Fractional Photothermolysis

A New Therapeutic Modality for Xanthelasma

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

Xanthelasma of the eyelid is an asymptomatic and not uncommon disease with cosmetic consequences that drive the patient to seek medical treatment.

REPORT OF A CASE

A 52-year-old Asian woman with skin type IV presented with a 4-year history of xanthelasma on her face, including her cheeks, upper eyelids, and inner canthi. She also reported a more than 20-year medical history of hypothyroidism, for which she had been taking thyroid hormone replacement during that time. No other medical history was reported. A punch biopsy specimen demonstrated aggregates of histiocytes with small round nuclei and abundant foamy cytoplasm extending 0.39 mm into the upper reticular dermis. These findings were consistent with xanthelasma. At that time, the patient was referred to her primary care physician to undergo workup for dyslipidemia. Her blood cholesterol levels were found to be elevated (total cholesterol, 303 mg/dL; low-density lipoprotein cholesterol, 195 mg/dL [to convert cholesterol values to millimoles per liter, multiply by 0.0259]). Therapy with a lipid-lowering agent was initiated, with a subsequent decrease in plasma lipid levels (after 6 months) to a total cholesterol level of 185 mg/dL and a low-density lipoprotein cholesterol level of 106 mg/dL. The patient noted no change in the appearance of her xanthelasma. Physical examination revealed multiple coalescing papules and plaques of both cheeks, temples, inner canthi, and upper eyelids (Figure 1).

THERAPEUTIC CHALLENGE

Xanthelasmas are usually found on the inner canthi and have a tendency to be permanent, progressive, and coalescent. Treatment options include surgical excision, which can cause scarring as well as an ectropion that may require reconstruction with a flap or a full-thickness skin graft. Xanthelasmas may also recur, requiring additional excisions, which may not be possible owing to a lack of redundant skin remaining on the eyelid. Other treatment modalities include fulguration, trichloroacetic acid cauterization, carbon dioxide laser ablation, erbium:YAG laser treatment, pulsed-dye laser treatment, and Q-switched Nd:YAG laser treatment.

SOLUTION

Because of the success of fractional photothermolysis in treating many dermal skin conditions, we thought that our patient's extensive xanthelasma could be treated with this technology. Treatments were performed using a 1550-nm-wavelength, erbium-doped laser (Fraxel SR 1500; Reliant Technologies Inc, Mountainview, California). The treatment area was cleansed with a mild soap (Cetaphil Gentle Skin Cleanser; Galderma Laboratories, LP, Fort Worth, Texas) before the procedure. A topical triple anesthetic composed of benzocaine, 10%, lidocaine, 6%, and tetracaine, 4% (BLT; New England Compounding Center, Framingham, Massachusetts) was applied under occlusion to the treatment area of the cheeks, temples, upper eyelids, and inner canthi for 1 hour before treatment. A water-soluble tint certified by the US Food and Drug Administration (OptiGuide Blue; Reliant Technologies Inc) was applied to the treatment area (first 3 sessions) to allow the laser's optical tracking system (Intelligent Optical Tracking System; Reliant Technologies Inc) to adjust the treatment pattern with respect to handpiece velocity. An ointment (LipoThene Inc, Pacific Grove, California) was applied over the water-soluble tint so that the laser handpiece could glide smoothly over the treatment area.

The patient underwent 7 treatment sessions at 4- to 11-week intervals. Energy fluence was started at 40 mJ, with 5-mJ increment increases for each subsequent treatment, to a final fluence of 70 mJ. The final densities were 250 to 408 microscopic treatment zones per square centimeter (MTZs/cm²). Each treatment included 8 passes at a density of 32 to 51 MTZs/cm² per pass (Table). Upper and lower eyelids were treated with only 4 passes to minimize eyelid swelling, which may account for the incomplete clearing of the lesions in this area. A cold-air cooling system (Cryo 5; Zimmer Medizin Systems, Irvine, California) was used to cool the skin during treatment and to minimize patient discomfort (fan power, 5;
10-14 cm from the skin). The patient was advised to begin using a daily broad-spectrum sunscreen with UV-A protection (minimum sun protection factor, 45) on treated areas and to avoid any unnecessary sun exposure for 7 days after treatment.

Photographic documentation using identical camera settings, lighting, and patient positioning was obtained at baseline, before each treatment, and at a 4-month follow-up visit. Medical evaluation was independently evaluated using the following well-established quartile grading scale: grade 1 (<25%) indicates minimal to no improvement; grade 2 (26%-50%), moderate improvement; grade 3 (51%-75%), marked improvement; and grade 4 (>75%), near-total improvement. During treatment, the patient experienced mild pain, with moderate postprocedural erythema and edema resolving in 24 to 48 hours. At the 4-month follow-up visit after the last treatment, the evaluating physician noted grade 4 improvement, with no postprocedural complications or recurrence (Figure 2). The patient’s degree of satisfaction agreed with the physician’s assessment of improvement.

**COMMENT**

Xanthelasma, a planar xanthoma, is a localized infiltrate of foamy macrophages containing lipids. Xanthelasma forms when lipoproteins, specifically total cholesterol and low-density lipoprotein cholesterol, are found in high levels in the blood, or when the lipoprotein levels are normal, but their biochemical structure is altered. It is hypothesized that these lipids may enter the xanthoma through capillary walls and that trauma and inflammation may alter vascular permeability. Xanthelmas are generally associated with type 2A hypercholesterolemia, while no dyslipidemia may be present in as many as 50% of patients. More common in women, xanthelmas increase in prevalence with age. Clinically, they are yellow-orange macular or papular plaques. Although they are most commonly found on the inner canthi, more extensive lesions can be found on the cheeks, temples, and other areas of the face. Corneal arcus is a common accompanying clinical finding. Histologic analysis shows perivascular collections of esterified cholesterol deposits in foamy macrophages. Touton giant cells are seen in the middle and superficial layers of the dermis, while the epidermis is normal.

In diagnosing xanthelasma, the dermatologist may be in a position to aid in uncovering underlying alterations.

<table>
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<tr>
<th>Session No.</th>
<th>Energy, mJ</th>
<th>Total Density, MTZ/cm²</th>
<th>Density per Pass, MTZ/cm²</th>
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<tr>
<td>1</td>
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<td>392</td>
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<td>7</td>
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The treatment parameters ranged from pulse energies of 40 to 70 mJ and total densities of 250 to 408 microscopic treatment zones per square centimeter (MTZ/cm²).
in lipid metabolism. Undetected atherosclerotic cardiovascular disease has been reported to be as high as 69% in patients with xanthelasma. Xanthelasma may also be the first clue to diseases such as diabetes, pancreatitis, thyroid disease, renal disease, and dysglobulinemia. Dermatologists who diagnose any xanthomas should have the patient evaluated by their primary care physician for possible dyslipidemia or associated conditions.

Fractional photothermolysis involves the process of separating a laser into smaller beams to deliver MTZs, which are converted to a density of MTZs/cm². Hundreds to thousands of these MTZs are created where thermal injury to the skin is produced. In the MTZs, dermal tissue is selectively damaged, leading to the formation of new collagen. As a result of the relatively small cross-sectional area of the MTZs, a limited number of the keratinocytes within the target area are removed in a single session. With multiple sessions, the entire target area is eventually treated. The 1550-nm-wavelength, erbium-doped nonablative fractionated laser that we used to treat our patient allows the physician to adjust the density (treatment level) and depth (mJ) of treatment desired. It is able to penetrate heat to a depth of 382 to 1379 µm when energy levels of 4 to 70 mJ are being used. Middle-range energy level settings were initially chosen for our patient because of the lesion’s location in the reticular dermis. Energy settings were increased to the maximum of 70 mJ, allowing greater depth of penetration.

Hantash et al described the process known as transepidermal elimination, which is induced by fractional photothermolysis. In this transport system, microepidermal necrotic debris is eliminated transepidermally via epidermal vacuoles. A portion of the vacuolar content was found to be dermal in origin. This mechanism, which has been coined laser-induced transepidermal biological resurfacing, may have caused extrusion of the dermal content (ie, esterified cholesterol and histiocyte aggregates) and may explain the clinical improvement that was observed in this case.

A relatively high recurrence rate has been reported with various treatment modalities for xanthelasma. Mendelson and Masson found a 40% recurrence rate after primary excision of xanthelasma and a 60% recurrence rate after secondary excision of xanthelasma. A 13% recurrence rate was noted after ultrapulsed carbon dioxide laser treatment of xanthelasma, while there was no evidence of recurrence during a follow-up period of 7 to 12 months after erbium:YAG laser treatment. Because this is the first report of fractional photothermolysis for the treatment of xanthelasma (to our knowledge), recurrence rates are unknown. This case demonstrates marked improvement of xanthelasma on the face after a series of fractional photothermolysis treatments. Controlled studies are warranted to better understand the efficacy, longevity, and optimal laser settings for this indication.

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Study concept and design: Katz and Friedman. Acquisition of data: Katz and Friedman. Analysis and interpretation of data: Katz, Goldberg, and Friedman. Drafting of the manuscript: Katz, Goldberg, and Friedman. Critical revision of the manuscript for important intellectual content: Katz, Goldberg, and Friedman. Obtained funding: Goldberg. Administrative, technical, and material support: Katz, Goldberg, and Friedman.
References


Submissions

Clinicians, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern. Manuscripts should be prepared double-spaced with right margins nonjustified. Pages should be numbered consecutively with the title page separated from the text (see Instructions for Authors [http://archderm.ama-assn.org/misc/ifora.dtl] for information about preparation of the title page). Clinical photographs, photomicrographs, and illustrations must be sharply focused and submitted as separate JPEG files with each file numbered with the figure number. Material must be accompanied by the required copyright transfer statement (see authorship form [http://archderm.ama-assn.org/misc/auinst_crit.pdf]). Preliminary inquiries regarding submissions for this feature may be submitted to George J. Hruza, MD (ghruza@aol.com). Manuscripts should be submitted via our online manuscript submission and review system (http://manuscripts.archdermatol.com).