Case Report

Imatinib Induced Melasma Like Pigmentation : A rare entity

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ABSTRACT

Imatinib mesylate, a tyrosine kinase inhibitor, is used for the treatment of chronic myeloid leukemia (CML), gastrointestinal stromal tumor (GIST), mastocytosis, myelodysplastic and myeloproliferative disorders. Cutaneous side effects of imatinib include xerosis, photosensitivity, pigmentary changes hypopigmentation and rarely hyperpigmentation. A 34-years-old male diagnosed case of CML currently on Imatinib 400mg once daily since 5 months presented with brownish discoloration of face since 4 weeks. Histopathology revealed increased epidermal pigmentation without interface dermatitis, lichenoid infiltrate and melanin incontinence. Considering the clinical, histopathological findings and temporal association with drug intake, a diagnosis of imatinib induced melasma like hyperpigmentation was made.

Key words : Hyperpigmentation, Melasma, Imatinib, Drug-induced hyperpigmentation, chronic myeloid leukemia

Introduction :

Imatinib mesylate is a tyrosine kinase inhibitor that targets BCR-ABL tyrosine kinase, platelet derived growth factor (PDGF), and c-kit.[1] FDA approved indications of imatinib are Philadelphia chromosome positive adult CML, KIT positive metastatic GIST, acute myelogenous leukaemia, myelodysplastic / myeloproliferative diseases, hypereosinoplilic syndrome, aggressive mastocytosis and refractory dermatofibrosarcoma protuberans.[1] There are many cutaneous adverse effects of imatinib of which hypopigmentation is a predictable sequelae.[2]

Case History :

A 34-year-old male, a diagnosed case of CML on treatment with Imatinib mesylate 400 mg OD since 5 months presented with asymptomatic brownish discoloration of face since 4 weeks.

Cutaneous examination revealed brownish hyperpigmented patches involving the malar areas of the face extending bilaterally to zygomatic areas and bridge of the nose. The pigmentation was more markedly seen on the lateral aspect of the face than on the centrofacial area. Few hyperpigmented macules were seen on chin. There was sparing of the upper and lower eyelids and the nasolabial folds ***(Figure 1)***. The palms, soles and nails were normal. The buccal mucosa and teeth were not involved.

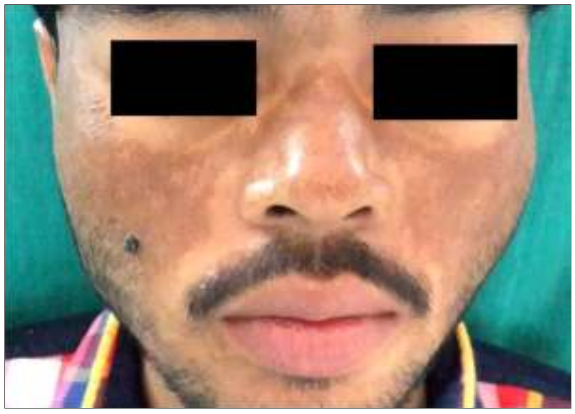

Fig. 1 : **Melasma like Pigmentation**

Histopathological examination of the hyperpigmented patch on the cheek revealed increased pigmentation of the basal layer. There was no evidence of basal layer vacuolar degeneration, interface change, melanin incontinence or lichenoid infiltrate in the dermis.

The patient was advised strict photoprotective measures and was treated with modified Kligman's regimen and sunscreens. Considering the reversible nature of the pigmentation, the patient was advised to continue the imatinib therapy.

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Discussion :

Imatinib mesylate is a tyrosine kinase inhibitor that targets BCR-ABL tyrosine kinase, platelet derived growth factor (PDGF), and c-kit. BCR-ABL acts through tyrosine kinase pathway to cause proliferation of leukemic cells in CML.[1] The common side effects of imatinib include nausea, myalgia, maculopapular rash and edema. Cutaneous adverse effects of imatinib include xerosis, photosensitivity, pigmentary changes, psoriasiform rash, angular chelitis, lichenoid reaction, acute generalized exanthematous pustulosis and painful oral erosions.[3] ***(Table 1)***

Pigmentary changes include hypopigmentation, hyperpigmentation, generalized skin lightening, vitiligo like lesions and hair graying.[1] ***(Table 2)*** In the melanogenesis pathway, c-kit and PDGF receptors' activation play a pivotal role, thus explaining hypopigmentation as a predictable and dose dependent side effect.[2] The reason behind hyperpigmentation may be linked to alterations in the c-kit signalling pathway.[4] In families carrying congenital tyrosine II domain mutations of c-kit, a similar cutaneous phenotypic expression is observed.[4] Other reasons postulated behind hyperpigmentation include paradoxical stimulation of melanocytes, drug - induced basal cell degeneration, and deposition of drug metabolite that chelates melanin.[1,2] Pigmentation may also involve palatal mucosa, nails, teeth, hair, gums.[5]

Other drugs causing melasma like pigmentation are oral contraceptive pills, hormone replacement therapy drugs causing phototoxic and photo-allergic reactions and antiepilepsy medications.[1] hence; drug history needs to be elicited properly.

Imatinib induced hyperpigmentation is usually seen after 2-6 months of starting of imatinib.[1] This hyperpigmentation is reversible and imatinib should not be discontinued for this side effect. Patient should be informed about this side effect to maintain the treatment compliance.

References :

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Table 1 : Orocutaneous side effects of Imatinib

Xerosis	Photosensitivity
Pigmentary changes	Graft-versus-host-like-disease
Maculopapular rash	Mycosis fungoides like reaction
Psoriasiform rash	Small vessel vasculitis
Pityriasis rosea-like eruption	Stevens-Johnson syndrome
Lichenoid reaction	Sweet syndrome
Acute generalized exanthematous pustulosis	Edema, Grey-blue pigmentation of palate
Follicular mucinosis	Angular chelitis
Erythroderma	Painful oral erosions

Table 2 : Pigmentary side effects of Imatinib

Sr. No.	Side effect	Mechanism
1.	Hypopigmentation	Inhibit melanogenesis via inhibition of the binding of ligands to c-kit receptors
2.	Hyperpigmentation	Paradoxical stimulation of melanocytes Drug-induced basal cell degeneration Deposition of drug metabolite that chelates melanin
3.	Generalized skin lightening	Inhibit melanogenesis via inhibition of the binding of ligands to c-kit receptors
4.	Vitiligo like lesions	Inhibit melanogenesis via inhibition of the binding of ligands to c-kit receptors
5.	Hair graying	Inhibit melanogenesis via inhibition of the binding of ligands to c-kit receptors