105 Cancer of the Skin

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MELANOMA

Pigmented lesions are among the most common findings on skin examination. The challenge is to distinguish cutaneous melanomas, which account for the overwhelming majority of deaths resulting from skin cancer, from the remainder, which are usually benign. Cutaneous melanoma can occur in adults of all ages, even young individuals, and people of all colors; its location on the skin and its distinct clinical features make it detectable at a time when complete surgical excision is possible. Examples of malignant and benign pigmented lesions are shown in Fig. 105-1.

EPIDEMIOLOGY

Melanoma is an aggressive malignancy of melanocytes, pigment-producing cells that originate from the neural crest and migrate to the skin, meninges, mucous membranes, upper esophagus, and eyes. Melanocytes in each of these locations have the potential for malignant transformation. Cutaneous melanoma is predominantly a malignancy of white-skinned people (98% of cases), and the incidence correlates with latitude of residence, providing strong evidence for the role of sun exposure. Men are affected slightly more than women (1.3:1), and the median age at diagnosis is the late fifties. Dark-skinned populations (such as those of India and Puerto Rico), blacks, and East Asians also develop melanoma, albeit at rates 10–20 times lower than those in whites. Cutaneous melanomas in these populations are diagnosed more often at a higher stage, and patients tend to have worse outcomes. Furthermore, in nonwhite populations, there is a much higher frequency of acral (subungual, plantar, palmar) and mucosal melanomas. In 2014, more than 76,000 individuals in the United States were expected to develop melanoma, and approximately 9700 were expected to die. There will be nearly 50,000 annual deaths worldwide as a result of melanoma. Data from the Connecticut Tumor Registry support an unremitting increase in the incidence and mortality of melanoma. In the past 60 years, there have been 17-fold and 9-fold increases in incidence for men and women, respectively. In the same six decades, there has been a tripling of mortality rates for men and doubling for women. Mortality rates begin to rise at age 55, with the greatest increase in men age >65 years. Of particular concern is the increase in rates among women <40 years of age. Much of this increase is believed to be associated with a greater emphasis on tanned skin as a marker of beauty, the increased availability and use of indoor tanning beds, and exposure to intense ultraviolet (UV) light in childhood. These statistics highlight the need to promote prevention and early detection.

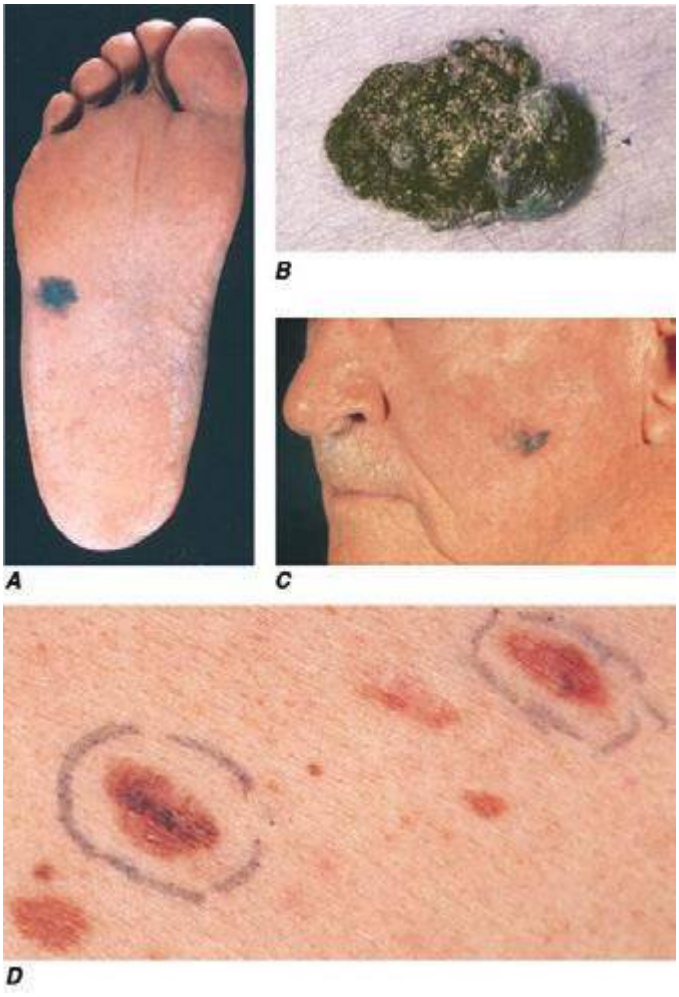

FIGURE 105-1 Atypical and malignant pigmented lesions. The most common melanoma is superficial spreading melanoma (not pictured). ***A.*** Acral lentiginous melanoma is the most common melanoma in blacks, Asians, and Hispanics and occurs as an enlarging hyperpigmented macule or plaque on the palms and soles. Lateral pigment diffusion is present. ***B.*** Nodular melanoma most commonly manifests as a rapidly growing, often ulcerated or crusted black nodule. ***C.*** Lentigo maligna melanoma occurs on sun-exposed skin as a large, hyperpigmented macule or plaque with irregular borders and variable pigmentation. ***D.*** Dysplastic nevi are irregularly pigmented and shaped nevomelanocytic lesions that may be associated with familial melanoma.

RISK FACTORS

Presence of Nevi The risk of developing melanoma is related to genetic, environmental, and host factors (Table 105-1). The strongest risk factors for melanoma are the presence of multiple benign or atypical nevi and a family or personal history of melanoma. The presence of melanocytic nevi, common or dysplastic, is a marker for increased risk of melanoma. Nevi have been referred to as precursor lesions because they can transform into melanomas; however, the actual risk for any specific nevus is exceedingly low. About one-quarter of melanomas are histologically associated with nevi, but the majority arise de novo. The number of clinically atypical moles may vary from one to several hundred, and they usually differ from one another in appearance. The borders are often hazy and indistinct, and the pigment pattern is more highly varied than that in benign acquired nevi. Individuals with clinically atypical moles and a strong family history of melanoma have been reported to have a >50% lifetime risk for developing melanoma and warrant close follow-up with a dermatologist. Of the 90% of patients whose disease is sporadic (i.e., who lack a family history of melanoma), ~40% have clinically atypical moles, compared with an estimated 5–10% of the population at large.

Congenital melanocytic nevi, which are classified as small (≤1.5 cm), medium (1.5–20 cm), and giant (>20 cm), can be precursors for melanoma. The risk is highest for the giant melanocytic nevus, also called the bathing trunk nevus, a rare malformation that affects 1 in 30,000–100,000 individuals. Since the lifetime risk of melanoma development is estimated to be as high as 6%, prophylactic excision early in life is prudent. This usually requires staged removal with coverage

TABLE 105-1 FACTORS ASSOCIATED WITH INCREASED RISK OF MELANOMA

Total body nevi (higher number = higher risk)
Dysplastic nevi (10-fold increased risk)
Family or personal history
Ultraviolet exposure/sunburns/tanning booths
Light skin/hair/eye color
Poor tanning ability
Freckling
CDKN2A, CDK4, MITF mutations
MC1R variants