Skin Cancer Risk (Nonmelanoma Skin Cancers/Melanoma) in Vitiligo Patients

Michelle Rodrigues

KEYWORDS

• Vitiligo • Leukoderma • Skin cancer • Cancer • Melanoma • Basal cell skin cancer • Squamous cell skin cancer • Nonmelanoma skin cancer • Phototherapy • Depigmentation

KEY POINTS

- The risk of skin cancer in vitiligo is still being debated.
- The genetic profile of those with vitiligo seems to be opposite to those with melanoma.
- The autoimmunity seen in vitiligo seems protective against melanoma.
- Current evidence suggests narrow-band ultraviolet B does not increase the risk of cutaneous malignancies, even with long-term therapy, especially in those with skin phototype IV to VI.

INTRODUCTION

Vitiligo affects approximately 0.5% to 2% of the population[1,2] and has no geographic or ethnic boundaries. Vitiligo results in patchy depigmentation of the skin, mucous membranes, and hair owing to a combination of genetic susceptibility, cellular stress, and an autoimmune cytotoxic CD8+-mediated melanocyte attack. Although an absence of melanin in lesional skin and prolonged administration of phototherapy may cause concern about the development of skin cancer in this population, the genetic and autoimmune profiles of vitiligo patients confer a degree of protection against melanoma and nonmelanoma skin cancers (NMSC). A growing body of evidence suggests there is no significant increased risk of melanoma or NMSC in vitiligo, even with prolonged narrow-band ultraviolet (UV) B light therapy. However, well-constructed, prospective studies are a lacking and are clearly needed to substantiate the recent published findings on the topic.

CONTENT

Exposure to UV is an important factor in the development of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and possibly other skin cancers. In Australia, 2 of 3 people will have skin cancer diagnosed by the time they are 70[3] with melanoma cited as the most common cancer in those between 15 and 44 years of age. High rates of skin cancer, however, are not unique to Australia. One in 5 Americans will have skin cancer in their lifetime,[4] and the estimated annual cost of treating skin cancers in the United States is 8.1 billion dollars.[5]

Those with black skin have an intrinsic sun protection factor of 13.4[6] resulting in lower rates of skin cancer compared with lighter skin types. Those with dark skin, however, are not immune to UV-induced cutaneous malignancies. The incidence of melanoma and nonmelanoma skin cancer is approximately 5% in Hispanics, 4% in Asians, and 2% in blacks.[7] Those with vitiligo

Disclosures: The author has no conflicts of interest to declare.
Department of Dermatology, St Vincent's Hospital, The Royal Children's Hospital, Skin and Cancer Foundation, Inc, 41 Victoria Parade, Fitzroy, Victoria 3065, Australia
E-mail address: michelleannerodrigues@hotmail.com

Dermatol Clin 35 (2017) 129–134
http://dx.doi.org/10.1016/j.det.2016.11.003

lack melanin in affected white patches of skin. It is, therefore, understandable that dermatologists around the world have been concerned about the development of melanoma and nonmelanoma skin cancer secondary to incidental and therapeutic UV light exposure in this subgroup of patients.

Genetic studies found polymorphisms in the TYR gene of vitiligo patients. This gene encodes tyrosinase, which is involved in melanin synthesis. The TYR allele that confers risk for vitiligo is also protective against melanoma.[8,9] In addition, human leukocyte antigen–A2 is the protective allele against melanoma development and was the risk allele for development of vitiligo in a meta-analysis.[10]

Further evidence to support this inverse relationship between vitiligo and melanoma is noted in the melanoma literature. Vitiligo has been reported to confer an enhanced 5-year survival in melanoma patients.[11] Furthermore, treatments used for metastatic melanoma have been reported to induce vitiligo including vemurafenib, a BRAF inhibitor,[12] and therapeutic immune checkpoint inhibitors such as anti–cytotoxic T-lymphocyte–associated protein 4 and anti–programmed cell death protein 1 (PD-1) agents. The development of vitiligo while on such therapy seems to improve treatment response (**Figs. 1** and **2**).[13,14] Inhibition of cytotoxic T-lymphocyte–associated protein 4 and PD-1 reduces regulatory T-cell activity, which may explain why they are associated with the development of autoimmune diseases.[13,15,16] This body of evidence suggests melanoma and vitiligo represent opposite ends of the genetic risk spectrum, which has led to vitiligo being recently labeled *the white armour*.[17]

Although autoimmunity in vitiligo confers protection against melanoma, the lesional skin of those with vitiligo lacks melanin. In normal skin, melanin affords an inherent skin protection factor that is proportional to the darkness of the skin. It has been assumed, therefore, that when melanin is reduced in amount or absent, the skin is more photosensitive and susceptible to UV light–induced carcinogenesis. The assumption that vitiliginous skin acts like Fitzpatrick skin phototype (SPT) I, however, has been challenged in the literature. Studies found that photoadaptation and tolerance seem to mirror the patient's normal skin phototype, even in vitiliginous lesions.[18,19] Studies also found that those with darker skin types tolerate higher doses of UVB, suggesting that photobiological properties such as epidermal thickness and chromophores play a more significant role in photoprotection than previously assumed.

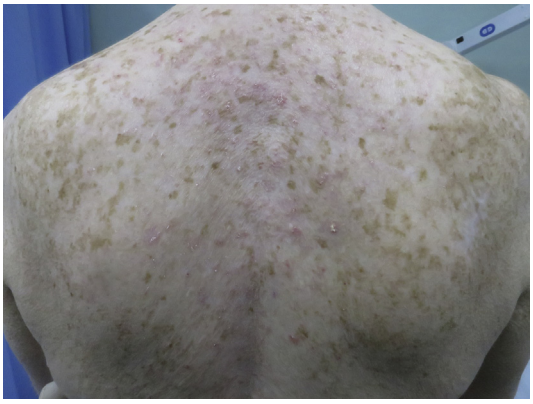

Fig. 1. Back of a patient with metastatic melanoma in whom vitiligo developed while on PD-1 inhibitor, pembrolizumab, with coexistant solar keratoses.

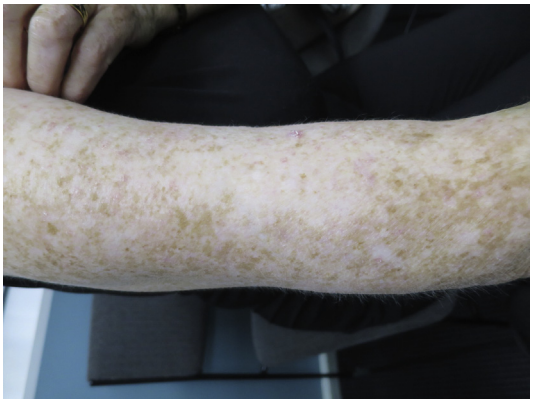

Fig. 2. Right arm of the same patient.

Therapeutic exposure to narrow-band UVB light (NB-UVB) (311 nm) is currently the treatment of choice for widespread or progressive vitiligo.[20] NB-UVB was first introduced in the Netherlands in the early 1980s[21,22] and is now a standard therapy for many dermatologic conditions including vitiligo for which it is commonly combined with topical corticosteroid and calcineurin inhibitors for widespread disease. Yones and colleagues,[23] in a randomized double-blind trial, found that NB-UVB had superior efficacy, better color matching of repigmented skin, and fewer side effects compared with psoralen and UV light A (PUVA). This superior safety and efficacy profile was also noted in prior studies.[24,25] Yones and colleagues[23] also found that approximately 6 months of NB-UVB was required to achieve 50% repigmentation and 12 months to regain 75% pigmentation. Studies examining optimal duration of phototherapy for vitiligo are lacking because of heterogeneous study designs, the use of variable outcome measures, and the paucity of prospective trials. What is clear is