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Case Report

Diffuse Universal Hyperpigmentation Induced by Imatinib Mesylate

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Abstract

Observations: Imatinib mesylate, a tyrosine kinase inhibitor, is increasingly being used in the treatment of chronic myeloid leukemia and other oncological disorders. It may cause a large number of cutaneous adverse effects. We are reporting here a case of diffuse universal hyperpigmentation following imatinib therapy, showing lichenoid interface dermatitis on histopathology, a hitherto unreported entity.

Introduction

A large number of anti-neoplastic and other drugs have been implicated in the causation of drug-induced hyperpigmentation of skin, mucosae, and nails. Among the anti-neoplastic agents, busulphan, bleomycin, and hydroxyurea are well known to cause various types of hyperpigmentery changes. We are reporting the occurrence of diffuse universal hypermelanosis, a hitherto unreported adverse effect imatinib mesylate, a tyrosine kinase inhibitor that is increasingly being used in the treatment of chronic myeloid leukemia.

Case Report

A 43-year-old woman from rural West Bengal, India, presented with a 2-month history of an extensive, asymptomatic progressive darkening of skin. She was on imatinib mesylate for chronic myeloid leukemia two months before the onset of the rash. The patient had been on no other significant medications immediately preceding or simultaneously with the pigmentation. On examination, there was slate gray hyperpigmentaion involving the entire body. The oral mucosa and nails were free from any lesion. Before receiving imatinib, the patient had stable localized vitiligo over limbs and lower lip for the last 8 years, which were spared by the hyperpigmentation. (**Figure 1**) and (**Figure 2**). Punch biopsy showed hyperkeratotis, mild acanthosis, a band of lymphocytic infiltrate at the papillary dermis, marked pigmentary incontinence, and basal cell degeneration (**Figure 3**). As imatinib seemed to be the most likely cause for this lichenoid pigmentation, it was subsequently stopped for a few weeks. This lead to mild improvement of the condition, but upon reintroduction of the drug, the pigmentary change intensified again and was seen to be persistent on follow-up after three months.

Discussion

Imatinib has become one of the first-line treatment options in chronic myeloid leukemia. Existing studies have shown that imatinib is well tolerated. Patients may experience hematological or non-hematological side effects during imatinib therapy

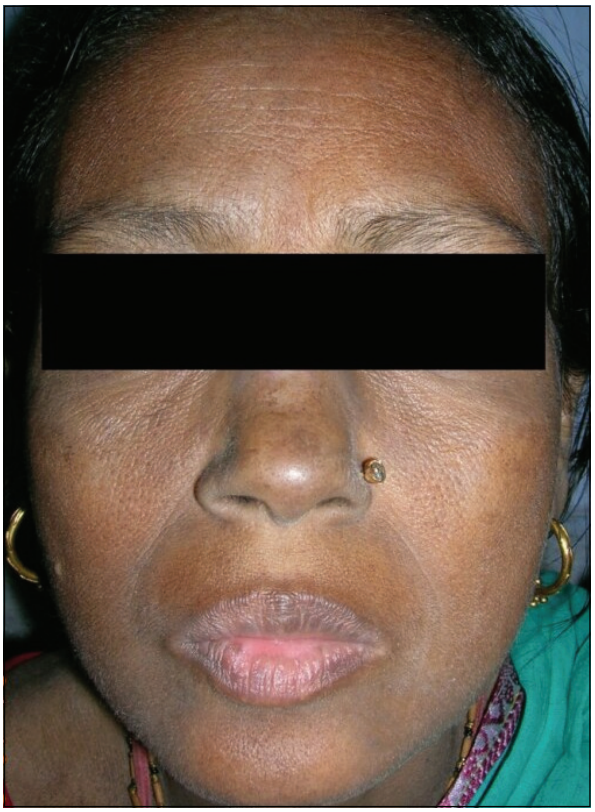

Figure 1. Showing hyperpigmentation of face sparing the vitiliginous areas on lip.

but these are usually mild to moderate in severity [**1**]. Skin change is the most common non-hematological toxicity of this drug [**2**] and commonly occurs in the form of rash, edema and pruritus [**3**]. The exact pathogenesis of the cutaneous reaction is obscure, but direct pharmacological effect is implicated owing to their high prevalence and dose dependence. These changes do not warrant interruption in treatment of imatinib. Among other adverse effects, hypopigmentation has been documented on

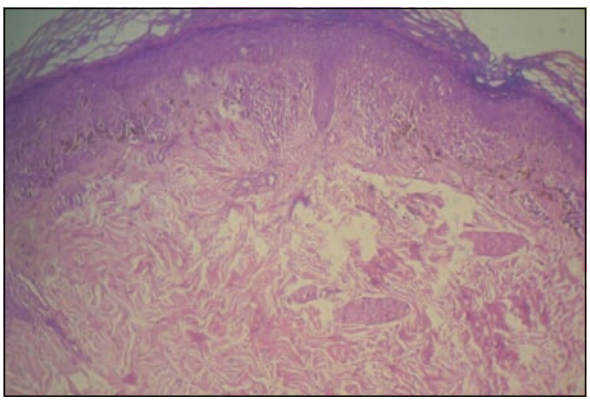

Figure 3. Histopathology showing lichenoid interface dermatitis with pronounced pigmentary incontinence. H & E. Original magnification X 100.

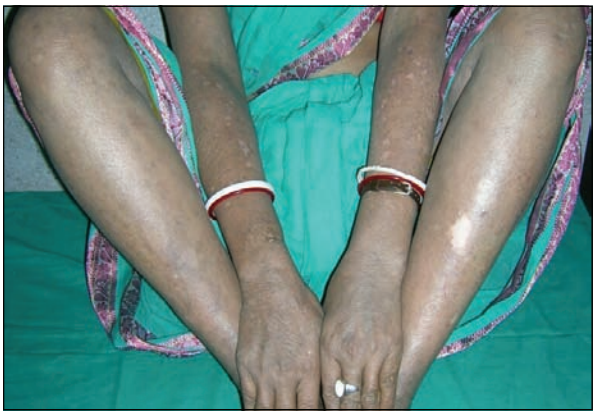

Figure 2. Showing hyperpigmentation over the limbs sparing the vitiliginous areas

several occasions but apart from a report of unspecified hyperpigmentation [**2**] and another on nail pigmentation [**4**], hyperpigmentery changes have not been reported. Pigmentary changes appear to be dose-related and it has a regulatory role in melanogenesis, melanocyte homeostasis, and pigmentation. The molecular mechanism for hyperpigmentation is not known [**4**].

The temporal relationship of the cutaneous change with the administration of imatinib and inability to document other possible causes for the condition is strongly suggestive of a causative role. Although the occurrence of imatinib-induced typical lichen planus-like papular eruption has recently been described [**5**], diffuse generalized hyperpigmentation with a lichenoid interface dermatitis has not been reported previously. As the use of this drug for patients with chronic myeloid leukemia and other oncologic conditions is increasing, clinicians should be aware of the fact that this type of pigmentary changes can occur as a rare adverse effect of imatinib therapy. On the other hand dermatologists should consider the possibility of prior imatinib therapy while evaluating a case of drug-induced hyperpigmentation.

References

1. Gupta DK, Saluja S, Bhasin S, Sharma M. Imatinib mesylate-induced generalized hypopigmentation in patients with chronic myeloid leukemia. Indian J Pharmacol 2006; 38: 66-67.

2. Arora B, Kumar L, Sharma A et al. Pigmentary changes in chronic myeloid leukemia patients

treated with imatinib mesylate. Ann Oncol 2004; 15:358-359. PMID:14760137

3. Valeyrie L, Bastuji-Garin S, Revuz J et al. Adverse cutaneous reactions to Imatinib (STI-571) in Philadelphia chromosome positive leukemias: A prospective study of 54 patients. J Am Acad Dermatol 2003; 48: 201–206. PMID:12582389
4. Prabhash K, Biswas G, Prasad N et al. Imatinib-induced nail hyperpigmentation in chronic myeloid leukemia. Indian J Dermatol Venereol Leprol 2006; 72: 63-64. PMID:16481719
5. Chan CYS, Browning J, Smith-Zagone MJ et al. Cutaneous lichenoid dermatitis associated with imatinib mesylate. Dermatol Online J 2007; 13(2): 29. PMID:17498448