Melasma like hyperpigmentation on face: A rare side effect of imatinib

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Abstract
Imatinib mesylate is a cytotoxic agent that is used in chronic myeloid leukaemia. Common reported side effect is hypopigmentation; here we report a 48 year old female who developed hyperpigmentation as melasma on her face while taking imatinib mesylate in a dose of 400 mg daily for chronic myeloid leukaemia.

Keywords: Drug-induced pigmentation, Imatinib-mesylate, Melasma, Chronic myeloid leukemia.

Introduction
Imatinib is a tyrosine kinase inhibitor that targets break cluster region-Abelson (BCR-ABL) tyrosine kinase, initial drug of choice for Philadelphia chromosome positive adult chronic myelogenous leukaemia.[1] Adverse cutaneous reaction is common in imatinib treated patients. Varying proportions of cutaneous reactions to Imatinib have been reported in different case series.[1-3] Reversible hypopigmentation is a well-recognized side effect of this drug; however, hyperpigmentation like melasma has been rarely reported. Melasma is an acquired hyper melanosis of sun-exposed areas which presents as hyper pigmented macules. They are symmetrically distributed over the cheeks, upper lip, chin, and the forehead. This can occasionally occur in other sun-exposed locations. Herein, we report 48 year old female who presented with melasma-like pigmentation on her face caused by this anti-tumor agent.

Case Report
A 48-year-old female known case of chronic myeloid leukemia on imatinib mesylate 400 mg daily came for follow up in our medicine out patient department. She was in follow up since last 6 month. This time she presented with pigmentation on her face. There was no pigmentation or active skin lesions on her face prior to this. There was no history of photosensitivity. Her thyroid profile was normal. She was not on any other medications. She had good improvement in the hematological parameters as well as spleen which were also reduced in size.

On examination, there were brownish hyperpigmented macules involving the forehead, malar and mandibular areas of the face. The pigmentation was more marked on the lateral aspect of the face than on the Centro facial area. There was sparing of the upper and lower eyelids and the nasolabial folds. There was no such pigmentation on neck, upper chest and other part of the body. The palms, soles and nails were normal. The buccal mucosa and teeth were not involved.

Fig. 1: Hyperpigmentation present diffusely over cheek

The patients were advised about sun protection and were counselled regarding the benign nature of the pigmentation. On follow up there was no increase in pigmentation so Imatinib was not stopped in this patient.

Discussion
Imatinib belongs to a new class of anti-cancer drugs that target the tyrosine kinase receptor. This agent blocks signaling via BCR-ABL, c-kit and platelet-derived growth factor receptor by binding to the adenosine triphosphate-binding pocket which is required for phosphorylation and activation of the receptor, resulting in inhibition of tumor proliferation. Its systemic side effects are less severe than those seen with other cytotoxic drugs. The most common toxicities are nausea, myalgia, skin rashes and edema. Among the dermatological side effects, maculopapular rash is the most common. Other side effects include xerosis, photosensitivity, angular cheilitis, psoriasiform rash and pigmentary changes. Rarer side effects include acute generalized exanthematous pustulosis, urticaria,

lichenoid reaction and painful oral erosions.[4] Among the pigmentary changes seen with this drug, hypopigmentation has been most commonly reported. The drug inhibits melanogenesis via inhibition of the binding of ligands to c-kit receptors. In one study, 41% of patients receiving imatinib were reported to develop hypopigmentation.[5] The morphological variants included generalized skin lightening, vitiligo-like lesions and hair graying. Only few case reports of imatinib-induced hyperpigmentation is available in the literature. Exact mechanism of this pigmentation is not known, probability may be due to formation of a drug–melanin metabolite, drug-induced cytotoxic response to epidermal 'neo antigen' and the presence of a specific KIT mutation and its interaction with other receptors.[4-6]

Other drugs which cause melasma-like pigmentation are oral contraceptive pills, hormone replacement therapy, drugs causing phototoxic and photo-allergic reactions and anti-epilepsy medications.[7] Both hyper- and hypopigmentation have been reported with imatinib, as well as a paradoxical presentation of both occurring in the same patient.[4] counselling of the patients about the possibility of these side effects may increase compliance to this anti tumor drug which has to be taken for longer duration.

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