Photoaging refers to the effects of long-term ultraviolet (UV) exposure and sun damage superimposed on intrinsically aged skin. The clinical signs associated with photoaging include dyspigmentation, laxity, a yellow hue, wrinkles, telangiectasia, a leathery appearance, and cutaneous malignancy. These changes often occur gradually as a person ages but can develop earlier if extensive UV exposure and photodamage have taken place. When patients present early with photodamage, their concerns are often cosmetic, inquiring about treatments for rhytides, skin roughness, laxity, and mottled appearance.

A number of therapies have now been advocated for the treatment of photodamaged and photoaged skin. Fractional photothermolysis (FP) with a 1,550-nm erbium-doped laser (Fraxel SR, Reliant Technologies Inc., San Diego, CA) is a fairly recent addition to the dermatologist’s therapeutic armamentarium. This laser is designed to generate microscopic columns of thermal tissue injury, leading to discrete areas of thermal necrosis (microscopic epidermal necrotic debris) in the epidermis and dermis while sparing surrounding tissue. Currently, FP is approved for the treatment of photodamaged skin, as well as rhytides, acne and surgical scars, and melasma. Adverse effects are reported to be minimal with this treatment. We report the development of keratoacanthomas (KAs) on the legs in two patients after FP. We discuss the potential etiology of these tumors and the consideration and precautions that must be taken when treating photoaged skin.

Case 1
A 42-year-old Caucasian woman with Fitzpatrick skin type III presented to our clinic complaining of scattered discoloration and erythema of both lower extremities. She had been treated previously with cryotherapy for actinic keratoses on her legs but was otherwise healthy, with no history of skin cancer. She took no medications and denied any drug allergies. Her surgical history was significant for a breast augmentation in 1991.

On examination, the patient was noted to have scattered lentigines, hypopigmented and erythematous macules, and a number of seborrheic keratoses (Figure 1A and B). The patient was diagnosed with photoaging and underwent two cycles of fractional photothermolysis treatment (Fraxel SR750) at 3-week intervals.
Briefly, the affected areas were cleansed with a mild soap before the procedure. Triple anesthetic cream (10% benzocaine, 6% lidocaine, 4% tetracaine; New England Compounding Center, Framingham, MA) was applied to the treatment area under occlusion. One hour later, the triple anesthetic cream was removed and a Food and Drug Administration–certified water-soluble tint (OptiGuide Blue, Reliant Technologies Inc., Mountain View, CA) was applied to the treatment area. The tint allowed the laser’s intelligent optical tracking system to detect contact with the skin and to adjust the treatment pattern.

Figure 1. Clinical photos of patient 1’s left medial (A) and right leg (B) before fractional photothermolysis. Six weeks after treatment, the patient presented with discrete scaly papules on the left (C) and right (D) legs. Frozen sections performed on Mohs surgery specimens revealed discrete and well-circumscribed epidermal strands and nests of glassy squamous cells surrounding areas of keratotic material (E & F) (toluidine blue, × 20 magnification).
with respect to handpiece velocity. Ointment (LipoThene, Lipothene Inc., Pacific Grove, CA) was applied over the OptiGuide Blue to allow the laser handpiece to glide smoothly over the treatment area. The device settings were as follows: energy 12 mJ, spot size 15 mm, wavelength 1,550 nm, 24% to 30% coverage. Eight to 10 passes were performed with a density of 2,000 to 2,500 microscopic treatment zones (MTZ)/cm². A cold-air cooling device (Zimmer Medizin Systems, Irvine, CA) was used at a setting of 4.

Six weeks later, the patient was noted to have four discrete erythematous papules with a central hyperkeratotic core on her left medial (n = 1) and right (n = 3) lower extremity (Figure 1C and D). Biopsies were performed for histopathologic examination, and all the lesions were consistent with KAs (Figure 2E and F).

Case 2
A 63-year-old Caucasian woman with Fitzpatrick skin type III initially presented in 2004 with discoloration and erythema of her bilateral lower extremities. Her past medical history was significant for gastroesophageal reflux disease, a neck lift, liposuction, and a cholecystectomy. There was no past history of skin cancer. Her medications included esomeprazole and cetirizine, and she was allergic to tetracycline and terbinafine.

Examination was significant for a number of hyperpigmented and erythematous macules that were clinically consistent with actinic keratoses and solar lentigines (Figure 2A). The patient underwent two rounds of laser-mediated photodynamic therapy treatment for photodamage, the first to both lower extremities in February 2004 and the second to the left posterior leg in September 2007.

In January 2008, the patient's bilateral lower extremities were treated with fractional photothermal treatment (Fraxel SR1500) for persistent photodamage. The treatment was performed in a similar fashion to that in Case 1, although the water-soluble tint was not applied because it was not required for this second-generation device. The following laser parameters were employed: energy 50 mJ, spot size 15 mm, treatment level 11, 32% coverage, with eight to 10 passes. A cold-air cooling device (Zimmer Medizin Systems) set at 4 was again employed during treatment.

One month later, the patient developed hyperkeratotic papules on the left anterior and posterior leg (Figure 2B). Biopsies of the lesions were consistent with KA and invasive squamous cell carcinoma (SCC), respectively (Figure 2C and D).

Discussion
KA is a rapidly growing cutaneous tumor that arises in sun-exposed areas of the skin. It tends to develop in individuals with fair complexions, and the incidence peaks in middle age, typically between 50 and 69 years of age. These tumors characteristically present as crateriform lesions, appearing as dome-shaped, skin-colored nodules with a central keratinous core.

A number of KA subtypes have been documented, including mucosal, subungual, keratoacanthoma centrifugum marginatum, and giant KA. Multiple KAs have been described in Grzybowski, and Ferguson-Smith, as well as other conditions such as Muir-Torre, nevus sebaceous of Jadassohn and xeroderma pigmentosa. In addition, KAs have been noted to arise in lesions of hypertrophic lichen planus, discoid lupus erythematosus, epidermolysis bullosa dystrophica, psoriasis, and herpes zoster sites. Still, the etiology of these tumors remains unknown. KAs appear to be follicular in origin, and potential causes have been attributed to genetic disorders, immunosuppression, viruses, chemical carcinogens, UV light exposure, and trauma.

Numerous reports of KA arising secondary to trauma exist. KAs have been documented after thermal burns, cryotherapy, radiation therapy, dog scratch, thorn injury, tattoos, and even surgery. Trauma-induced KAs have further
been demonstrated in animal models, and it has been postulated that epithelial disruption may be involved in the development of KAs in humans.\textsuperscript{9}

UV exposure has also been epidemiologically proven to be a cause of cutaneous tumors in humans, including KA.\textsuperscript{2,9,23} It is believed that specific UV-induced mutations accumulate in the skin after exposure. This, combined with the immunosuppressive and other detrimental effects of UV light on the skin, as well as an individual’s efficiency or inefficiency at repairing the damage inflicted, predispose

\textbf{Figure 2.} Clinical photos of patient 2’s left leg before fractional photothermolysis (A). Although overall improvement in photodamage is observed, a new hyperkeratotic papule is noted in the treatment area 1 month after therapy (B). On histologic examination, an atypical squamoproliferative lesion consisting of keratinocytes with abundant glassy cytoplasm is observed (C) (hematoxylin and eosin, \times 20 magnification). These cells extend into the dermis forming cysts and some microabscesses (D) (hematoxylin and eosin, \times 100 magnification).
mutated epidermal cells to tumor development. Photocarcinogenesis is considered to be the extreme of the photoaging spectrum and the end result of chronic photodamage.¹

Treatments available for photoaged skin are now numerous. For example, cryotherapy is commonly used in the treatment of actinic keratoses and pigmented changes.¹⁵ Trichloroacetic acid peeling and carbon dioxide laser resurfacing have been proposed as prophylactic treatments to prevent the development of nonmelanoma skin cancer in individuals with photoaged skin. Investigators have shown a lower incidence of tumors and a longer time to development of new skin cancers in subjects treated with these modalities than in controls.²⁴ More invasive approaches to the treatment of severe photodamage and cutaneous malignancies such as KA include curettage and electrodesiccation, excision, and Mohs microscopic surgery.⁷,⁸,²¹,²⁵–²⁸ All of these modalities designed to treat photoaging have also been associated with KA development.¹⁴–¹⁶,²²,²⁸,²⁹

FP with the 1,550-nm erbium-doped laser has been advocated as a safe and effective treatment for photodamaged and photoaged skin. FP creates coagulated microscopic columns of epidermis and dermis while sparing the surrounding tissue from injury.³,⁴ A study examining 50 patients with mild to moderate facial and nonfacial cutaneous photodamage, rhytides, and dyspigmentation who underwent three successive treatments of FP at 3- to 4-week intervals showed only transient erythema and edema in the majority of patients. No prolonged pigmentedary changes or scarring was observed at 9 months of follow-up.⁵ In a larger retrospective study of 961 patients treated with FP, complications were found in 7.6%. Acneiform eruptions (1.9%) and herpes simplex virus outbreaks (1.8%) were most frequently observed. Adverse events appeared equally across age groups, skin types, body locations, and laser parameters. No tumors were reported in this study.⁶ The sites treated in this study included the face, neck, chest, and hands.

Both of our patients had their legs treated with FP and subsequently developed KAs in this area. It is possible that there is something unique about the legs that predisposed our patients to tumor development. Furthermore, the acneiform eruptions reported with this treatment⁶ might suggest some type of follicular disruption. This trauma to the follicular unit could represent a possible mechanism for KA development.

FP has been advocated as a safe and effective treatment modality for photoaging. To our knowledge, these are the first reported cases of KA developing after FP therapy. Eruptive KAs may therefore be considered a rare complication of FP treatment.

References


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