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A Review for Melanoma Risk Factors

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ABSTRACT

Melanoma, the most common cutaneous sarcoma, poses a significant health threat due to its metastatic potential. This review explores the causes, risk factors, and associations of melanoma, emphasizing its diverse presentations and diagnostic considerations. UV light exposure, genetic predisposition, and somatic mutations contribute to melanoma development. The disease affects individuals of all races, with varied clinical manifestations. Prevention strategies involve sun protection behaviors, and early detection through surveillance is crucial for optimal outcomes. Treatment modalities, including surgical excision and adjuvant therapies, are contingent on disease stage. Ongoing monitoring and counseling play key roles in comprehensive care. This review aims to enhance understanding of melanoma, guiding efforts toward prevention, early detection, and effective management.

KEYWORDS: Melanoma, UV exposure, risk factors, early detection, prevention, adjuvant therapy, surveillance, comprehensive care.

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INTRODUCTION

Cutaneous melanoma, a malignancy with significant metastatic potential, becomes more concerning as the depth of invasion increases or ulceration is present [1, 2]. While it is most commonly found in the skin, it can occasionally affect the uveal tract of the eye or mucous membranes in various areas such as the head and neck, gastrointestinal tract, and genital tract. Identified risk factors encompass exposure to UV light, particularly intense exposures leading to sunburn, use of tanning beds, fair skin types with limited tanning ability, characteristics like blonde or red hair and blue eyes, a family history of melanoma, dysplastic nevi, and congenital nevi. Melanoma can either develop in a preexisting nevus or emerge de novo. Suspicion arises when a pigmented lesion exhibits features aligned with the ABCDE criteria—namely asymmetry, border irregularities, color variation, dimensions/diameter, and evolution/change [3, 4].

Diagnosis confirmation is achieved through an excisional biopsy, with the thickness of invasion being a pivotal prognostic factor [5]. Initial management entails wide local excision. The spread of melanomas typically begins through lymphatic channels to locoregional lymph nodes, prompting the use of sentinel lymph node mapping and biopsy in specific clinical scenarios [6]. Locoregional lymph node involvement designates stage III, and the recommendation for adjuvant systemic therapy is based on the extent of lymph node involvement. In cases of metastatic disease, available treatment options include surgical excision followed by adjuvant immunotherapy or combinations of BRAF and MEK inhibitors for limited, resectable cases. Unresectable disseminated disease is managed medically, utilizing immune checkpoint inhibitors or BRAF and MEK inhibitor combinations [7].

Monitoring patients for at least 5 years post-treatment, with intervals adjusted based on disease stage, is integral. The survival outlook hinges on the stage and extent of disease at the initial presentation, with localized disease showing excellent 5-year survival rates and ongoing improvements noted in metastatic melanoma outcomes [8].

CAUSES AND RISK FACTORS

The specific cause behind the malignant transformation of melanocytes remains uncertain, with factors such as UV light exposure, genetic susceptibility, and somatic mutations playing significant roles in many patients. Risk factors include age, with an increasing incidence in children and adolescents, particularly in teenaged girls, potentially linked to the widespread use of artificial tanning. The lifetime risk is 1 in 34 for women and 1 in 53 for men, and about 10% of melanoma patients have a positive family history. Susceptibility genes, including CDKN2A (P16), show mutations in 25% to 40% of melanoma-prone families, while carriers of mutations in BRCA2 exhibit an elevated risk of

cutaneous melanoma. The MC1R gene's variability plays a role in pigmentation and melanoma predisposition [7, 9, 10].

Germline mutations in BAP1, PALB2, MBD4, or NF1 are associated with familial uveal melanoma, and somatic mutations/amplifications, like the activating mutation of BRAF found in approximately half of metastatic melanomas, guide treatment strategies. Mutations or amplifications of the KIT gene are commonly linked to acral and mucosal melanoma, and NRAS and NF1 mutations are present in a significant percentage of cases [11].

While melanoma is most common in light-skinned individuals, it can occur in people of any race or skin color, with a lifetime risk of 1 in 52 across all populations and less than 1 per 1000 in Black individuals [12]. Darker-skinned populations often present with more advanced disease at the initial diagnosis, with a higher proportion of lower-extremity disease and acral lentiginous subtype compared to White populations. The proportion of mucosal melanomas varies by ethnicity/race, with 1% in non-Hispanic White people, 4% in Hispanic people, 9% in non-Hispanic Black people, and 15% in Asian/Pacific Islanders [13].

Other risk factors for cutaneous melanoma include a history of prior melanoma or nonmelanoma skin cancer, dysplastic nevi, or an increased number of typical melanocytic nevi. Sun exposure, especially intermittent intense exposure, and the use of indoor tanning beds are associated with higher risks. Light complexion, blond or red hair, blue eyes, freckles, and a tendency to burn rather than tan are additional risk factors. Conditions such as xeroderma pigmentosum and immunosuppressed states also contribute to risk [14].

For ocular melanoma, risk factors include light eye color, light skin color, little or no ability to tan, a propensity to sunburn, occupational history of welding, chronic occupational sun exposure, congenital ocular melanocytosis, and the presence of uveal nevus. In the case of mucosal melanoma, smoking is a risk factor for oral cavity melanomas, while exposure to formaldehyde may be a risk factor for sinonasal cavities [15].

PREVENTION

Prevention strategies for skin cancer, including melanoma, involve behavioral interventions to promote sun protection. However, there is limited consistent evidence demonstrating a reduction in the frequency of sunburn or skin cancer outcomes in both children and adults. Sun protection behaviors recommended include the use of sunscreen with a sun protection factor (SPF) of 15 or more (covering both UV-A and UV-B), especially in childhood, wearing sun-protective clothing such as broad-brimmed hats, avoiding sun exposure during midday, and steering clear of tanning parlors [16].

According to the US Preventive Services Task Force, counseling is advised for young adults, adolescents, children, and parents of young children to minimize exposure to UV radiation, particularly for individuals aged 6 months to 24 years with fair skin types. Selective counseling is recommended for adults older than 24 years with fair skin types. However, the current evidence is insufficient to assess the balance of benefits and harms of counseling adults (regardless of skin type) about skin self-examination to prevent skin cancer [17].

CONCLUSION

Skin cancer, particularly melanoma, poses a significant health concern with the potential for metastasis and associated risks. Diagnosing melanoma involves careful consideration of clinical criteria and may necessitate histological examination. Early detection through surveillance and behavioral interventions for sun protection remains crucial. While treatment options vary based on the stage of melanoma, surgical extirpation with adequate margins is a common approach. Adjuvant therapies, including immunotherapy and targeted inhibitors, play a role in managing advanced cases. Ongoing monitoring and counseling on sun protection behaviors are essential components of comprehensive care. Overall, addressing risk factors, promoting awareness, and fostering preventive measures are integral to minimizing the impact of melanoma on individuals and public health.

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