Q-Switched Laser-Induced Chrysiasis Treated With Long-Pulsed Laser

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 70-year-old woman presented for elective treatment of lentigines on her face. This was her first treatment with any laser. She was treated with a Q-switched alexandrite laser (755 nm, 50 nanoseconds, 3.5 J/cm², 15 pulses of 4-mm spot diameter; Candela, Wayland, Mass), causing what appeared to be usual purpura immediately following laser exposure of 8 tan macules. Several weeks later, blue-black discoloration was present, and was attributed to postinflammatory hyperpigmentation, but failed to lighten over the next 4 months.

Her medical history was significant for rheumatoid arthritis, treated with methotrexate and prednisone. Further questioning revealed that she had received a 3-year course of oral gold therapy 20 years prior. The total dosage taken could not be determined.

Four months following Q-switched alexandrite laser therapy, her examination revealed 8 blue macules without texture changes located at the laser treatment sites on her cheeks and forehead ranging from 2 to 6 mm (Figure 1). The lesions did not enhance on Wood’s light examination, suggesting dermal pigmentation. In some areas, portions of the original lentigo were still visible in the center of the blue macule. There was no discoloration of the sclera, nails, or hair. A subtle blue-gray hue in the patient’s general skin color was noted at the time of reexamination.

A punch biopsy specimen of a representative area demonstrated numerous black particles within macrophages in the dermis. A diagnosis of Q-switched laser-induced chrysiasis was made.

Initially, an attempt was made to clear the hyperpigmentation using the same Q-switched laser, a technique that can often lighten or clear laser-induced cosmetic tattoo darkening.1 A test spot was created on the inner aspect of the right arm with the original Q-switched alexandrite laser, and the hyperpigmented macule was pulsed again with the same laser. While the center of the lesion did show some clearing, a new rim of blue hyperpigmentation was induced around the treated spot. Further treatment with a Q-switched alexandrite laser was therefore not pursued, because blue pigmentation would always be induced at the border of the treated area. Surgical excision was considered but not pursued, given the number and location of the lesions.

Therapeutic Challenge

Chrysiasis refers to the effects of gold in tissues, in particular the skin. There is no known effective treatment for either generalized or local chrysiasis. Gold salts are widely used for the treatment of rheumatoid arthritis and are administered in both oral and intramuscular formulations. All show a propensity to accumulate in tissues and are particularly concentrated in the reticuloendothelial system, but they are also present in the skin, cornea, and lens.2 Typically, patients present with an irreversible blue to slate-gray discoloration affecting sun-exposed areas on the face, neck, and dorsal aspect of the hands. The cutaneous features often present insidiously, months to years after the ingestion of gold so that the association is not always obvious. In the skin, the deposition of gold occurs in the re-

Figure 1. Blue macules of chrysiasis approximately 1 year after Q-switched alexandrite laser treatment for lentigines.
ticular and papillary dermis in a perivascular pattern. Electron microscopy demonstrates electron-dense areas called aurosomes within macrophage lysosomes.3-5

The mechanism for the hyperpigmentation is not fully understood, but there is a clear association of disease severity with total cumulative dosage of gold. There is also a strong association with ultraviolet exposure.6,7 While the gold is deposited in both sun-exposed and non–sun-exposed skin,7,9 the hyperpigmentation occurs in areas exposed to sunlight. Hypopigmentation in an area normally protected from sun has been induced with experimental ultraviolet exposure.7 It is thought that gold-associated melanogenesis and physiochemical changes in gold structure within the skin account for these changes.6-8

Localized forms of chrysiasis have also been reported in association with implanted gold-plated needles,10 and more recently after laser treatment with a Q-switched ruby laser in a patient receiving parenteral gold therapy.8 The deposits were examined with transmission electron microscopy and confirmed to be gold. There is no effective treatment for chrysiasis. Our challenge was to find a treatment that could remove the chrysiasis pigmentation, without inducing further pigmentation at the margins of the treatment field.

**SOLUTION**

**SPECTRAL ANALYSIS**

We hypothesized that the laser-induced chrysiasis pigment might be removed by a combination of wavelength and pulse duration, which did not induce pigmentation in surrounding skin. As a first step, we characterized the pigment absorption in her skin using reflectance spectrophotometry, to define the wavelength region in which the darkened skin absorbed substantially more light than adjacent normal skin. An integrating sphere reflectance spectrophotometer (model 5270; Beckman Instruments, Fullerton, Calif) was used to measure the diffuse reflectance spectrum from 400 to 1200-nm of a darkened chrysiasis macule on the face and of an adjacent area of normal-appearing skin. Subtraction of the 2 reflectance curves yielded a difference spectrum (Figure 2). The difference spectrum has a broad band between about 550 nm and 850 nm, consistent with causing a bluish skin hue. The wavelength region near 700 nm was chosen for subsequent testing.

As a second step, we tested how laser-induced chrysiasis depends on pulse duration. This was done by exposing normal-appearing skin on her right inner upper arm to lasers with widely different pulse durations and irradiances, at nearby wavelengths within the chrysiasis pigment absorption band. A long-pulsed ruby laser (694 nm, 3 milliseconds; Epilaser, Palomar Medical Products, Burlington, Mass), a coaxial flashlamp-pumped dye laser (680 nm, 0.3 microsecond; Candela), and a Q-switched ruby laser (694 nm, nominally 30 nanoseconds; Spectrum, Lexington, Mass) were used. Immediate bluish hyperpigmentation was induced at low fluences with all but the normal mode ruby laser (Table). Even at the highest fluence of 50 J/cm², skin response to the 3-millisecond ruby laser consisted of mild erythema appearing a few minutes after exposure, with no skin darkening. Next, the test sites on her arm with laser-induced chrysiasis were treated with the long-pulsed ruby laser, which resulted in complete or substantial clearing.

**TREATMENT**

The original chrysiasis lesions on her face were then treated using the long-pulsed ruby laser at a fluence of 35 J/cm² with a 10-mm spot size and chilled tip (4°C). Two treatments were performed given about 1 month apart. Two months after the second treatment, the blue macules had resolved almost completely without induction of any new pigmentation (Figure 3).

**COMMENT**

We present the first successful treatment of chrysiasis of the skin. Previous reports have established that development of localized chrysiasis is a risk for any patient with a history of gold intake in sun-exposed skin or after Q-switched laser therapy.8 Surgical excision was previously the only option for removing discrete lesions. We have shown that a normal mode ruby laser can effectively clear the hyperpigmentation and, more important, does so without inducing new hyperpigmentation at the periphery of the treated area.

Based on our observations, laser-induced chrysiasis in patients treated with gold is primarily an irradiance-dependent rather than fluence-dependent phenomenon (Table). The irradiance (power delivered per unit area,
W/cm²) of Q-switched and other submicrosecond-pulsed lasers used in dermatology is very high and may induce chrysiasis. These lasers include Q-switched versions of alexandrite, ruby, Nd:YAG, and frequency-doubled Nd:YAG lasers, a short-pulsed 510-nm dye laser, as well as the quasi-continuous KTP laser and a xenon chloride excimer laser recently approved for psoriasis phototherapy. Our findings suggest that these high-irradiance devices may be prone to causing laser-induced chrysiasis. For attempting laser treatment of chrysiasis, we suggest that a millisecond-second-domain laser emitting between about 550 and 850 nm can be used. These include the long-pulsed versions of dye, ruby, and alexandrite lasers. It is interesting that long pulses can be effective for clearing chrysiasis pigment, which is similar in size and anatomic distribution to tattoo ink. While short-pulsed lasers are superior in treating tattoo pigment, the normal-mode ruby laser has been reported to be effective in the treatment of tattoos.12

Its irradiance dependence suggests that laser-induced chrysiasis is due either to mechanical alteration of the aurosome particles, as suggested by Trotter et al,8 or to a chemical alteration caused only at high irradiance. The situation is strongly analogous to tattoo ink darkening observed in some cosmetic tattoos after Q-switched laser treatment. Ferric oxide1 and titanium dioxide13 tattoo inks have been shown to convert to dark-colored, reduced chemical forms after high irradiance laser exposure. Tattoo ink darkening is also irradiance dependent, similar to our case of laser-induced chrysiasis. Ink darkening could not be induced with pulse durations greater than 1 millisecond.14 We propose that a multiphoton process is a plausible explanation for both tattoo ink darkening and laser-induced chrysiasis. Laser irradiances greater than about 10⁶ W/cm² are capable of promoting multiphoton events including dielectric breakdown, electron avalanche, plasma formation, and multiphoton photochemical reactions. Ultraviolet-induced chrysiasis occurs at low irradiances and suggests that a single-photon quantum energy of about 4 eV is necessary. At the visible and near-infrared wavelengths of Q-switched lasers in dermatology, 2 or 3 photons are necessary to deliver this energy.

Although their mechanisms for formation may be similar, laser-induced chrysiasis is more challenging to treat than laser-induced tattoo ink darkening. Tattoos that have darkened can often be cleared by repeated treatment with the same Q-switched laser that caused the ink darkening.1 In contrast, the entire skin of a chrysiasis patient contains gold deposits that darken upon Q-switched laser treatment, such that no “margin” exists at the edge of the treatment field. For chrysiasis treatment, a laser which does not induce further pigment darkening is needed. We demonstrate here that a long-pulsed ruby laser can be used successfully.

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