

Skin Cancer in Asians

Part 2: Melanoma

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ABSTRACT

The Asian population in the United States is expected to increase in the next 50 years. Concurrently, there is an overall rise in the incidence of melanoma. It is therefore crucial to obtain a better understanding of this deadly skin cancer in this minority population, as little information is currently available and prognosis remains poor. Through a review of the literature, this paper explores melanoma in the Asian population, including the most common subtype encountered, prognosis, theories on pathogenesis, and molecular biology. (*J Clin Aesthetic Dermatol.* 2009;2(10):34–36.)

The National Cancer Institute estimates that 39,080 men and 29,640 women will be diagnosed with cutaneous melanoma (CM) in 2009.¹ It is further estimated that of those diagnosed with melanoma, 8,650 men and women will die in the United States.¹ The US census bureau projects that the Asian population will triple in the next 50 years.² With an overall rise in melanoma and anticipated increases in the Asian population, clinicians and patients alike must be aware of the potential for skin cancer in this minority population. Currently, there is limited available data on skin cancer in Asians, including melanoma.

CM is predominantly an ultraviolet (UV) light-induced skin cancer more commonly associated with light-skinned Caucasians than in individuals with darker skin.³ Traditionally, clinical features associated with CM included Fitzpatrick skin types I to III with lighter color hair and eyes, an increased tendency to burn, history of multiple nevi, and strong family history of CM.⁴ Therefore, it is generally recognized that CM rarely affects individuals of ethnic backgrounds other than Caucasians, including those of Asian, Indian, Hispanic, or African descent. It is believed that greater concentrations of melanin in these darker skin populations provides photoprotective activity against the carcinogenic effects of UV radiation.³ More specifically, increased levels of melanin in darker skin

tones are thought to allow less damage to deoxyribonucleic acid (DNA) in the lower epidermis, and more effectively prevents proliferation of UV-damaged cells via apoptosis.³ Consequently, CM in these individuals tends to occur at anatomic locations that are not continually sun-exposed, such as the feet.

MELANOMA SUBTYPES

There are four major histological subtypes of CM. In decreasing order of frequency, they are superficial spreading melanoma (70%), nodular melanoma (15%), lentigo maligna melanoma (13%), and acral lentiginous melanoma (2–3%).⁵ Acral lentiginous melanoma (ALM) is a less commonly encountered subtype with a predilection for the palms, soles, subungual region, and mucous membranes.⁶ Among these sites, the plantar portion of the foot is the most common area of involvement.⁷ Histologically, ALM is characterized by a distinct radial or “lentiginous” growth phase.⁶ In contrast to Caucasians, ALM is the most common type of CM seen in deeply pigmented or Asian skin.^{5,8} Internationally, epidemiological studies conducted in Japan during 1997 to 2001 found that ALM accounted for 47 percent of all melanomas.⁹ A study of 63 Chinese people from Hong Kong diagnosed with CM reported greater than 50 percent were ALM.¹⁰ According to reports examining ALM, the mean age at

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diagnosis was 62.8 years, with incidence rates increasing with advancing age.⁵ Asian and Pacific Islanders exhibited the highest percentage of ALM diagnosis at Stage III.⁵

PROGNOSIS

Unfortunately, prognosis is poor in Asian patients with ALM.^{7,11} The five and 10-year survival rates for patients with primary ALM without metastasis is reported to be 80.3 and 67.5 percent, respectively, compared to 91.3 and 87.5 percent, respectively ($p < .001$), for all CMs in the United States.⁵ Many variables have been investigated as possible reasons for this grim prognosis. Among these, ulceration and tumor thickness were reported to be among the most significant predictors of outcome.^{12,13} In fact, studies have demonstrated that non-Caucasian patients with CM consistently had thicker tumors and had more frequent ulcerations than their non-Hispanic Caucasian counterparts.¹⁴ Such tumors are often detected at a more advanced stage, which subsequently leads to a poorer outcome. Other contributing factors may include the natural aggressive nature of ALM, unusual sites of involvement (palms and soles), and socioeconomic status (SES).^{15,16} An analysis of the California Cancer Registry database showed that higher SES was associated with earlier stage of tumor on presentation ($p < .0001$) and prolonged survival ($p < .0001$).¹⁵ Further, earlier recognition and diagnosis of CM is a challenging and contributing factor. A retrospective study of plantar melanoma from 1990 to 1997 showed the mean time between initial detection of the skin lesion by the patient and the first visit with a physician was 4.8 years, and on average, an additional seven months would pass before surgical treatment was performed.¹⁷ These results indicate that efforts need to be directed toward decreasing delays in seeking diagnosis and treatment.

PATHOGENESIS

CM is generally associated with increased exposure to UV light. However, with the predominant subtype of melanoma being in acral sites that are infrequently exposed to sunlight, one descriptive study showed no significant association between UV exposure and CM development in Asian populations.¹⁸ This has led investigators to search for other potential causes for the development of CM in non-sun-exposed sites of the body. Previous reports indicate local trauma to acral sites as well as heavy exposure to agricultural chemicals as possible risk factors for ALM development.^{19–21} In a case-controlled study of 311 CM patients in Australia and Scotland, authors found a positive association with penetrative trauma of the hands and feet with an adjusted relative risk (RR) of 5.0 and confidence interval (CI) of 3.0 to 8.6.¹⁹ With agricultural chemical exposure the RR was reported to be 3.6 and the CI was 1.5 to 8.3.¹⁹ A study of CM in Taiwan echoed this hypothesis as some of their farming patients worked outdoors without protection of hands and feet and subsequently were subjected to trauma in addition to being exposed to agricultural

chemicals.²² Opponents to the trauma theory state that increased trauma in acral sites is common and that CM may occur coincidentally along with the traumatic event.²³

MOLECULAR BIOLOGY OF ALM

Molecular pathology reveals a genetically distinct pattern of alteration unique to ALM.²⁴ First, ALM is shown to have a greater frequency of focal gene amplifications and losses when compared to other melanoma subtypes.^{24,25} Secondly, BRAF and NRAS genes encode proteins that are a part of the mitogen-activated protein kinase (MAPK) pathway, which is responsible for the proliferation and differentiation of cells.²⁶ It is hypothesized that mutations in the BRAF gene may be one of the early events in the pathogenesis of some CMs. In fact, BRAF mutations are seen in two thirds of CM with much of the remainder having NRAS mutations.²⁶ In contrast, studies indicate that ALM has low frequency of BRAF mutations and high levels of NRAS mutations, although the reasons for this remain unclear.²⁶ Therefore, recent reports searched for alternative pathways that might mediate tumor formation in ALM. Studies from Taiwan suggest an over expression of Ankyrin repeat-rich membrane spanning (ARMS) as a possible pathogenic mechanism for ALM by inhibiting apoptosis of the cancerous cell via regulation of the MEK/ERK signaling pathway.²⁷

DISCUSSION

CM is a relatively rare occurrence in the Asian population compared to fair-skinned populations. Limited data are available on skin cancer in Asians, including information on prevalence rates on CM in different Asian populations. Research shows that ALM is the most common subtype found in Asian populations in the United States as well as in many native Asian countries, such as China and Japan. Asians diagnosed with CM were more likely to have thicker tumors with an advanced disease state at time of presentation ultimately resulting in poorer overall prognosis and greater morbidity and mortality. There is evidence that delays in seeking diagnosis and treatment are major contributing factors. As a result, educational efforts should be put in motion to decrease delays in diagnosis. Skin cancer is no longer attributed solely to fair-skinned individuals with light-colored hair and eyes. Skin cancer has a new face, and that face is multicultural. Increasing awareness about CM in both Caucasian and non-Caucasian populations may facilitate early diagnosis and treatment, and ultimately will save lives.

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