Atypical Lentigines in a Man With Mixed African American and White Race/Ethnicity Receiving Long-term Voriconazole Therapy

Voriconazole, an antifungal agent frequently used in systemic fungal infections, has been implicated in phototoxicity and photoaging.1 Chronic voriconazole phototoxicity and accelerated photoaging may contribute to the development of melanoma and squamous cell carcinoma.1,2 We describe the development of multiple lentigines and atypical melanocytic lesions in a dark-skinned man receiving long-term voriconazole therapy.

Report of a Case | A man in his 40s with mixed African American and white race/ethnicity, Fitzpatrick skin type IV, and history of pulmonary sarcoidosis and secondary pulmonary aspergillosis presented for a follow-up dermatologic examination. Unremarkable findings from a skin examination had been noted 3 years previously. The patient returned for dermatologic examination and was noted to have new hyperpigmented lesions on his forearms that were present for a few months. At the time, the patient had been receiving voriconazole, 200 mg twice daily, for 32 months for treatment of his fungal disease. In addition, the patient had a history of long-term prednisone use (varying doses of up to 60 mg/d) since 2008 to manage his pulmonary sarcoidosis. Because of progressively deteriorating pulmonary function and intermittent, worsening hemoptysis, an evaluation for lung transplant was initiated.

The patient had no history of atypical melanocytic lesions, and there was no family history of melanoma. The patient reported sun exposure with no history of increased occupational exposure or sunburns.

Physical examination revealed numerous hyperpigmented macules clinically consistent with lentigines on his face, with darker and multicolored macules on his sun-exposed forearms (Figure 1A). Other signs of chronic sun exposure were absent. Biopsies of the most clinically suspicious hyperpigmented lesions were obtained and were remarkable for epidermal hyperplasia with pigmentation along the basal layer consistent with a lentiginous growth pattern. The largest, darkest lentiginous macule (Figure 1B) demonstrated single atypical melanocytes crowding in the lower epidermal layers without exhibiting a normal nesting pattern (Figure 2), while other lesions had moderate cytologic atypia (not shown). The atypical lesions were excised, and the patient was counseled on appropriate sun protection measures and self-skin examination, with close dermatologic follow-up.

Discussion | Voriconazole inhibits fungal 14 α-demethylase, a cytochrome p450 enzyme essential to ergosterol biosynthesis of fungal cell membranes and is first-line therapy for the treatment of invasive aspergillosis.3 It has multiple cutaneous adverse effects, including UV-A photosensitivity manifesting as erythema, blistering, pruritus, cheilosis, eczema, and lentigo formation.3

Figure 1. Clinical Images

New onset growth of lentigines on the forearms of a man with mixed African American and white race/ethnicity (A) with an irregularly pigmented macule that was biopsied (B).
The mechanism for voriconazole-induced photosensitivity and phototoxicity remains unknown. One current hypothesis includes a potentially phototoxic UV-B–absorbing N-oxide metabolite of voriconazole. Alternatively, inhibition of CYP450 with voriconazole therapy is thought to possibly increase serum retinol level, a known photosensitizer.

Malignant skin conditions associated with chronic voriconazole use, including melanoma in situ and squamous cell carcinoma, have been reported in patients with Fitzpatrick skin types III or below and more commonly in individuals with some degree of immune compromise. More recently, the development of lentigines in a dark-skinned patient receiving long-term voriconazole therapy was described. Our patient is similar in the abrupt development of lentigines and photodamage characterized by mild poikiloderma but differs from the prior report owing to the severe melanocytic atypia observed.

Cutaneous adverse effects of long-term voriconazole therapy are not only burdensome but also lead to morbidity and mortality. Product labeling recommends discontinuation of voriconazole therapy if a squamous cell carcinoma or melanoma develops, which can lead to adverse outcomes if alternative antifungal therapies are limited. In addition, for patients awaiting transplant, the development of a melanoma also could compromise the ability to receive an organ donation.

This report highlights the development of atypical melanocytic lesions in a dark-skinned individual receiving concurrent voriconazole and immunosuppression therapy and reinforces the importance of counseling patients on appropriate sun protection and sun avoidance. These patients, regardless of skin type, require frequent dermatologic follow-up and surveillance with a low threshold for biopsy of atypical lesions.

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Onychocytic Matricoma: A New, Important Nail-Unit Tumor Mistaken for a Foreign Body

Onychocytic matricoma (OCM) is a benign acanthoma of the nail unit that presents with localized thickening of the nail plate and melanonychia. This newly described entity has suggestive clinical features and distinctive histopathologic changes.

Report of a Case | A man in his 40s presented with a history of traumatic injury to the nail unit, after which he noted a dark line under the nail, which he assumed to be a splinter. It persisted for 3 years without any notable change. The patient reported removing portions of it when he wouldclip the nail back.

Physical examination demonstrated a 2-mm-wide black longitudinal streak extending to the distal lunula with localized nail plate thickening on the right second digit (Figure 1A and B). Dermatoscopic findings were consistent with a foreign body under the nail (Figure 1C and D). Nail clippings of