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Treatment of refractory dermal melasma with the MedLite C6 Q-switched Nd:YAG laser: Two case reports

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CASE REPORT

Treatment of refractory dermal melasma with the MedLite C6 Q-switched Nd:YAG laser: Two case reports

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Abstract

Objective: Dermal melasma in Fitzpatrick skin types III–V usually does not respond to topical treatments. Laser resurfacing often either fails to treat these lesions or results in severe postinflammatory hyperpigmentation (PIH) or permanent hypopigmentation. Two cases of refractory dermal melasma are reported, which responded to treatment with the MedLite C6 Q-switched Nd:YAG laser. **Methods:** Case 1: A 50-year-old Asian female with refractory dermal melasma and severe PIH received 10 weekly laser treatments combined with 7% alpha arbutin and a broad-spectrum sunscreen. Case 2: A 45-year-old Asian female with refractory dermal melasma received 10 weekly laser treatments combined with 7% alpha arbutin and a broad-spectrum sunscreen. **Results:** In both cases, there was a greater than 80% reduction in epidermal and dermal hyperpigmentation. The melanin index at the site of the lesions decreased from 50 to 35 and 45 to 33, respectively. There was no recurrence of melasma at 1 year (case 1) or 6 months (case 2). **Conclusion:** Even in cases of long-standing refractory dermal melasma in a darker skin type, combination therapy has been shown to be an effective treatment for this difficult condition.

Key words: *Melasma, Nd:YAG laser, postinflammatory hyperpigmentation, Q-switched laser*

Introduction

Melasma is the most common hyperpigmentation disorder in Asian individuals, and is one of the most difficult to treat. Treatment of this disfiguring condition accounts for more than 50% of aesthetic consultations in Asian countries. The pathogenesis of melasma is complex and related to genetics and hormonal factors, as well as to photodamage. The lesions occur mainly in middle-aged women on sun-exposed areas of the face, especially on the cheeks, forehead and upper lip. Lesions begin as a brownish asymptomatic irregular border of macules and then slowly spread out, forming brownish patches. Spontaneous remission after menopause is possible, but most of these patients will have the lesions for life. Even though total clearing in up to 50% of cases is possible with a topical agent such as Kligman's formula, recurrence is inevitable (1). Topical treatments result in only temporary clearing, with the added possibility of long-term complications. Lasers have been evaluated only recently for the treatment of this condition. Most of the early studies reported poor results and complications (2–4). However, the

author has used the MedLite C6 laser (HOYA ConBio, Fremont, CA, USA) as part of combination therapy in over 500 cases of melasma in Asian skin types with good to excellent results, no downtime and rare adverse effects.

Pathogenesis

In melasma, specific clones of melanocytes are hyperactive, leading to the stimulation of the melanin synthesis pathway and hyperpigmentation. Melanin granules are synthesized in epidermal and follicular melanocytes by stimulation with ultraviolet light, especially in the range of UVA (320–400 nm). UV stimulation of specific binding proteins and receptors (stem cell factor [SCF] and C-kit proteins) activates the binding of keratinocytes and melanocytes. This leads to the release of epidermal cytokines (endothelins). Endothelins bind to receptors on melanocyte cell membranes. These cytokines are potent stimulators in the synthesis of tyrosinase enzymes. Endothelin stimulation leads to an increase in melanin synthesis in melanosomes. The mature melanin granules (stage

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IV–V) in melanosomes are then transferred to keratinocytes (epidermal melanocyte units). Melanin granules in keratinocytes are shed daily. In order for melasma lesions to be clinically stable, the hyperactive state of melanin synthesis must be continuously suppressed for a long period of time.

In an Asian individual's skin type (Fitzpatrick skin types III–VI), there is a wide range of melanin synthesis, aggregation and distribution, leading to different shades of brown coloring. The darker the color, the higher the density of large, mature clumps of melanin in both keratinocytes and melanocytes. For reasons that are still unexplained, strong ultraviolet light activates clones of melanocytes from hair follicles in only some specific locations of the face. These hyperactive melanocytes will populate the areas and synthesize more mature melanin granules. Large melanized melanosomes (stage IV–V) are found in epidermal melanocytes and keratinocytes. In normal skin these mature melanin granules will be found mainly in keratinocytes. In more than two-thirds of melasma cases, macrophages containing melanin granules (melanophages) are detected in the upper dermis. These result from the dropping of melanin granules through damaged basement membranes into the dermis. Basement membrane damage can result from the use of topical agents in a chemical peel or from treatment with an ablative laser or high-energy pigment-selective laser.

To treat melasma effectively (and for long-lasting results) we should strive to control epidermal melanin synthesis, reduce melanin aggregation in both melanocytes and keratinocytes, increase melanin transportation into keratinocytes and also mobilize melanophages from the dermis. This is not possible with a single treatment method. From a theoretical point of view, combination treatments will ensure better, faster and longer-lasting results than a single treatment modality.

Mechanisms of action for the treatment of melasma can be grouped as follows.

1. Reduction of melanin synthesis

Tyrosinase enzyme is the most important enzyme in melanization. It changes dopa to dopaquinone and eumelanin. Topical application of tyrosinase inhibitors is the most widely used method in the treatment of melasma. Even though there are many new chemical agents claiming to be effective bleaching agents, hydroquinone (2–4%) is still the most widely prescribed topical bleaching agent. Hydroquinone usually results in short-term improvement. Between 30% and 40% of patients have total clearing within 3 months, followed by recurrence. However, long-term maintenance with even 2% hydroquinone is often related to many side effects (e.g. skin irritation, hypopigmentation, rebound hyperpigmentation and ochronosis). Other newer agents include kojic acid, arbutin (hydroquinone bound to glucose), licorice

and ascorbic acid, but these seem to be less effective than hydroquinone (1). In order to enhance the effectiveness of hydroquinone, it has been combined with 0.05% retinoic acid and a steroid (0.1% dexamethasone) in a recipe known as Kligman's formula. With the addition of this formula to hydroquinone, the percentage of cases with total clearing is increased to 50–60% (1–3). However, the side effects are increased as well, especially skin irritation, dryness, acneiform eruption, rosacea-like dermatitis, skin atrophy and telangiectasia. Many patients develop steroid-dependent rosacea-like facial dermatitis after prolonged application (1).

2. Increased melanin transfer and shedding

This is possible by the superficial, repetitive peeling of keratinocytes. This interferes with melanin transportation, enhances desquamation and reduces hyperpigmentation. Retinoic acid (0.1%), glycolic acid (30–50%), and salicylic acid (20%) work on this principle. The clinical effectiveness of superficial peels for melasma is only mild to moderate (1). Periodic peelings are necessary to sustain the result. This often increases side effects, most notably skin irritation. Better results are obtained if peeling has been combined with topical bleaching.

3. Skin resurfacing

Despite the reported results of good treatment of melasma with dermabrasion (5), this modality has not gained wide acceptance. The prolonged post-operative downtime and the risk of complications seems to discourage both patients and physicians (5). Carbon dioxide laser resurfacing has been studied in melasma, but with poor results and unacceptable side effects. Intra-epidermal laser resurfacing has often resulted in severe post-treatment hyperpigmentation, while deep resurfacing (down to the mid-dermis) has resulted in persistent hypopigmentation. Erbium:YAG laser resurfacing has been studied with a similar result. Intense pulsed light works by the production of epidermal necrosis from absorbed light that had been converted into heat. The effects are similar to intra-epidermal laser resurfacing. Postinflammatory hyperpigmentation (PIH) and persistent hypopigmentation are common, especially in dark skin types (6).

4. Pigment-selective lasers

High-energy pigment-selective lasers (e.g. 694 nm Q-switched ruby laser, 755 nm Q-switched alexandrite laser, 532 nm frequency-doubled Q-switched Nd:YAG laser, and 1064 nm Q-switched Nd:YAG laser) have been studied for the treatment of melasma with poor results (4). Balanced normal skin color was rarely achieved. However, a few studies demonstrated better results after a combination of pulsed CO₂ laser and Q-switched alexandrite laser treatments (7,8). The efficacy of this combination technique was believed to be due to the elimination of melanophages and a reduction of

hyperactive epidermal and follicular melanocytes (8). Owing to the complexity of these procedures, this combination laser treatment is still not widely accepted.

5. Fractional laser

Pigment lightening was a coincidental finding after the application of a new type of laser delivery system. A fractional laser delivers a pattern of tiny laser beams, producing microthermal necrotic zones or wounds that are a stimulus for skin rejuvenation. The original technology involved a diode laser but other lasers have since been modified to produce a similar result (e.g. pulsed CO₂, pulsed erbium:YAG). Preliminary data from non-control studies have shown fair to moderate results in the treatment of melasma (9). The mechanism of pigment lightening may be explained by the partial destruction of epidermal melanocytes and the trans-epidermal elimination of dermal melanophages. In Asian skin types, PIH is not an uncommon result of this process.

The author has had extensive clinical experience with the MedLite C6, one of the most powerful Q-switched Nd:YAG lasers commercially available. Several properties make this laser useful in the treatment of melasma: large spot size (6 mm and 8 mm in diameter); collimated and flat-top beam profiles; high-energy pulse (up to 2 Joules); high repetition (10 Hz); and coaxial aiming beam.

By delivering repetitive energy from the 1064 nm Q-switched Nd:YAG laser with a sub-photothermolytic fluence (<5 J/cm²) over a large spot size, melanin granules will be fragmented and dispersed into cytoplasm. The total accumulative dose should be lower than the total toxic accumulative energy that will destroy the cells. This will lead to pigment lightening. Subsequent treatments at weekly intervals will gradually reduce hyperpigmentation. This reaction can be classified as the biostimulation effect of the Q-switched Nd:YAG laser at the subcellular level, without cellular damage or cell death. On average, about 8–10 weekly treatments are required to reduce the hyperpigmentation so that it appears close to normal skin color. Recurrence is then prevented by the application of topical bleaching agents (e.g. 7% alpha arbutin or Kligman's formula) together with UVB+UVA blocker sunscreen (SPF > 30, PFA > ++++) (10).

Case 1

Case 1 was a 50-year-old Asian female with persistent marked grayish-brown patches on both cheeks. The patient had a history of application of many topical bleaching creams (including Kligman's formula) without benefit. Laser resurfacing with an erbium:YAG laser and a Q-switched ruby laser had resulted in severe PIH. She denied any oral hormone therapy. She worked in an office with minimum

exposure to direct sunlight. On the first consultation she was found to have Fitzpatrick skin type IV with severe epidermal and dermal hyperpigmented patches on bilateral cheeks and on the forehead. She was diagnosed with dermal melasma with severe PIH.

Treatment protocol

Five standard digital photographs were taken (Olympus, SP 500uz, 6.0 megapixel) and the melanin index was recorded (Dermatospectrometer; Cortex, Denmark). Before treatment, the skin was thoroughly cleansed and pre-cooled to 5°C with cool air (Criojet; Medizintechnik, Germany). A MedLite C6 laser with 1064 nm, 6 mm spot size, 10 Hz, and an energy fluence of 3.4 J/cm² delivered 10% overlap pulses: 10 passes in one direction and 10 passes perpendicular to the previous direction. The treatment was done for each small area (approximately 3 × 3 cm²) to cover the entire face. Perilesional erythema with whitening of fine hairs was observed. Post-treatment cooling with cool air to reduce the burning sensation was then performed. Ten weekly treatments were performed. The patient was advised to apply 7% alpha arbutin solution twice daily with a broad-spectrum sunscreen (SPF 50, PFA ++, Anthelios XL; La Roche Posay, France). After completing 10 treatments, the patient was followed monthly for more than a year.

Results

There was a reduction in both epidermal and dermal hyperpigmentation of more than 80% after 10 treatments (Figures 1 and 2). The melanin index at the site of the lesions also decreased from 50 to 35. After 1 year of follow-up, there was no recurrence of melasma. She was prescribed topical 7% alpha arbutin solution (Skin Advanced Laboratory, Japan) together with topical sunscreen (Anthelios XL, SPF 50, PFA +++) for maintenance. The patient was also observed to have a reduction in the appearance of fine wrinkles and an improvement of acne scars.

Case 2

A 45-year-old Asian female with Fitzpatrick skin type III presented with persistent grayish-brown hyperpigmentation on both cheeks. She had been diagnosed with dermal melasma and had received topical treatments with Kligman's formula bleaching cream with only minimal lightening. She had also been treated with intense pulsed light without any effects.

Treatment protocol

Five standard digital photographs were taken (Olympus, SP 500uz, 6.0 megapixel) and the melanin index was recorded (Dermatospectrometer). Before

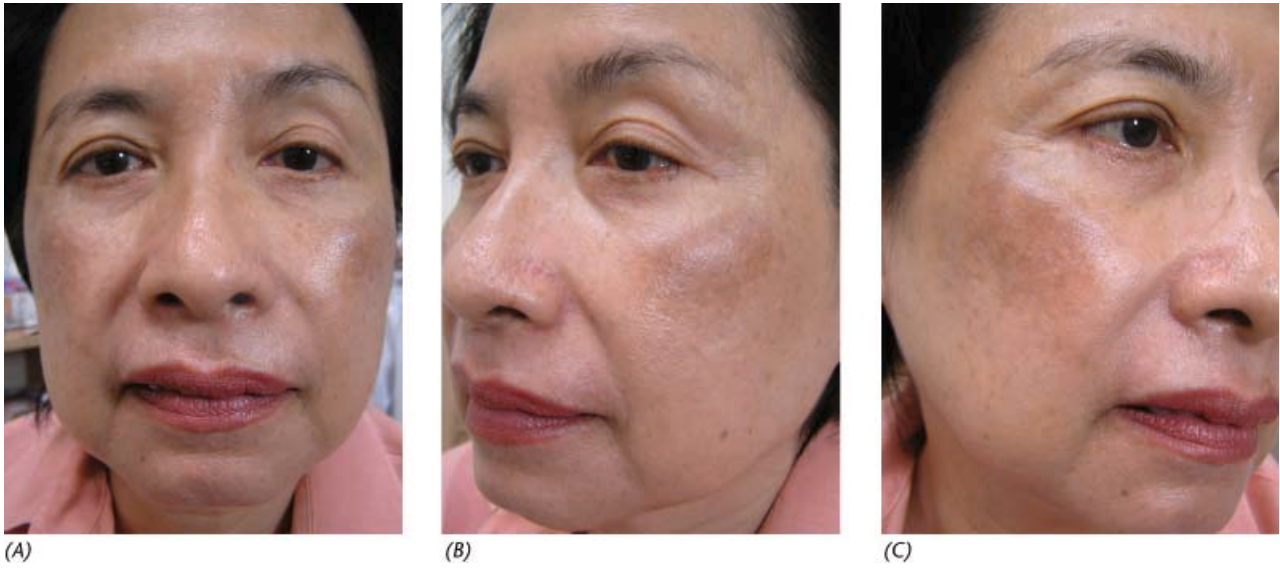


Figure 1. Case 1 (A–C): pretreatment (dermal melasma and PIH).

treatment, the skin was thoroughly cleansed and pre-cooled to 5°C with cool air (Criojet). MedLite C6 laser treatment (1064 nm, 3.4 J/cm², 6 mm spot size, 10 Hz, 20 passes to cover the whole face: 10 passes in one direction and then another 10 passes perpendicular to that direction) was administered. The clinical end point was immediate perilesional erythema and whitening of fine facial hair. The treatment was performed once a week for a total of 10 treatments. After that the patient continuously applied a topical 7% alpha arbutin solution (Skin Advanced Laboratory) together with sunscreen (Anthelios XL, SPF 50, PFA +++) for maintenance.

Result

There was a greater than 80% reduction of hyperpigmentation after 10 treatments (Figures 3

and 4). Figure 4A is at the 6-month follow-up visit. The average melanin index at the site of the lesions decreased from 45 to 33.

Results

Epidermal melasma seems to respond better and faster than dermal/mixed melasma. Complete clearing of the lesions should be expected in more than 50% of cases of epidermal melasma. Complete clearing of dermal/mixed melasma will be between 30% and 50%, while the remaining cases will show moderate improvement. PIH and rebound melasma are sensitive to the treatment. Lower energy and fewer repetitions are adequate to produce a marked improvement.

After 8–10 treatments, the maximum result will be obtained. The delivery of additional treatments

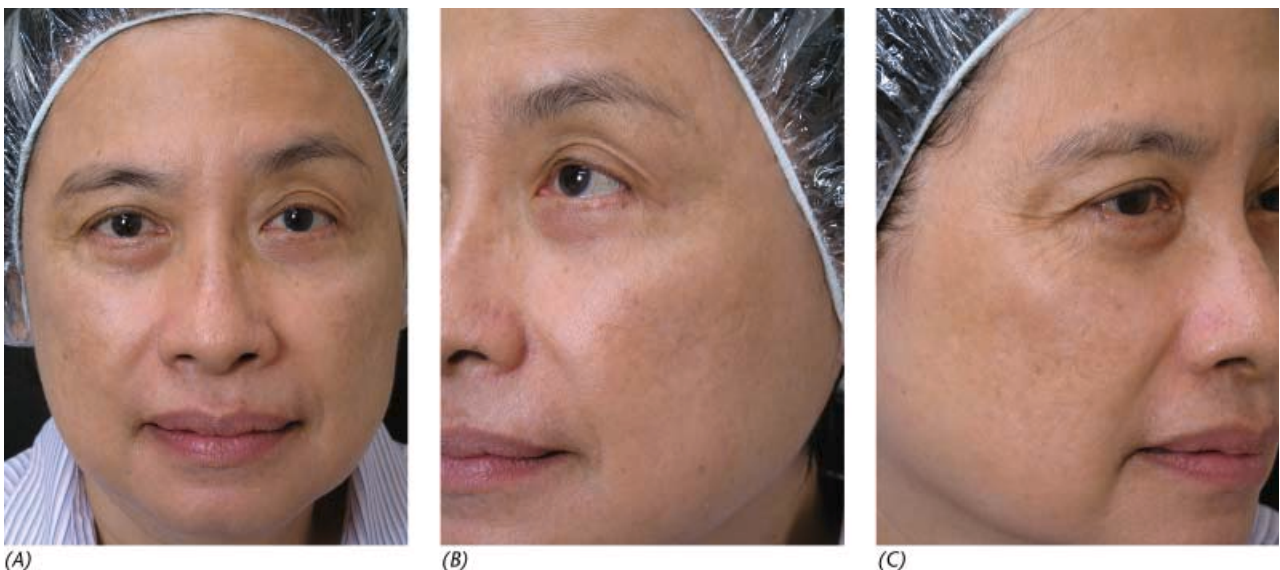


Figure 2. Case 1 (A–C): 1 year after the completion of 10 MedLite C6 laser treatments.

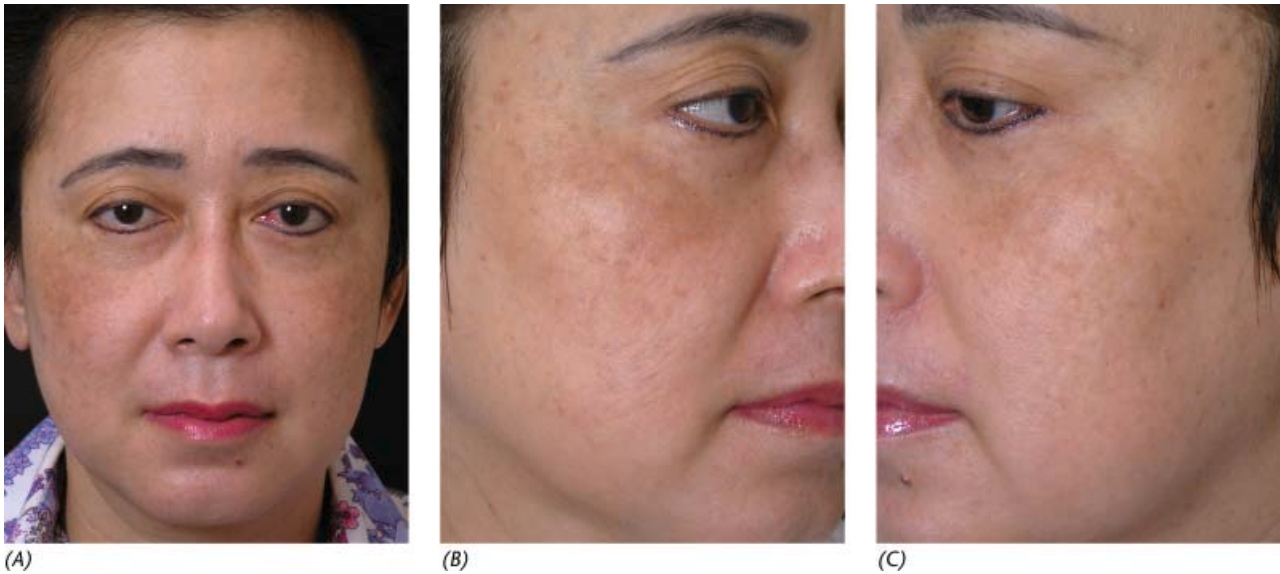


Figure 3. Case 2 (A–C): pretreatment (dermal melasma).

should be carefully judged on a case-by-case basis. In dermal melasma or for dermal melanocyte lesions, continued treatments may be justified if there is already fair to moderate improvement without any sign of side effects. Usually, clearance of epidermal melasma is maintained by topical bleaching agents (e.g. 7% alpha arbutin or Kligman's formula). Long-term monthly treatment of melasma is not justified. Only when there is relapse of moderate melasma should another course of MedLite C6 treatment be considered.

The following technique is advocated:

1. Cleanse the face thoroughly and dry with a clean towel.
2. Take standard photographs (front, side views, close-ups).
3. Measure the melanin index at the site of the lesions and in areas of normal facial skin (by either Dermatospectrometer or Mexameter).
4. The patient should wear a cap and protective eye goggles. Safeguard the hair of the patient's eyebrows with tape.
5. Pre-cool the treatment area with cool air (-20°C) for a few minutes.
6. Adjust the MedLite C6 setting parameters as described in both cases.
7. Divide the face into multiple treatment areas and treat one area at a time.
8. Deliver the laser pulses perpendicular to the surface and move the beam slowly in such a way that there is 10% overlapping between pulses. Usually, the laser beam is moved along the

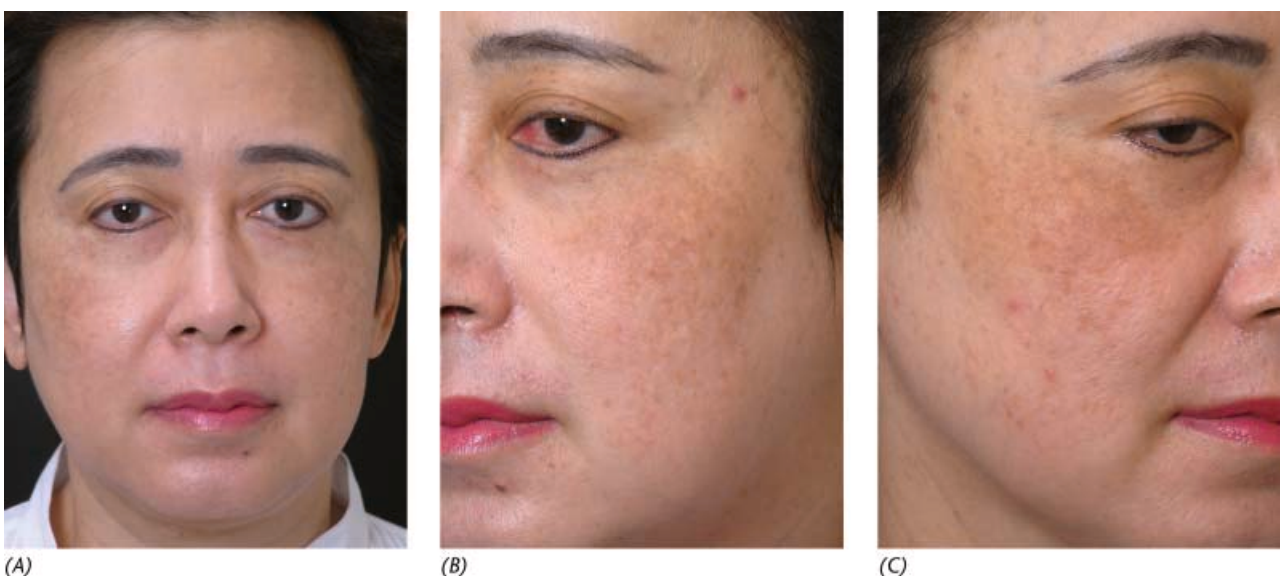


Figure 4. Case 2 (A–C): 6 months after the completion of 10 MedLite C6 laser treatments.

linear lines. The beam is moved forward and backward along that line 10 times before moving to an adjacent area. After completion of the first pass of treatment to an area, the second pass will be performed in a similar manner, perpendicular to the direction of the first pass.

9. Observe the following clinical end points, according to indication:

epidermal melasma: immediate pigment lightening, immediate whitening of fine hair and perilesional erythema

dermal/mixed melasma: immediate darkening of lesions, immediate perilesional erythema

rebound melasma: immediate pigment lightening, immediate perilesional erythema

postinflammatory hyperpigmentation: immediate lightening of lesions, perilesional erythema

rejuvenation: immediate improvement of skin texture, pore size and the appearance of wrinkles

atrophic scar: immediate minute petechiae at the base of the scar.

For melasma, treatment is performed at weekly intervals for a total of 8–10 treatments. The number of treatments depends on the clinical response. The goal of treatment is to reduce hyperpigmentation so that it appears close to normal skin color. Treatment is then augmented with topical bleaching agents (e.g. 7% alpha arbutin, 20% azelaic acid, Kligman's formula) and a broad-spectrum sunscreen to maintain long-term remission. Other choices for combination therapy include intralesional transxemic acid (5 mg/ml) and chemical peels (20–30% glycolic acid). For skin rejuvenation, treatment is performed every week for 4–6 weeks, then once every 1–3 months for maintenance. For PIH, owing to large melanins and fewer melanocytes, fewer treatments are required. For ephelides and solar lentigos, a single pass of 1–2 J/cm², 4–6 mm spot size with the 532 nm wavelength is required at monthly intervals. This is sufficient to reduce hyperpigmentation without inducing hypopigmentation. Most of the cases will develop mild to moderate PIH. A few sessions with the 1064 nm wavelength, similar to the treatment algorithm described herein for the treatment for melasma, should resolve this symptom within 1 month.

The following complications are transient reactions and do not require termination of treatment: immediate erythema, physical urticaria, acneiform eruption, minute petechiae and whitening of fine hair. However, the following complications are considered serious and justify the suspension of treatment: mottling hypopigmentation, leucoderma, severe urticaria, severe acneiform eruption and

Herpes simplex activation. These complications are uncommon. Mottling hypopigmentation can be visible after a few treatments, but it can also develop gradually after multiple treatments. In the author's experience, patchy hypopigmentation was reversible after the termination of treatment. Rebound hyperpigmentation was common after the reduction of bleaching agents containing hydroquinone. Such hyperpigmentation can be re-treated with the MedLite C6 laser at a lower energy fluence (2.5–3 J/cm²) with 5–10 treatments spaced at weekly intervals. This condition will respond faster than ordinary melasma.

Discussion

Melasma in Asian individual's dark skin is difficult to treat. The majority of cases should be classified as mixed or dermal-type melasma (2,3). Even though there were reports of good to moderate improvement after many types of topical treatments (especially the combination known as Kligman's formula), the best results were achieved only with the epidermal type of melasma (11). Dermal and mixed melasma often had poor results, with either recurrence or complications (11). Since the introduction of lasers in dermatology, these instruments have been tried in the treatment of melasma with variable results. Erbium:YAG lasers have been found to be ineffective, with recurrence in all cases (6). Pigment-selective lasers, continuous or quasicontinuous (e.g. KTP at 532 nm) lasers or copper bromide (570 nm) lasers often caused severe PIH (4). Nanosecond pulsed lasers (e.g. Q-switched ruby lasers at 695 nm), Q-switched Nd:YAG lasers (1064 nm) and Q-switched alexandrite lasers (755 nm) have been studied in the treatment of melasma, also with variable results (12). Only with a combination of ablative lasers (CO₂ and Q-switched alexandrite) did the author find good results after 6 months with a split-face design study (13).

The author has since instituted a new approach for the treatment of dermal melasma with repetitive sub-threshold photothermolysis using the pulsed 1064 nm MedLite C6 laser in more than 500 cases over a period of 2 years. The two case studies presented here were among the most severe of those cases: they had long-standing refractory dermal melasma which did not respond to any known topical treatments. The first case had been treated with both an ablative erbium:YAG laser and a Q-switched ruby laser with recurrence and PIH. After 10 treatments with the technique described above for the MedLite C6 laser, hyperpigmented lesions faded by more than 80%. The melanin index came down to a level resembling normal. The patients were followed for 1 year and 6 months respectively, without recurrence in either case. The author has postulated that melanin fragmentation, and

dispersion and superficial ablation of the epidermis are the causes of the lightening of epidermal hyperpigmentation, while destruction of melanophages or the enhancement of melanophage migration is the cause of a reduction in dermal pigmentation. The combination of these mechanisms of action enables this new technique to be effective in both epidermal and dermal melasma. Overtreatment with the MedLite C6 laser is not recommended due to the risk of hypopigmentation, and control of recurrence with a broad-spectrum sunscreen and a topical tyrosinase inhibitor (e.g. alpha arbutin) is recommended for at least 6 months after finishing the course of laser treatment.

In conclusion, this new technique of repetitive sub-threshold pulsed laser treatments with the MedLite C6 laser has been shown to be effective for the treatment of refractory dermal melasma.

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