Incidence of nonmelanoma skin cancer in a cohort of patients with vitiligo

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Background: Nonmelanoma skin cancer (NMSC) incidence in patients with vitiligo has not been studied.

Objective: We sought to quantify the incidence of NMSC in patients with vitiligo.

Methods: A cohort of 477 patients with vitiligo and no history of NMSC seen in an outpatient academic center between January 2001 and December 2006 was established. All charts for patients with vitiligo were reviewed for incident NMSC, and histopathology verified. Age-adjusted (2000 US Standard Million) incidence rates were calculated and compared to US rates.

Results: Six patients with NMSC were identified; all were Caucasian (>61 years). Age-adjusted incidence rates were: basal cell carcinoma, male 1382/100,000; basal cell carcinoma, female 0; squamous cell carcinoma, male 465/100,000; squamous cell carcinoma, female 156/100,000. Except for basal cell carcinoma in females, all rates were higher than US rates but not statistically significant.

Limitations: Comparison incidence rates from the general patient population during the same time period were unavailable.

Conclusion: Health care providers should be aware of the possible risk of NMSC in Caucasian patients with vitiligo. (J Am Acad Dermatol 2008;60:929-33.)

Vitiligo affects approximately 1% of the US population and is characterized by idiopathic destruction of melanocytes, possibly immune mediated, resulting in depigmented or hypopigmented macules and patches.[1] Melanin is thought to be protective against the harmful effects of ultraviolet (UV) radiation,[2] such as skin cancer. Fitzpatrick skin phototypes I and II are more susceptible to skin cancer, and skin phototypes V and VI, with high levels of constitutive pigmentation, have the lowest incidence of skin cancer.[3-5] Hence, it is counterintuitive that, despite the loss of photoprotective melanin and considering that UV radiation is used therapeutically for vitiligo, only anecdotal reports of nonmelanoma skin cancer (NMSC) in patients with vitiligo have been published.[6-11]

Psoralen plus UVA (PUVA) photochemotherapy was reported for the treatment of psoriasis in 1974.[12]

Abbreviations used:

BCC:	basal cell carcinoma
HFHS:	Henry Ford Health System
KPNW:	Kaiser Permanente Northwest
NH:	New Hampshire
NMSC:	nonmelanoma skin cancer
PUVA:	psoralen plus ultraviolet A
SCC:	squamous cell carcinoma
UV:	ultraviolet

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In 1976, a follow-up study of the long-term impact of PUVA in psoriasis was initiated in 16 US centers. In the first year after PUVA therapy, 18 skin cancers (13 basal cell carcinoma [BCC] and 5 squamous cell carcinoma [SCC]) were detected; by 2.1 years of follow-up, 48 NMSCs (19 BCC and 29 SCC) were reported.[13] Conversely, PUVA was reported for the treatment of vitiligo in 1976,[14] and two subsequent studies, involving 326 and 59 patients, failed to show an association of skin cancer in patients with vitiligo treated with PUVA.[15,16] An initial case report of SCC in vitiligo after prolonged PUVA therapy was not reported until 2 decades later.[17] It is commonly believed that patients with vitiligo do not have an increased risk, and perhaps have even a lower incidence of skin cancer than the general population.[8]

Because skin cancer has been rarely reported in patients with vitiligo and its incidence among these individuals is currently unknown, we designed a study with the purpose of determining the incidence of NMSC in a cohort of patients with vitiligo seen in a large group practice health care system in the Detroit, MI, metropolitan area (academic department of dermatology), and to compare these data with available incidence rates in the United States.[18]

METHODS

Data sources

This study was approved by the Henry Ford Hospital Institutional Review Board. Our design was a cohort study with a population derived from the comprehensive electronic medical record database of the Henry Ford Health System (HFHS), Detroit, MI. The HFHS is comprised of a large multispecialty and primary care group practice and a health maintenance organization. Payor distribution, as of 2006, was composed of health maintenance organization 32%, Medicare 34%, Medicaid 11%, commercial insurance 14%, and other insurers/self-pay 9%, which demonstrates that the HFHS patient population encompasses all age groups, races, and social settings. Approximately 3.1 million outpatient visits per year occur at HFHS with patients from both urban and suburban areas.

Design and patients

As designed a priori, patients had to have the *International Classification of Diseases, Ninth Revision* diagnostic code for vitiligo (709.01) recorded from January 1, 2001, to December 31, 2006, in the HFHS medical record database to be included in the cohort. To ascertain that the patients were being followed up in HFHS, it was required that the *International Classification of Diseases, Ninth Revision* code be recorded in at least two separate encounters by a dermatologist during this time range. A total of 518 patients were identified, and all patients had been examined in the department of dermatology. To validate the diagnosis, all 518 medical records (100%) were individually reviewed to ascertain the confirmed diagnosis of vitiligo given by a dermatologist, which was verified in 479 patients. Two additional patients with vitiligo had NMSC before the study's start date (January 1, 2001) and, hence, were also excluded (477 patients; 92%). The medical records of these 477 patients were further reviewed to identify any incident biopsy-confirmed NMSC during the study period. All histopathology slides of patients who developed skin cancer during the study inclusion period were obtained, and Melan-A and Fontana-Masson stains were performed on the original tissue blocks to determine whether the skin cancers were located on vitiliginous or normal-appearing skin. These slides were re-reviewed for confirmation of skin cancer and the presence of pigmentation by a board-certified dermatopathologist (Marsha Chaffins, MD). Skin type, history of phototherapy, and sun-exposure history were also documented during chart review of the encounter notes of the patients who developed skin cancer.

Data analysis

The records of all 518 cohort members (100%) that fit inclusion criteria were individually reviewed. Our final sample is comprised of only those patients who had confirmed diagnosis of vitiligo given by a dermatologist and no history of NMSC (n = 477). Age was calculated as of January 1, 2001. Entry into the study was defined using date of enrollment in the health system, which was set as either January 1, 2001, for established patients, or for those who were new to the health system (enrolled after January 1, 2001), as the date on which they were first seen in the system. To determine censorship or end of follow-up, the study end date (December 31, 2006), date of last office visit to the HFHS (if left health system during study period), or date of histopathologic diagnosis or skin cancer was used. Total person-years of observation were calculated. Crude annual incidence rates per 100,000 population were calculated and age-adjusted rates, using the 2000 US Standard Million (2000 US Census Bureau population estimates), the most recent age distribution of the US population available.

The annual incidence rates reported in this study refer to persons with NMSC, not the number of tumors, so a person with more than one skin cancer was counted once. Incidence is a key measure for