

The histopathological characteristics of male melasma: Comparison with female melasma and lentigo

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Background: Knowledge of the histopathology of melasma is a prerequisite for understanding its pathogenesis. However, the histopathological characteristics of male melasma are not well characterized.

Objective: We sought to investigate the histopathological characteristics of melasma in men compared with those of women with melasma and solar lentigo.

Methods: Biopsy specimens were obtained from both the lesional skin and the adjacent nonlesional skin in 8 men with melasma, 10 women with melasma, and 5 men and women each with solar lentigo. The samples were stained using Fontana-Masson and Verhoeff-van Gieson. Immunohistochemistry for melanocytes, the estrogen receptor, progesterone receptor, factor VIIIa-related antigen, stem cell factor, and c-kit was performed.

Results: Increased vascularity was found in the lesion of male melasma. The lesion to nonlesion ratio of the vessel area was increased in male melasma compared with lentigo groups. In the lesion of male melasma, there was a significant increase of stem cell factor and c-kit expression. In addition, the lesion to nonlesion ratio of stem cell factor was increased in male melasma compared with female melasma and lentigo groups. The lesion to nonlesion ratio of c-kit was also increased in male melasma compared with lentigo groups.

Limitations: This study did not include clinical data regarding social habits and was not confirmed by other molecular techniques.

Conclusion: The results suggest that chronic ultraviolet radiation associated with signaling of paracrine cytokines plays an important role in the mechanism associated with hyperpigmentation in male melasma. (J Am Acad Dermatol 2012;66:642-9.)

Key words: c-kit; estrogen receptor; male melasma; progesterone receptor; stem cell factor.

Melasma in men is much less common than in women.¹ Approximately 10% of Caucasian patients with melasma, 26% of Indian patients with melasma, 4% of Korean patients with melasma, and 14.5% of Latino patients with melasma are men.²⁻⁴ Classically, in previous studies conducted largely on women, it has been generally believed that ultraviolet (UV) irradiation, sex hormones, and genetics are involved in the development of melasma.

Abbreviations used:

ER:	estrogen receptor
LS/NL:	lesion to nonlesion ratio
PR:	progesterone receptor
SCF:	stem cell factor
UV:	ultraviolet

In many cases, a direct relationship with female hormone activity appears to be present; this is

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because melasma has been associated with pregnancy and with the use of oral contraceptive pills. In addition, previous studies have shown increased expression of the estrogen receptor (ER) in melasma-affected skin, which suggests the role of hormone receptors in the pathogenesis of melasma.⁵ However, a recent epidemiologic study showed that melasma is not always associated with pregnancy or a history of contraceptive use.⁶

It has been demonstrated that the skin lesions associated with melasma have more prominent solar elastosis compared with the skin without lesions; this suggests that dermal changes may induce the development of melasma.¹ We have previously suggested that dermal inflammation, induced by accumulation of UV radiation, may be associated with activation of fibroblasts, resulting in the up-regulation of the stem cell factor (SCF) in the dermis of melasma lesions, which leads to the increased melanogenesis associated with melasma.⁷ In addition, in our previous study on the vascular characteristics of the dermis of melasma skin there was an increased vascularity identified as one of the major findings of female melasma.⁸ Therefore, in most female patients with melasma, a combination of factors including UV exposure, hormone factors, family history, and age are likely to play a role in the development of melasma. On the other hand, previous studies have suggested that the main associated factors of melasma in men are: UV irradiation, genetic influences, and subtle testicular resistance.^{2-4,9}

Knowledge of the morphologic and histopathological characteristics of melasma in men is essential to understand its pathogenesis. The aim of the current study was to investigate the histopathological differences between male melasma skin and the adjacent control skin, and to compare the histopathological characteristics of male melasma skin with those of female melasma and nonmelasma skin with solar lentigo.

METHODS

Tissue samples

Skin biopsy specimens were obtained from 8 male patients with melasma, 10 female patients with

melasma, and 5 men and women each with solar lentigo recruited from January 2002 to June 2008. In each patient, the diagnosis of melasma and solar lentigo was made by physical examination. Two-millimeter punch biopsy specimens from lesional and adjacent nonlesional skin (usually within 1 cm) were obtained from each patient under local anes-

thesia. Their mean age was 35 ± 5.2 (mean \pm SD) years and all groups were age-matched. All of the patients had Fitzpatrick skin type IV or V. Informed written consent was obtained from each patient before skin sampling. Dermal melanocytosis such as acquired bilateral nevus of Ota-like macules, based on positive dermal NKI/beteb staining, were excluded from this study. In addition, the clinical diagnosis was confirmed histologically by performing Fontana-Masson and NKI/beteb staining. This study was approved by the institu-

tional review board (number: AJIRB-CRO-08-185).

Stains and immunohistochemistry

Paraffin-embedded tissue sections of 3- μ m thickness were processed for light microscopy. The Fontana-Masson stain for melanin pigment and the Verhoeff-van Gieson stain for elastotic materials were performed by the usual methods without eosin background staining for image analysis.

Immunohistochemistry for melanocytes, ER, progesterone receptor (PR), factor VIIIa-related antigen, SCF, and c-kit were performed using standard techniques. The primary antibodies included: NKI/beteb (diluted 1:20; Monosan, Uden, The Netherlands) for melanocytes, ER- α (diluted 1:100; Cell Marque, Rocklin, CA), ER- β (diluted 1:50; Novocastra, Newcastle upon Tyne, United Kingdom), PR (diluted 1:100; Thermo Scientific, Fremont, CA), factor VIIIa-related antigen (diluted 1:50; Invitrogen, Camarillo, CA), SCF (diluted 1:100; Santa Cruz Biotechnology Inc, Santa Cruz, CA), and c-kit (diluted 1:100; Cell Marque).

Image analysis

For quantification of melanin pigmentation, melanocytes, and expression of SCF and c-kit in the epidermis, the stained area per epidermal area was measured in the lesional skin and in the adjacent

CAPSULE SUMMARY

- Melasma in men is much less common than in women; the histopathological characteristics of male melasma are not yet clearly defined.
- Based on histopathological findings, the main factor involved in the development of male melasma appears to be chronic ultraviolet radiation. In contrast to common belief, hormonal factors were not predisposing factors for male melasma.
- This study suggests that the key factor in prevention of male melasma is avoidance of sun exposure.

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