

SHORT COMMUNICATIONS

Imatinib-Induced Acquired Dermal Melanocytosis

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ABSTRACT

Background: Imatinib, a tyrosine kinase inhibitor, is commonly used to treat gastrointestinal stromal tumors and hematologic malignancies. Hyperpigmentation is a known side-effect of imatinib, with intradermal hemosiderosis being the most common histologic finding.

Case Presentation: We report a rare case of hyperpigmentation secondary to dermal melanocytosis following imatinib treatment in an African American patient with acute lymphoblastic leukemia.

Conclusion: The efficacy of imatinib and the benign nature of the pigment abnormalities should be emphasized to prevent unnecessary treatment cessation in patients presenting with imatinib-induced dermal melanocytosis.

INTRODUCTION

Imatinib, a tyrosine kinase inhibitor, is commonly used to treat gastrointestinal stromal tumors and hematologic malignancies.¹ Cutaneous reactions occur in up to 69% of patients, most commonly manifesting as superficial edema and an exanthem-like rash.² Recent literature documents changes in pigmentation, with higher rates of hypopigmentation (40.9%) as compared to hyperpigmentation (3.6%).³ While the histologic appearance of imatinib-induced hyperpigmentation varies, intradermal hemosiderosis is the most common finding.⁴ We report a rare case of hyperpigmented patches secondary to dermal melanocytosis following imatinib treatment in an African American patient with acute lymphoblastic leukemia (ALL).

CASE PRESENTATION

An 81-year-old African American woman with a history of ALL presented to dermatology clinic with diffuse hyperpigmented patches of her face, upper back, and shoulders in February of 2020. She was initially diagnosed with ALL in August of 2014, and complete remission was achieved shortly thereafter with 2 cycles of hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) and initiation of imatinib therapy. At the time of presentation, imatinib use had been continuous for more than 5 years. Physical examination revealed diffuse, ill-defined, slate-grey hyperpigmented patches distributed symmetrically on the bilateral temples, forehead, upper back, and shoulders. Hyperpigmented patches of her face were first observed in September of 2015, with

Figure 1. Clinical examination showed ill-defined, slate-grey hyperpigmentation of (A) forehead, (B) temples, (C) and upper back.



later expansion to her shoulders and neck. A punch biopsy of the right shoulder was obtained, revealing occasional pigmented spindled cells in the superficial and deep reticular dermis. An iron stain was negative. The pigment stained positive with Fontana-Masson and the cells stained with antibodies

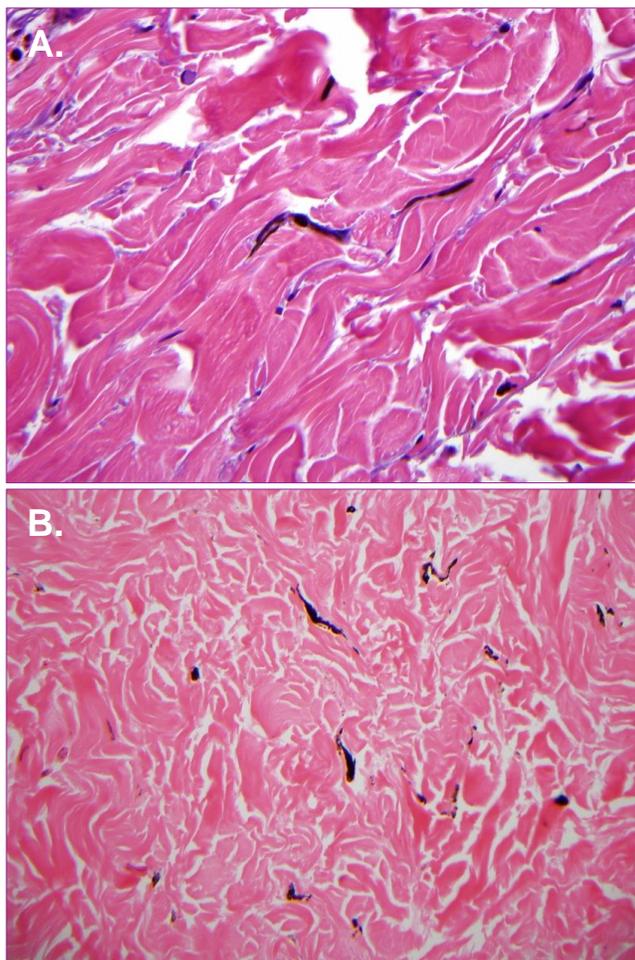
against Melan-A. A final diagnosis of dermal melanocytosis was made. Given the patient's positive response to imatinib, the favorable side effect profile of imatinib compared to other tyrosine kinase inhibitors, and the benign nature of the pigmentation abnormalities, she remains on imatinib.

DISCUSSION

Imatinib has been known to induce dyspigmentation.⁵ Although Imatinib-induced hypopigmentation has been attributed to inhibition of the c-Kit/SCF pathway which is responsible for the differentiation, survival, and proliferation of melanocytes, the mechanism of paradoxical imatinib-induced hyperpigmentation is unclear and the histologic findings are diverse.¹ Among patients with imatinib-induced hyperpigmentation, intradermal hemosiderosis is the most common finding on biopsy.⁴ The pathophysiology involves damage to the dermal vessels and subsequent deposition of iron in the skin. As later development of hepatic hemosiderosis has been reported, these patients should be closely monitored for signs of liver disease.⁶ Rarely, imatinib-induced hyperpigmentation has been attributed to dermal melanocytosis. Kok et al reported 3 cases of generalized hypopigmentation and progression of existing dermal melanocytosis.⁷ Although dermal melanocytosis appears bluish-grey and the pigmentation of intradermal hemosiderosis is classically dark brown, color changes vary and can be difficult to distinguish clinically. Biopsy is therefore essential to ensure appropriate diagnosis and subsequent management.

Although dermal melanocytosis is evidence of melanocyte activation, there are only 5 reported cases of primary cutaneous

Figure 2. Histopathologic examination revealed (A) heavily-pigmented superficial spindled cells in the dermis (H&E, 40x). (B) Fontana-Masson staining showed spindled melanocytes in the dermis (40x).



melanoma arising in the context of acquired dermal melanocytosis.^{8,9} The precursor lesion was a nevus of Ota in all 5 of these cases, in contrast to our patient.⁹ Furthermore, imatinib may offer a protective benefit as it inhibits the c-Kit/SCF pathway and has been used in the treatment of melanoma with KIT mutations.^{10,11} For these reasons, we are doubtful our patient's dermal melanocytosis confers an increased risk of melanoma, although there is a lack of literature regarding this topic. The efficacy of imatinib and the benign nature of the pigment abnormalities should be emphasized to prevent unnecessary

treatment cessation in patients presenting with imatinib-induced dermal melanocytosis.

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