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Imatinib-induced nail hyperpigmentation in chronic myeloid leukemia

Sir,

Imatinib mesylate has revolutionized the treatment of chronic myeloid leukemia (CML) and has been recently approved as first-line treatment. Most of the patients receiving imatinib experience hematological or non-hematological side effects. Skin changes are the most common non-hematological toxicities but nail changes have not been described.[1] The prevalence and their relationship with the dose suggest a direct pharmacological effect of imatinib.[2] There is one report of hyperpigmentation of the skin owing to imatinib but no report of nail pigmentation alone.[3] We report on a patient with CML who developed hyperpigmentation of the nails while receiving imatinib.

A 40-year-old man presented with the complaint of heaviness in the abdomen in September 2003. He had splenomegaly of 8 cm below the costal margin. Bone marrow aspiration was suggestive of a chronic myeloproliferative disorder. The leukocyte alkaline phosphatase score was 5. A cytogenetic study showed that he was Philadelphia–chromosome-positive.

The patient was diagnosed as a case of chronic myeloid leukemia and was started on 400 mg/day imatinib. There was complete hematological response within 1 month and major cytogenetic response at 6 months. In January 2004, he noticed hyperpigmentation of the fingernails, which gradually increased. The pigmentation was initially brown in color but darkened with time. It started at the nail bed and gradually involved approximately two-thirds of the nails. The hyperpigmentation was darker in the middle of the nails than in the nail-bed area and tip. All fingernails were affected. Similar pigmentation was also present on the toenails but they were relatively less dark. There was no change in the color of the skin.

The common skin changes owing to imatinib are superficial skin edema, skin rashes, hypopigmentation, and pruritus.[1] Rarely, it can cause severe toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and hyperpigmentation.[3–5] A study from India in CML patients on imatinib found 40.9% of them having hypopigmentation.[3] Hyperpigmentation of the skin owing to imatinib has been reported only once.[3] The median time of onset of the hypopigmentary changes is 4 weeks. Pigmentary changes (mainly hypopigmentation) are initially localized and then become diffuse after a few weeks or months. Such changes do not call for imatinib dose changes or interruption in treatment. These changes appear to be dose-related.[3]

Pigmentary changes in the nails have not been reported, but it is expected that the same mechanism as that for the skin pigmentary changes would be responsible. A molecular mechanism has been hypothesized for hypopigmentation. Imatinib targets tyrosine kinases of BCR-ABL, *c*-kit, and platelet-derived growth factor receptor-α. C-kit is normally expressed in skin basal cells, melanocytes, and epithelial cells of breast tissue, mast cells, and other cells.[3] It has a regulatory role in melanogenesis, melanocyte homeostasis, and pigmentation.[6] The molecular mechanism for hyperpigmentation is not known.

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