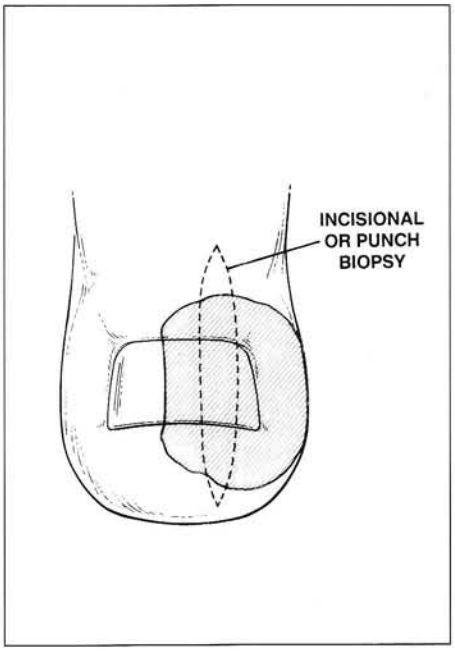

Figure 5. Incisional or punch biopsy.

Proper management includes a thorough problem-focused history and physical exam, oncological consultation and management, and definitive treatment based on the pathological diagnosis. If total excisional biopsy is performed for a clinical stage I lesion, and circumferencial margins of skin are identified and confirmed microscopically to be normal, no further surgical intervention is necessary as long as the oncological evaluation and ongoing periodic follow-up reveals no other evidence of disease.

Large stage I lesions, following appropriate incisional or punch biopsy, require definitive excision, effecting a clear margin of normal skin surrounding the biopsy site. Past guidelines have described excising a 5 cm margin of normal appearing tissue around a superficial (less than 1 mm depth of penetration) lesion, and up to 30 cm

for deeper lesions (greater than 1 mm depth of penetration). However, these guidelines serve only as general rules designed to assure complete removal of melanoma cells. The use of dilute sodium hypochlorite lavage following excision of the lesion, has also been described as an additional method of diminishing the chance of leaving melanoma cells in the deeper tissues. Proper excision of a large lesion often requires the use of a split-thickness skin graft for coverage of the surgical wound (Figs. 6A-6C).

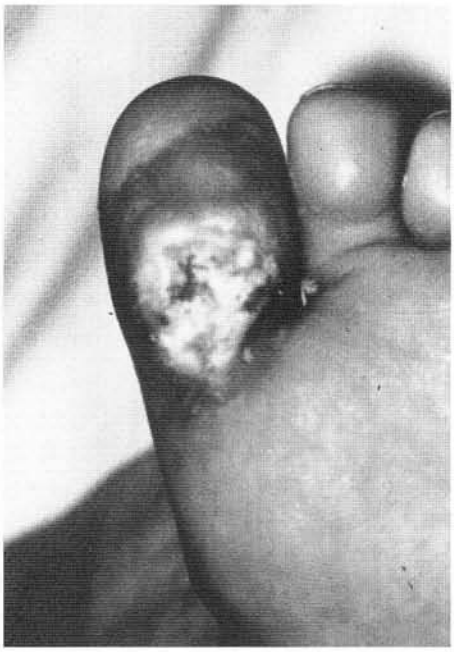

Figure 6A. Primary superficial spreading malignant melanoma involving the hallux.

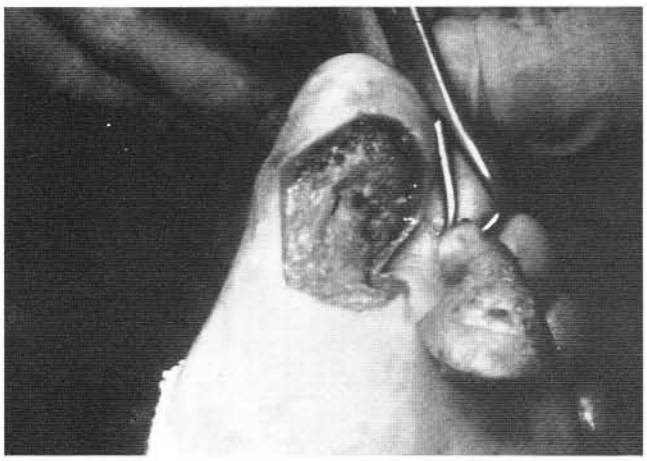

Figure 6B. Excision of the primary lesion.

Management of clinical stage II disease includes definitive excision of the primary lesion, but may also include lymph node dissection by an oncological surgeon, as well as adjunctive chemotherapy or immunotherapy in certain cases. Inguinal lymph node dissection can lead to significant morbidity, and is therefore, carefully considered from the oncological and surgical perspectives prior to undertaking this form of treatment. Clinical stage III disease conveys a severely poor prognosis. The primary lesion is excised in conjunction with chemotherapy, although lymph node dissection is generally not performed.

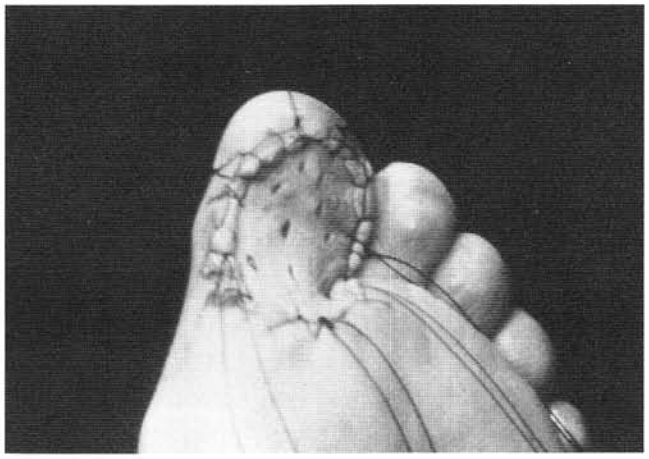

Figure 6C. Split-thickness skin graft coverage of definitive surgical wound.

SUMMARY

Malignant melanoma in the lower extremity can present in a variety of forms, and successful treatment requires early identification and appropriate surgical excision. Many stage I lesions can be completely eradicated using proper excisional biopsy technique. Proper diagnosis of a large lesion can be achieved with the use of an incisional or punch biopsy, followed by appropriate definitive therapy. The podiatric physician must maintain a high index of suspicion at all times, and not hesitate to biopsy a questionable lesion. Because malignant melanoma is a systemic disease, oncological evaluation and management are essential to proper management. Moreover, clinical stage II or stage III disease will require evaluation and management by an oncological surgeon.

REFERENCE

1. Mastrangelo MJ, Baker AR, Katz HR: Cutaneous melanoma. In DeVita VT, Hellman S, Rosenberg SA (eds):*Cancer: Principles and Practice of Oncology* Philadelphia, J.B. Lippincot, 1986, p 1372.