Skin Cancer in Asians

Part 1: Nonmelanoma Skin Cancer

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ABSTRACT

Since the 1960s, basal cell carcinoma and squamous cell carcinoma among the Caucasian population have increased 3 to 8 percent annually. Although Asians display relative protection from basal cell carcinoma and squamous cell carcinoma, incidence rates of these nonmelanoma skin cancers have been increasing over the past three decades. With changing demographics and a steady rise in the minority population in the United States, there is an increased need for further studies of cutaneous malignancies within Asian and other ethnic populations. This article reviews nonmelanoma skin cancers in the Asian population with an insight into contributing factors, such as skin type, occupation, cultural practices, and genetic components. (*J Clin Aesthetic Dermatol.* 2009;2(8):39–42.)

Since the 1960s, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) among the Caucasian population have increased 3 to 8 percent annually.[1,2] Nonmelanoma skin cancer (NMSC) is not as extensively studied in the Asian population as it is in the Caucasian population. It has been proposed that Asians in general have skin types that protect them from NMSC.[3] Darker-skinned individuals have confirmed protection provided by increased epidermal melanin; increased melanocyte activity; and larger, more dispersed melanosomes, which can filter twice as much ulatroviolet B (UVB) radiation than lighter-skinned Caucasians.[4] Although Asians have lower incidence rates than Caucasians, NMSC is on the rise in Pacific Rim locations, such as Japan.[3] It is often difficult for many second- and third-world countries in Asia to establish uniform tumor registries in hospitals or large clinics due to logistical considerations and associated costs.[5] Many NMSC incidence rates from Asia are from locations such as Japan and Singapore because of limited financial and organizational resources in various parts of Asia.[5] In addition, Asians as a whole are not a homogenous population, with different regions having a wide range of skin types.[5] There are as much as 50-fold to 100-fold differences in incidence rates for BCC and SCC, even within populations of Asians with the same Fitzpatrick skin type.[6] NMSC also varies according to geographic location and latitude within countries and across the globe.[3]

RISK FACTORS AND PRECANCEROUS LESIONS

The total ozone layer has decreased over the last 20 years resulting in an increase in UVB radiation exposure.[7] UVB has been known to yield high concentrations of cyclobutane pyrimidine dimers and photoproducts in the epidermis of people with Fitzpatrick type I skin.[8] In Japan, during the last three decades, NMSC has shown a twofold increase in incidence, with Fitzpatrick skin type I being a risk factor that is of higher prevalence among rural residents.[3]

There have also been studies showing actinic keratosis (AK) as a risk factor for NMSC in Asians.[9] In recent years, AK incidence rates have been increasing among the Japanese population, as have SCC rates.[9] In Caucasians, SCCs on sun-exposed areas are sometimes found in association with AKs and usually have low metastatic potential. This is in contrast to SCCs that develop in association with AKs among the Japanese, which appear in some cases to be more biologically aggressive and metastasize more frequently.[9]

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Studies strongly suggest that photoprotection, especially from sunlight, is the major preventative approach to reducing precancerous lesions, such as AKs and NMSCs in Japan.[9] In 1992, studies comparing Kasai City (34º 56'N) and Ie Island (25º 10'N) revealed that twice the dose of UVB radiation causes a threefold to fourfold higher incidence of AK with a mean prevalence rate of 203.33 and 756.26, respectively.[10] Further studies from 27 university hospitals suggest that NMSC and AK prevalence rates were approximately fivefold higher in southern parts of Japan as compared to northern Japan.[7] An increase in the latitudinal-UVB gradient has been identified as one of many factors that have contributed to NMSC rates in Japan.[3] The incidence of AK in Japan is 414 per 100,000, occurring more commonly among men that participate in outdoor activities.[11,12] The significantly higher prevalence of AKs in outdoor workers indicated that the lifetime-dose exposure of solar UV plays a key role in the development of precancerous lesions in Japan.[7] In the city of Kasai, it was found that prevalence rates of AK in males and in outdoor workers were significantly higher than females and indoor workers.[7] Use of cosmetics after 20 years of age was a protective factor for precancerous lesions and having Fitzpatrick type I skin with a history of severe sunburns during childhood were found to be important risk factors.[10]

BASAL CELL CARCINOMA

Development of BCC has been correlated with prolonged, intensive UV exposure, with BCC occurring most commonly after the fifth decade of life.[4] More than 90 percent of BCCs develop in sun-exposed areas of the head and neck region regardless of the degree of pigmentation in an individual.[4] BCC is the most common skin cancer in Caucasians, Hispanics, Chinese, and Japanese.[4] According to one study of 101 institutions in Japan from 1987 to 1996, BCC accounts for 47 percent of all cutaneous malignancies.[11] BCC rates are less in pigmented individuals because of the inherent photoprotection of melanin and the nature of melanosome dispersal.[4] The incidence of BCC per 100,000 populations is 6.4 in Chinese men; 5.8 in Chinese women; 15 to 16.5 in Japanese overall; 29.7 in Japanese residents of Kauai, Hawaii; and 26.1 in Japanese residents of Okinawa.[4] There has also been an increased trend of BCC development in Japan. The ratio of BCC to SCC in Japan in the 1960s was reported to be 1–1.4:1 as compared to the 1990s with an increased BCC:SCC ratio of 4.5:1.[13] Study results indicate that BCC incidence was higher in 1986 to 1990 compared to 1979 to 1980, while SCC rates held steady.[3] Studies were conducted in Ie Island, Okinawa, the southern part of Japan, where the annual cumulative dose of UV is assumed to be the highest in Japan.[13] There was also a higher incidence among people with outdoor occupations, such as farmers, fishermen, and laborers.[14]

NMSC is the seventh most common cancer in Singapore accounting for 9.6 per 100,000 cases among men and 8.1 per 100,000 cases among women during 1993 and 1997.[15] Singapore is situated one degree north of the equator and has a population of four million people, comprising 77 percent Chinese, 14 percent Malay, and nine percent a mixture of other races.[5] The age-standardized incidence rate (ASR) of BCC has increased at a rate of 2.8 per year among Asian residents in Singapore between 1968 and 1997.[5] Among females in Singapore, BCC accounts for 4.5 percent of all cancers in Chinese, 3.4 percent in Malays, and 2.5 percent in Asian Indians.[5] BCC incidence rates among the Chinese (Fitzpatrick skin types III–IV) were more than 2.5 times that of the Malays (Fitzpatrick skin types V–VI) and the Asian Indians (Fitzpatrick skin type VI).[16]

Similarly with Caucasians, 70 to 90 percent of BCCs occur on sun-exposed skin in Asians, thus emphasizing that photoprotection should not be ignored, even in more darkly pigmented individuals.[4] Rare BCC sites include nipple, penis, anus, groin, popliteal fossae, ankle, and scalp.[4] Other risk factors include history of radiation, scars, ulcers, arsenic ingestion, immunosuppression, trauma, albinism, and nevus sebaceus.[4] The clinical presentation and histological features of BCC in Asians include characteristics shared from darker-pigmented individuals and Caucasians.[17] Clinically, approximately 75 percent of tumors in one study of Japanese patients showed a brown-to-glossy dark pigmentation.[4] Presence of pigmented BCC may confound clinical differentiation of BCC from other skin lesions, including melanocytic neoplasms. Pigmented BCC represents 50 percent of BCCs in Asians in contrast to six percent in Caucasians.[4] The most common histopathological type of BCC in Asians is the solid (nodular) type similarly seen in Caucasians; however, the incidence of adenoid BCC is relatively higher in Asians and African-Americans compared to Caucasians.[4]

SQUAMOUS CELL CARCINOMA

SCC is the second most common skin cancer in the Chinese and Japanese.[5] SCC in the Chinese was reported to be 2.6 to 2.9 per 100,000 and has decreased 0.9 percent from 1968 to 1997.[3] SCC accounts for 30 percent of all skin cancers in Japan.[4] The male/female ratios for Chinese, Malays, and Asian Indians are 1.5 to 1.9, 1.1 to 6.2, and 0.3 to 0.9, respectively.[5] The annual incidence rates of SCC for Chinese, Malays, and Asian Indians are 2.6, 1.3, and 1.4 per 100,000 persons, respectively.[5] Among males, SCC accounts for 4.3 percent of all cancers in Chinese, 3.1 percent in Malays, and 3.2 percent of cancers in Asian Indians.[5] For SCC a small decline of 0.9 percent per year was noted in contrast to the increased rates seen in other countries, such as Australia and Canada.[5] The incidence of SCC has been reported to be 118 per 100,000 in Caucasian residents of Kauai, Hawaii, and 23 per 100,000 in Japanese residents in Kauai, Hawaii.[4] SCC is the most frequent type of malignant tumor arising in scarred skin.[17–20] According to reports, the fraction of scar carcinoma versus non-scar SCC in Japan is reported to be 31.8 and 44.0 percent, versus 1.9 and 2.5 percent in other countries.[21] In addition, the overall prognosis of scar SCC is less favorable

compared to non-scar SCC.[21] The rate of recurrence of scar carcinoma was reported to be 2.53 times higher than that of non-scar SCC, with a metastasis rate ranging from 10 to 100 percent, as compared to one percent in non-scar carcinoma.[22,23] Risk factors for the development of SCC in darkly pigmented individuals are chronic scarring and areas of chronic inflammation. These risk factors have been associated with a greater potential for metastasis and are reported to occur in 20 to 40 percent of cases as compared to 1 to 4 percent in sun-induced SCC in Caucasians.[4] SCCs in Asians have a greater tendency to occur in non sun-exposed sites, with a higher potential for metastasis possibly due to advanced disease stage at the time of diagnosis.[3]

MOLECULAR PATHOGENESIS

Although environmental factors play a significant role in NMSC, molecular components have been implicated in the pathogenesis of this disease. UV-induced DNA damage in keratinocytes causes mutation, promotes the initiation step of carcinogenesis, and triggers the production of interleukin-10 (IL-10), which may contribute to tumor escape from the host immune response.[24] IL-10 production by keratinocytes or tumor infiltration cells may contribute to the immunosuppressive and anti-inflammatory effects allowing the tumor to escape from the immune response.[24] IL-10 expression has been associated with the inhibition of antitumor T-cell immune response leading to tumor growth in both melanoma and NMSC.[1] Reports demonstrate that Japanese have a low incidence of IL-10 expression (0–1%) compared to Caucasians (12–19%).[24] In addition, UV-induced DNA damage is a vital component of cutaneous carcinogenesis by producing alternations in oncogenes and tumor suppressor genes, such as p53 and patched gene, which are responsible for keratinocyte transformation.[25] Apoptosis induced by radiation or other DNA-damaging agents is controlled by the p53 suppressor gene.[26] Loss of p53 tumor suppressor gene function represents the most common genetic alteration identified in human malignancy, occurring in >50 percent of all tumors.[27] Caucasians had a reported incidence of p53 gene mutations of approximately 50 percent in BCC as compared to nine percent in Koreans and 12 percent in Japanese, thus suggesting that reasons other than UV radiation contribute to the pathogenesis of BCC.[28] Studies in Korean patients showed that either dysfunctional p53 or Bcl-2 expressions enhance skin tumor formation by suppressing apoptosis.[28] Results showed that mutations in p53 suppressor genes, BAX genes, or dysfunction of Bcl-2 protein expression could also contribute to the development of BCC.[28] Research suggests that the role of a frameshift mutation of Bax gene could be responsible for BCC formation in Asians.[29] In aggressive SCC in Asians, there have been reports of several indices that correlate with tumor behavior, such as p53 suppressor gene over-expression, decreased expression of E-cadherin and beta-catenin, and Ki-67 LI.[30] Ki-67 LI is considered to be a reliable marker for assessing the growth activity of tumors and is useful for estimating the prognosis of patients.[28] Several studies in Asians demonstrated abnormal or reduced expression of E-cadherin or B-catenin in various carcinomas and the reduction of these markers has been related to the loss of differentiation as well as to tumor invasion and metastasis.[28]

COMPARISON OF ASIANS TO OTHER COUNTRIES

Variations between ethnicities encompass a wide range of Fitzpatrick skin types, sociocultural differences, and inherent genetic variabilities. Studies revealed a three-percent increase in BCC and a 0.9-percent decline in SCC in Singapore, which is lower than other countries with fair-skinned individuals, such as Australia, Canada, and Finland.[30–32] NMSC rates vary according to ethnicities and Fitzpatrick skin types as demonstrated by rates of BCC and SCC among Japanese in Hawaii, which were 1/40 of the rates among Caucasians living in the same geographic areas.[9] In addition, the incidence rates of BCC, SCC, and SCC *in-situ* in the Japanese-American population in Kauai, Hawaii, are 12, 4, and 11 times lower, respectively, as compared to rates in Caucasian Kauaiians.[9] The incidence of BCC is twice as high among ethnic Japanese who live in Kauai, Hawaii, as compared to those living in Japan, possibly due to intense UV exposure and an emphasis on more outdoor activities in Hawaii.[9] In contrast, Caucasian Kauaiians exhibit substantially lower incidence rates of NMSC compared to Caucasian Australians, although many Kauaiians have very active outdoor lifestyles with marked exposure to intense sunlight. When evaluating geographic variability, sun exposure alone does not account for NMSC differences between ethnicities.[34] Some BCC incidence rates are increasing more quickly than SCC rates in some countries, while the reverse is true in other countries.[34] Although people have speculated that changes in sun exposure with a given race can greatly affect NMSC rates, it is important to know that variability exists based on gender, sex, tumor type, and ethnic background.[34]

DISCUSSION

General trends in the numbers of deaths from NMSC in Japan have risen since 1995.[4] It is a misconception that all Asians possess inherent relative protection from NMSC because of their skin type. It seems that NMSC development among Asians varies greatly, and solar UV exposure and Fitzpatrick skin type are useful indices to determine relative risk. Although UV radiation plays an important role in the pathogenesis of NMSC in Asians, there also seems to be other genetic and molecular components at work. It is suggested that individuals with darker skin utilize the same photoprotection precautions as recommended for individuals with lighter skin since immune surveillance is the main protection against the development of many skin malignancies.[35] It is also important to keep in mind that NMSC rates are frequently under-reported and underestimated in the Asian population due to limited resources in many countries. NMSCs in Asians are often associated with greater morbidity and

mortality, necessitating increased efforts to assess risk factors in Asian individuals, to encourage periodic self examination and professional evaluation of skin, and to optimize strategies for earlier diagnosis and treatment.

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