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Imatinib Mesylate-Induced Hyperpigmentation of the Nose and Palate

Hyo Sang Song, Hee Young Kang

Department of Dermatology, Ajou University School of Medicine, Suwon, Korea

Dear Editor:

Imatinib mesylate, a tyrosine kinase inhibitor targeting c-kit and platelet-derived growth factor, has been used for the treatment of hematologic malignancies. Its cutaneous adverse effects are diverse, including maculopapular exanthema, vasculitis, and Stevens-Johnson syndrome[1]. A well-established pigmentary change is hypopigmentation, which is characterized by generalized skin lightening, vitiligo-like lesions, and hair graying[2]. However, paradoxical hyperpigmentary changes were rarely observed[3,4]. We present a case of hyperpigmentation of the nose and hard palate associated with imatinib mesylate.

A 58-year-old man was referred for discoloration of the nose. He was diagnosed with chronic myelogenous leukemia and was treated with imatinib mesylate (Gleevec; Novartis, Basel, Switzerland). Not long after imatinib treatment, he noticed insidious pigmentary changes on his nose. He had no history of skin eruptions or use of other medication. Physical examination revealed an ill-defined, slate-gray patch on the nose and on the hard palate, which suggested a diagnosis of dermal pigmentary disorders including acquired bilateral nevus of Ota-like macules (Fig. 1). Biopsy of the lesional skin and perilesional normal skin of the nose was performed. Fontana-Masson staining showed increased basal pigmentation and dermal melanophages in the lesional skin compared with the perilesional normal skin (Fig. 2A). Imunohistochemical staining with the NKI/beteb antibody confirmed the absence of melanocytes in the dermis (Fig. 2B). Therefore, the pigmentation was speculated to be imatinib-associated hyperpigmentation. Although hypopigmentation is a well-known pigmentary change due to imatinib treatment, paradoxical hyperpigmentation has been rarely reported. In hyperpigmentation, the changes are not generalized like hypopigmentary changes. The disorder pigmentation is localized in the oral cavity, including the hard palate and gum,

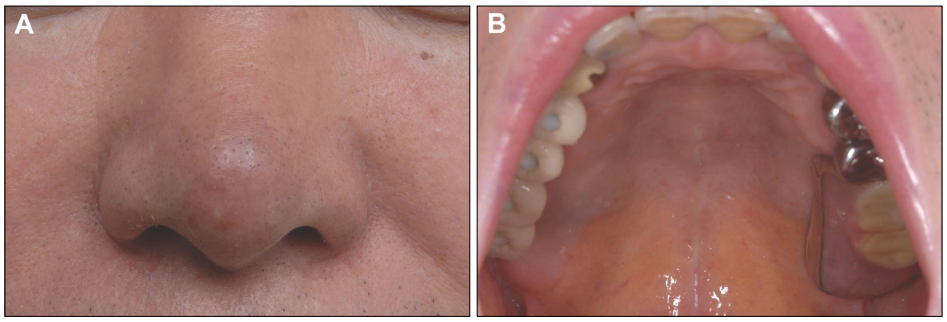

Fig. 1. Ill-defined slate grey-colored pigmentation on nose (A) and palate (B).

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Corresponding author: Hee Young Kang, Department of Dermatology, Ajou University School of Medicine, 164 World Cup-ro, Yeongtong-gu, Suwon 443-380, Korea. Tel: 82-31-219-5190, Fax: 82-31-219- 5189, E-mail: hykang@ajou.ac.kr

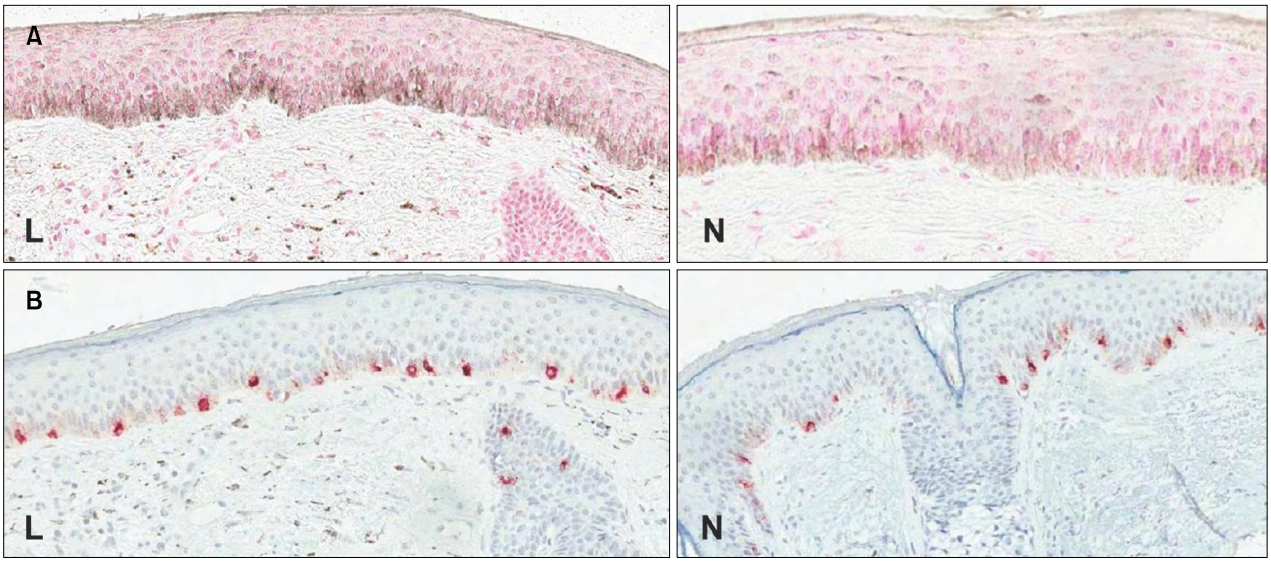

Fig. 2. (A) Increased epidermal pigmentation and dermal melanophages in the lesional skin (L) compared with perilesional normal skin (N) (Fontana-Masson stainining, ×200). (B) There were no melanocytes in the dermis (gp100, ×200).

nose, ear lobe, or nails[3,4]. The present case was consistent with these features, and the patient showed localized pigmentation on the nose and hard palate. There has been no report about the prognosis of this pigmentary change. In case of hypopigmentation, it could be reversible when the doses are tapered or the treatment is stopped[2]. Our patient is continuing imatinib treatment, and there has been no change in the pigmentation. It has been suggested that imatinib- induced hypopigmentation is mediated by c-kit inhibition, resulting in reduced tyrosinase activity in melanocytes[5]. The mechanism of this paradoxical hyperpigmentation is unclear. However, an *in vitro* study has shown the stimulating effect of imatinib on the tyrosinase activity of cultured melanocytes, which suggests the target-dependent stimulating effects of imatinib mesylate on pigmentation. Further studies are required to elucidate these pigmentary changes related to imatinib mesylate medication. Herein, we report a case of paradoxical hyperpigmentation of the nose and hard palate after imatinib mesylate treatment, warranting further evaluation of this mechanism.

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