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Changes in Melanin and Melanocytes in Mottled Hypopigmentation after Low-Fluence 1,064-nm Q-Switched Nd:YAG Laser Treatment for Melasma

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Dear Editor:

Melasma is a common acquired hyperpigmentary disorder of the face, but its treatment remains challenging. A procedure called "laser toning" that uses a low-energy 1064-nm Q-switched Nd:YAG laser was recently introduced for the treatment of melasma, demonstrating good results[1-3]. However, the possibility of mottled hypopigmentation is a major concern with this treatment, because it rarely recovers spontaneously[4]. The underlying mechanisms of mottled hypopigmentation are not completely understood. Whether the hypopigmentation is caused by reduced pigmentation with intact melanocytes or a decrease or absence of melanocytes remains to be elucidated.

Therefore, this study investigated the changes in melanin and melanocytes in hypopigmented lesions that develop after low-fluence 1,064-nm Q-switched Nd:YAG laser treatment for melasma. This study was approved by the institutional review board of Ajou University Hospital (AJIRB-MED-KSP-12-374).

Patient 1, a 41-year-old woman with Fitzpatrick skin type IV, presented with typical mottled hypopigmentation after treatment with 1,064-nm Q-switched Nd:YAG laser for melasma (Fig. 1A). The duration of hypopigmentation was 7 years. Skin biopsies were obtained from the hypopigmented, hyperpigmented (i.e., melasma), and adjacent perilesional normal skin areas. Hematoxylin and eosin and Fontana-Masson staining as well as immunohistochemical staining using melanocyte-specific markers including monoclonal antibodies against human gp100 (NKI/beteb; Monosan, Uden, the Netherlands), tyrosinase (Thermo Scientific, Fremont, CA, USA), and microphthalmia- associated transcription factor (MITF; Leica Biosystems, Newcastle, UK) were performed. The numbers of MITF+ melanocytes per 1-mm length of rete ridge were counted. The expression levels of gp100 and tyrosinase were measured as the ratio of stained area to measured epidermal area.

The general histological findings of the hypopigmented skin were unremarkable. There was no collagen remodeling or scarring. Fontana-Masson staining demonstrated the almost complete absence of melanin pigment in hypopigmented skin (Fig. 1B). The number of melanocytes, as determined by MITF expression, was not substantially different in lesional skin (n=4) compared to perilesional normal skin (n=5) or melasma skin (n=3). Consistently, tyrosinase level was not lower in lesional skin than perilesional normal skin but was higher than that in melasma skin as expected. Interestingly, gp100 expression was higher in the hypopigmented lesion than perilesional normal skin and even melasma skin. Similar findings were observed in patient 2, a 49-year-old woman with Fitzpatrick skin type III who presented with typical mottled hypopigmentation after laser toning for 1 year (Fig. 2A). Lesional skin biopsy showed the complete absence of melanin pigment in hypopigmented skin. However, there was no reduction in the number of melanocytes, and gp100 expression was elevated (Fig. 2B).

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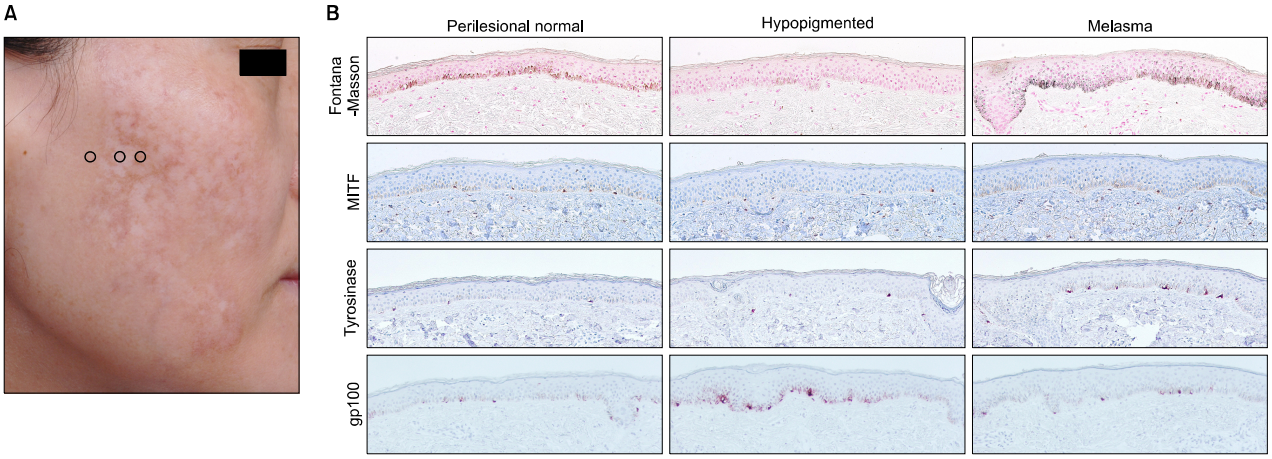

Fig. 1. (A) Mottled hypopigmentation developing after laser toning for melasma treatment in a 41-year-old woman with Fitzpatrick skin type IV. Hypopigmented, hyperpigmented (i.e., melasma), and adjacent perilesional normal skin were evaluated. Circles indicate biopsy sites of perilesional normal (left), hypopigmented (middle), and melasma (right) skin. (B) Histopathologic examination showed melanin pigmentation was markedly reduced in the basal layer of lesional skin (Fontana-Masson staining). The number of melanocytes, determined according to microphthalmia-associated transcription factor (MITF) expression, did not differ much between lesional skin and perilesional normal skin or melasma skin. The expression of gp100 was higher in hypopigmented lesional skin than perilesional normal skin or even melasma skin (×200).

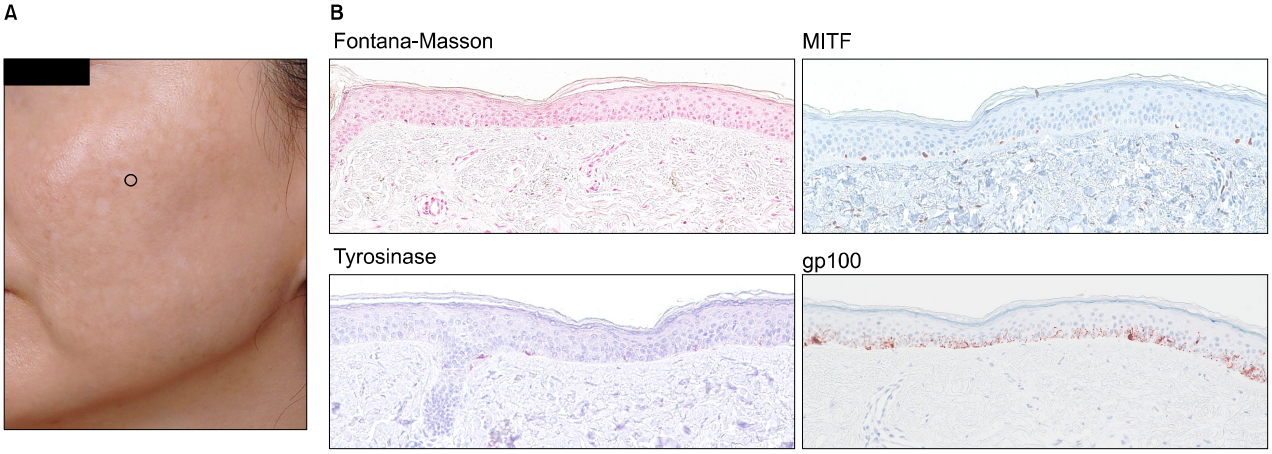

Fig. 2. (A) A 49-year-old woman with Fitzpatrick skin type III presented with typical mottled hypopigmentation after laser toning for 1 year. Circle indicates biopsy sites of the hypopigmented lesion. (B) Lesional skin biopsy showed the complete absence of melanin pigment in hypopigmented skin. However, there was no reduction in the number of melanocytes and rather increased gp100 expression (×200). MITF: microphthalmia-associated transcription factor.

The results of the present study clearly demonstrate that the histologic features of laser toning-induced hypopigmentation are characterized by almost destroyed melanosome pigments and a preserved the number of melanocytes. However, it is unclear whether the number of melanocytes is reduced in the hypopigmented skin. One study indicates hypopigmentation might be due to melanocytopenia[5]. However, in that study, lesional skin was not compared with adjacent perilesional normal skin. The other studies suggest the number of melanocytes in hypopigmented skin is normal[6,7]. In the present study, there was no difference in the mean numbers of MITF-stained melanocytes between lesional skin and perilesional normal skin. Interestingly, we noticed that the levels of the structural protein gp100 were preserved and rather elevated in lesional skin compared to perilesional normal skin. Moreover, in patient 1, gp100 levels of hypopigmented skin were clearly elevated compared to that in hyperpigmented skin. Although the reason for this result is unclear, these findings nonetheless suggest the melanogenic activity in the melanocytes was impaired and the cells failed to produce fully matured melanosomes.

Considering that the proposed action mechanism of laser toning is subcellular selective photothermolysis of melanosomes and not melanocytes, it is speculated that melanocytes survived but were functionally downregulated such that they did not produce fully matured melanosomes. The cumulative dose of repetitive laser treatment may affect melanocyte function, resulting in the development of hypopigmentation. Therefore, treatment activating or stimulating melanogenesis in the melanocytes would be required. To this end, treatment with focused narrowband ultraviolet B therapy has been used with some success[8].

In conclusion, laser toning-induced hypopigmentation is characterized by almost destroyed melanosome pigments and a preserved number of melanocytes, which seem to be functionally downregulated not to produce fully matured melanosomes. Thus, early intervention aiming to restore melanocyte function would be required.

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