Minocycline induced pigmentation treated with Q- Switched Alexandrite laser. Report of 2 cases, and review of the literature.

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Abstract:

Long term administration of Minocycline has been associated with rare occurrence of abnormal cutaneous pigmentation an few treatment options have been reported in the literature. Treatment with different Q- Switched Alexandrite laser has been described to be effective. We report two cases of Minocycline- induced pigmentation which were effectively treated with the Q- Switched Alexandrite (755nm) laser.

Introduction:

Cutaneous pigmentation caused by Minocycline intake is well-described entity that may present in up to 14% of facial dermatosis.1The pigment fades over times in most cases, but may present for months, or never fade entirely.2

We report two cases of minocycline induced pigmentation which cleared completely when treated with Q- Switched Alexandrite (755nm) laser.

Case 1:

A 35 years old man with a history of Rosacea for which he has been taking minocycline (minocine 100 mg/day) for two years. He had no history of other medications taken at that time. He noticed a progressive hyperpigmentation on his legs after one and half year, from the start of minocycline intake.

On physical examination, he had diffuse macular dark blue hyperpigmentation, on the anterior aspect of his both legs and on the dorsum aspect of his feet. (Fig.1 and 2). There was no mucosal, ocular, dental, nail plate, or nail bed pigmentation. There was no inguinal lymphadenopathy. He stopped using minocycline but without any progression of the pigmentation nor improvement. He was treated with Tretinion cream 0.025% and Hydroquinone craem 4% daily for months but without improvement.

A skin biopsy was done and sent to pathologist for hematoxylin and eosin (H & E), Fontana Masson (M), a0nd Perl's iron (PI) stain. Histological examination revealed multiple pigment-laden macrophages as well as free coarse, granular dark brown dermal pigment (figure 3 and 4). The pigment stained positively with both FM stain (Figure 5), and PI stain .

From the above data, type II minocycline induced pigmentation was confirmed, so we decided to treat the patient with Q- Switched Alexandrite laser. At first we did test spots with different Fluence (expressed in J/ cm2) to determine the maximum fluence that could be administered without producing apparent epidermal devitalization. Three different sites on the anterior aspect of the left leg were treated with a double pulse of a three mm in Diameter beam of light, each with different fluence, which were 5.0, 5.5, and 6.0, J/cm2 . None of these sites demonstrated any epidermal devitalization at the time of treatment or one week later. Accordingly we gave the patient 8 sessions using double pulse, with a fluence of 6.0 J/ cm2 with 3-mm. Diameter beam of Q- Switched Alexandrite (755nm) laser.

All areas of pigmentation were cleared (figure 6 and 7), and there was no recurrence of the pigmentation after a period of 18 months of follow up.

Case 2:

A 21 years old woman with a history of acne vulgaris for which she was taking minocycline (minocine 50 mg/day) for the past 3 years. She was applying tretinoin cream 0.025% on her face at night, and Benzoyl peroxide (Benzac AC gel) on her face in the morning. Beside these topical creams, she didn't take any other medication. She noticed a progressive darken pigmentation on her both legs over one year. So she discontinued all her medications including her topical therapy, and was only using 2.5% Benzoyl peroxide soap for her face. She used Tretinion cream 0.025% and Hydroquinone craem 4% daily for several months on her legs, but with no improvement.

On physical examination, she had a diffuse macular, very dusky blue hyperpigmentation, on her anterior aspect of the legs. There was no mucosal, ocular, dental, nail plate, nor nail bed pigmentation.

Skin biopsy was done, and revealed multiple coarse granular pigment on the upper dermis, and around the blood vessels, as well as the eccrine

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glands. Pigment stained strongly with the FM, and PI stain, thus, type II minocycline induced pigmentation was diagnosed, and the patient had 6 sessions of treatment with Q- Switched Alexandrite (755nm) laser, using a fluence of 6.0 J/cm2. all pigment was cleared, with no recurrence of the pigment for a period of 20 months of follow up.

Discussion:

Minocycline belongs to tetracycline antibiotics group, which is characterized by four ring carbocyclic structure.[3] they differ in the constituents of the ring.[4]

The mechanism of action of minocycline is by inhibiting protein synthesis, by binding to the 30S ribosomal-mRNA unit. This blocks the binding of amino acids to the growing peptides.4 Minocycline is metabolized by the liver, and concentrated in the bile, but its metabolism has not been well defined. [3] the main route of excretion is urinary, and to a lesser extent, fecal.4

The most common dermatologic uses of minocycline are in the treatment of acne vulgaris, rosacea, perioral dermatitis, and some infections, such as chlamydial, ricketsial and lyme diseases. [3] In addition to the common uses of minocycline, there have been anecdotal reports on the successful uses of minocycline for a variety of other non-infectious cutaneous diseases such as bullous pemphigoid, intestinal bypass dermatitis, pityriasis lichenoides, pyoderma gangrenosum, and even sarcoidosis.[5]

A variety of cutaneous reactions to minocycline have been reported such as hypersensitivity reactions, ranging from morbilliform eruption to urticaria and anaphylaxis, but they rarely occur.[6] Other adverse effects have been described with long term use of minocycline include pneumonitis[7], drug induced lupus[8, 9], serum sickness like reaction, and hypersensitivity syndrome.[10] Sweat syndrome has also been reported with minocycline use.[11] Minocycline has also been associated with gynaecomastia[12], and black tongue.[13] Also fixed drug reaction has been reported as an adverse reaction to minocycline.10 Minocycline induced cutaneous hyperpigmentation is a well-recognized phenomenon in skin[14], nail beds[15], thyroid16, bones[17], mucus membranes[18], and teeth[18]. It also causes scleral pigmentation[15], and black discoloration of breast milk.[10] The hyperpigmentation in the internal organs is likely to be irreversible in most patients, presumably due to formation of insoluble salts from minocycline degradation.[10] All tetracyclines are contraindicated during pregnancy because they deposit in the teeth and bones of fetus.[17]

In spite of all the above adverse effects of minocycline, it still remains a valuable drug in the therapeutic dermatological armamentarium.[5]

Although minocycline induced pigmentation is rare, but it has been associated with long term minocycline intake for months to years, or even after only three weeks of use.[19]

There are three types of minocycline induced pigmentation, and it can be distinguished on the basis of clinical and histological features.1 The first types consist of dark bluish- black macules developing in areas of inflammation and trauma, including contusions, ulcerations, lacerations, and within existing scars, such as acne scars.[19]

The pigment is primarily localized within the dermis and reacts with PI but not with FM stain, which would be consistent with iron, or hemosiderin, possibly complexed with a minocycline moiety.[19]

The second type is characterized by more generalized brown, or blue – gray pigmentation, with accentuation on sun exposed skin, especially on the legs, and forearms, although other sites may be involved.20 Histologically, the pigment appears to stain like melanin with both PI, and FM stain.[21]

The third type consists of a diffuse muddily brown discoloration, with also accentuation on sun exposed areas. It is usually more generalized than type II pigmentation.[20] Histologically, it shows an increase in melanin deposition in the basal cell layer of the epidermis, and in the macrophages in the upper dermis.[19] It appears to stain with FM stain, but not with PI stain.[21]

Unlike type I, both type II, and type III pigmentation are directly correlated with the cumulative dose and the duration of minocycline intake.[20]

However, all types of the pigmentation don't improve after discontinuation of minocycline.[19]

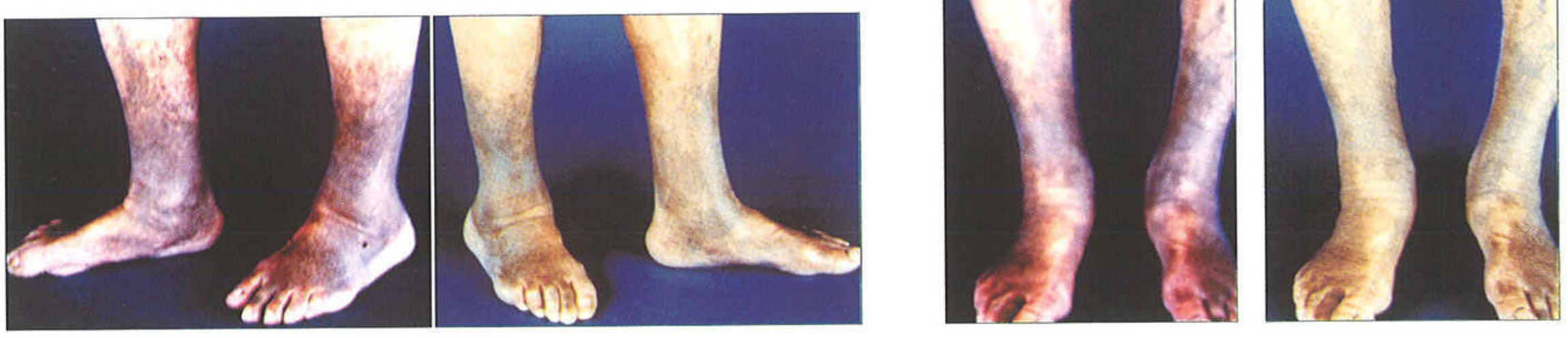
All of our reported patients in this article belong to type II pigmentation, which developed on a normal skin of the legs and arms. Both of them had an excellent result in clearance of the pigment after treatment with the Q- Switched Alexandrite (755nm) laser.

Review of the literature has revealed few reports of successful clearance of minocycline-induced pigmentation using the same procedure. Green D. et al, had recently reported an excellent result in both the cosmetic appearance, and histological clearance of type II pigment in 22 years old woman who was treated with 9 sessions of Fluence 6.0 J/cm2, using a 3 mm.

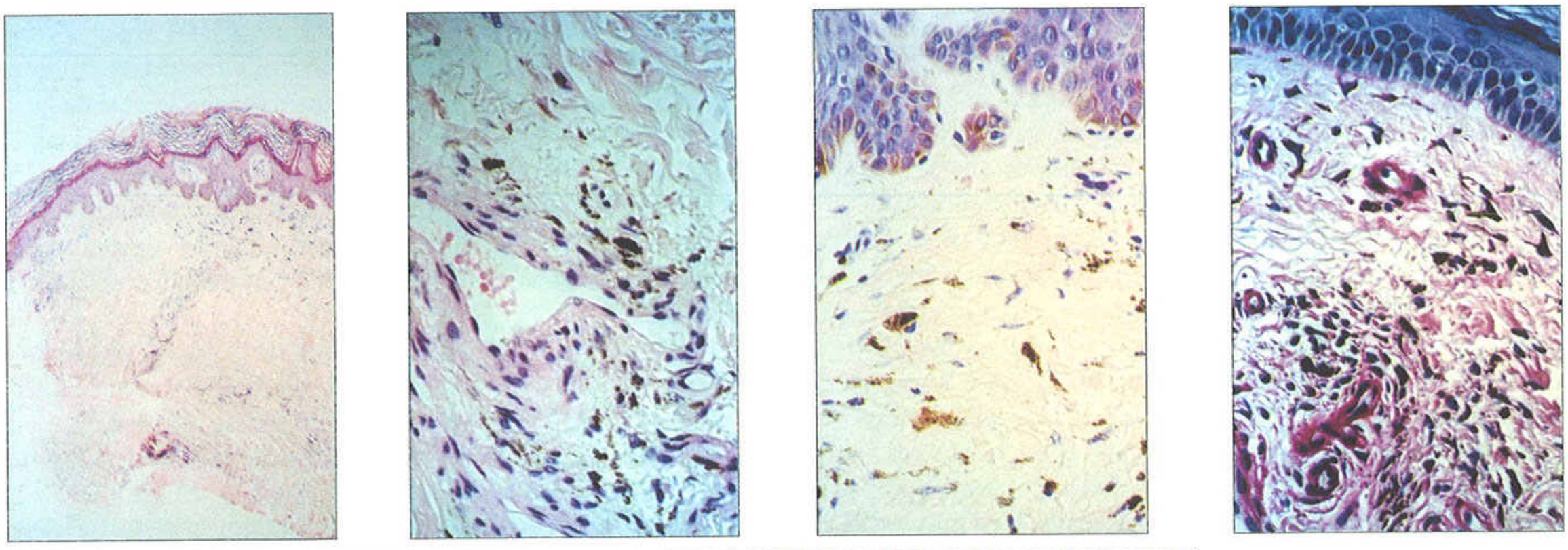
diameter beam of Q- Switched Alexandrite (755nm) laser, and there was no recurrence of the pigment after thirty four months of follow up, from the last treatment session.20 Others have reported the lack of success in using other lasers, such as the Q- Switched Neodynium:YAG (1064) laser.[22,23] while other reports had a good result in using both the Q- Switched, frequency doubled Neodynium:YAG (532)[23] and the Q-Switched Ruby (694) lasers.[22,24,25]

Although the mechanism of the laser removal of minocycline induced pigmentation and tattoos, is still unknown[24], it is postulated to be due to the fragmentation of the intracellular, and extracellular pigment as well as transport through lymphatic vessels into the regional lymph nodes. [25]

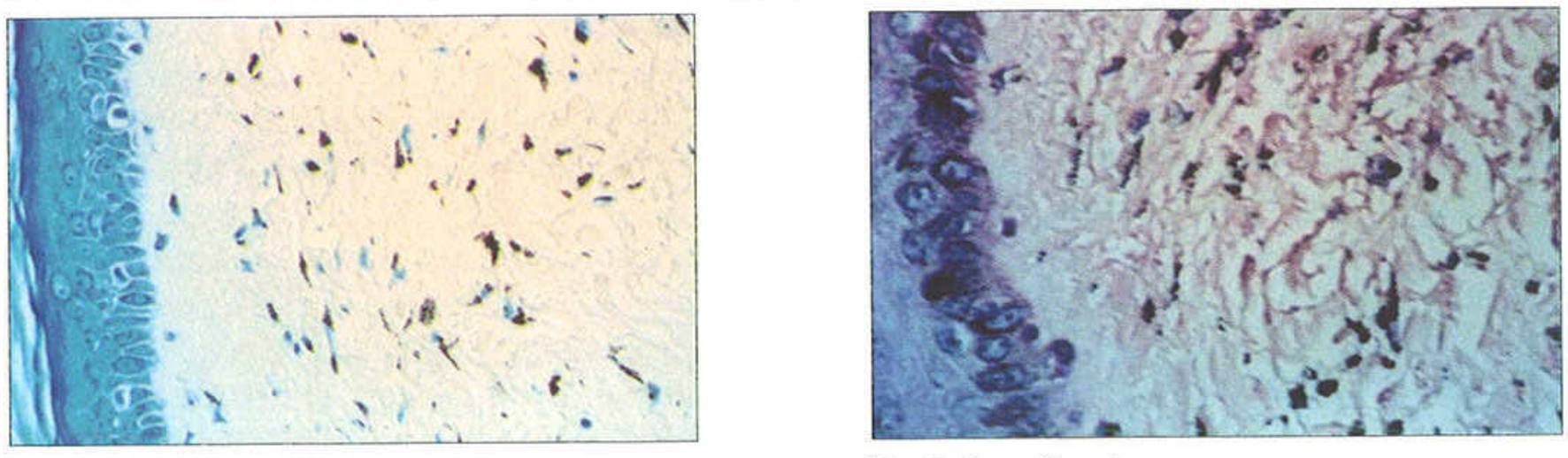
We conclude that the Q- Switched Alexandrite (755nm) laser is a possible therapeutic tool in treatment of type II minocycline induced pigmentation, because of the greater depth of penetration that the longer wave- length laser would be expected to achieve , allowing interaction with dermal pigment-laden histeocytes.



Case number one: Fig. 1 & 2 showing pigmentation of legs and feet.

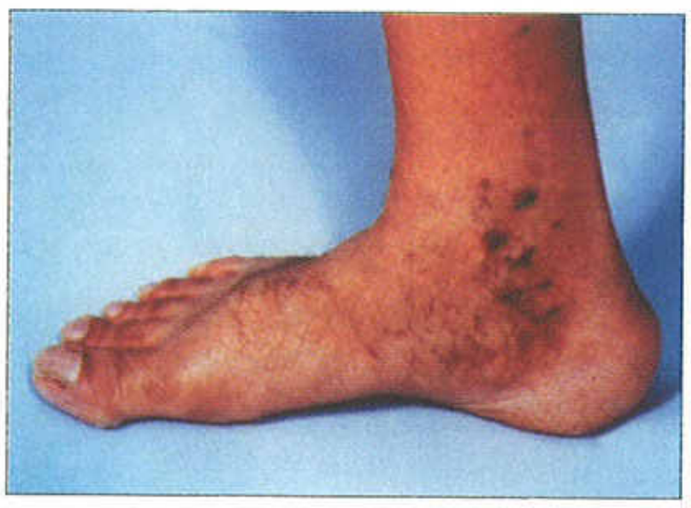


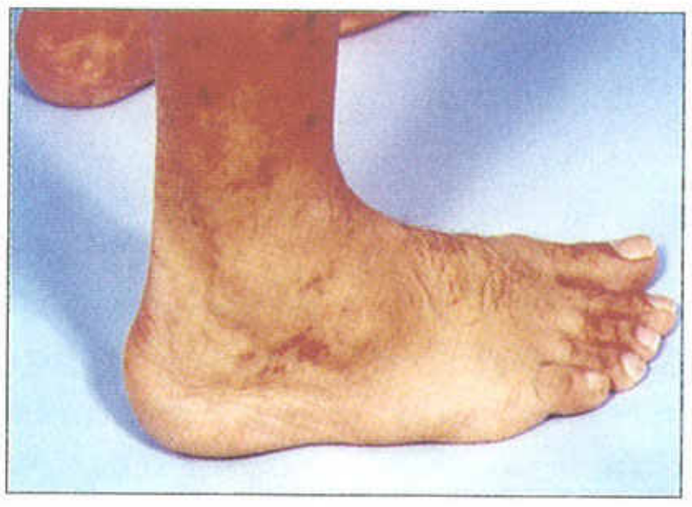
Fontana Masson Strain

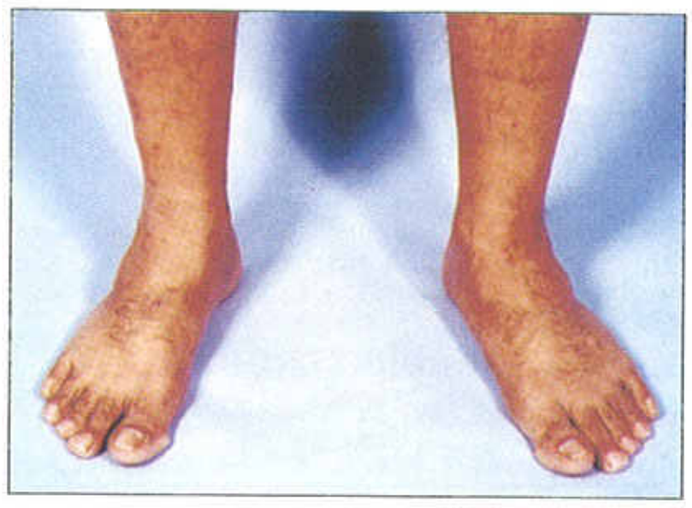


Perls Iron Strain

Case number one: Fig. 3, 4 and 5 Dermal pigmentation.







Case number one: Fig. 6 & 7 After laser treatment.

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