Imatinib- and Nilotinib-Induced Lichenoid Eruption in Chronic Myeloid Leukemia: A Rare Case Report

Abstract

Imatinib and nilotinib are inhibitors of tyrosine kinases (TKIs) generated from the bcr-abl fusion protein, c-Kit, and platelet-derived growth factor receptors. Cutaneous adverse effects (AEs) of TKI are the most frequent non-hematological sequelae. In our case, the common molecular target raises the possibility that cross-intolerance, in which similar AEs occur with both agents, can arise. We hereby report a rare case report on cross-intolerance of cutaneous AEs of imatinib and nilotinib in chronic myeloid leukemia.

Keywords: *Chronic myeloid leukemia, cross-intolerance, lichenoid eruption, tyrosinase kinase inhibitors*

Meenakshi Sachdeva, Jayanti Singh, Surabhi Dayal, Aanchal Gupta[1]

Departments of Dermatology and [1]Pathology, Pandit Bhagwat Dayal Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

Introduction

Imatinib and nilotinib are inhibitors of tyrosine kinases (TKIs) generated from the bcr-abl fusion protein, c-Kit, and platelet-derived growth factor receptors.[1] Cutaneous adverse effects (AEs) to imatinib and nilotinib are the most frequent non-hematological sequelae.[2] Lichenoid drug eruptions (LDE) due to imatinib are well described in the various studies while nilotinib-induced LDE are very few.[2] In our patient, LDE was seen as cutaneous AEs to both imatinib and nilotinib, thereby showing cross-intolerance. The common molecular target raises the possibility that cross-intolerance, in which similar AEs occur with both agents, can arise. So, we hereby report a rare case report on cross-intolerance of cutaneous AEs of imatinib and nilotinib in chronic myeloid leukemia (CML).

Case Report

A 61-year-old male, a known case of CML on treatment with imatinib 400 mg once daily for the last 1 month, presented with an acute onset, itchy, raised light-to-dark-brown colored skin lesions all over the body for the last 1 week. Cutaneous examination revealed bilaterally symmetrical, well-demarcated, violaceous, discrete plaques of size varying from 0.5 × 0.5 cm^2 to 2 × 1 cm^2 involving the whole body except scalp. Palms and soles showed confluent thickening. Oral cavity showed white lacy plaques over bilateral buccal mucosa [Figure 1]. External genitalia showed whitish-colored plaques over glans penis. Laboratory investigations including complete hemogram, liver and kidney function test, and triple viral serology (human immunodeficiency virus [HIV], anti-hepatitis C antibodies, hepatitis B surface antigen) were normal. Histopathological examination revealed orthokeratosis, wedge-shaped hypergranulosis, mild acanthosis, basal cell vacuolization, and band-like lymphocytic infiltrate in upper dermis [Figure 2]. Considering both clinical and histopathological findings, a diagnosis of generalized cutaneous and mucosal LDE was made. Patient was advised to stop imatinib and was started on topical steroids. Lesions resolved completely healing with hyperpigmentation after 2 weeks of treatment [Figure 3].

Imatinib was reintroduced on lower dose of 200 mg OD, after 2 weeks of which patient again presented to us in erythroderma with similar lesions. Imatinib was immediately stopped and short course of oral steroids for 4 weeks was given and lesions got resolved with hyperpigmentation.

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Address for correspondence:
Dr. Meenakshi Sachdeva, 271E, Model Town Near Haryana School Circle, Sonipat - 131 001, Haryana, India.
E-mail: ms1051993@gmail.com

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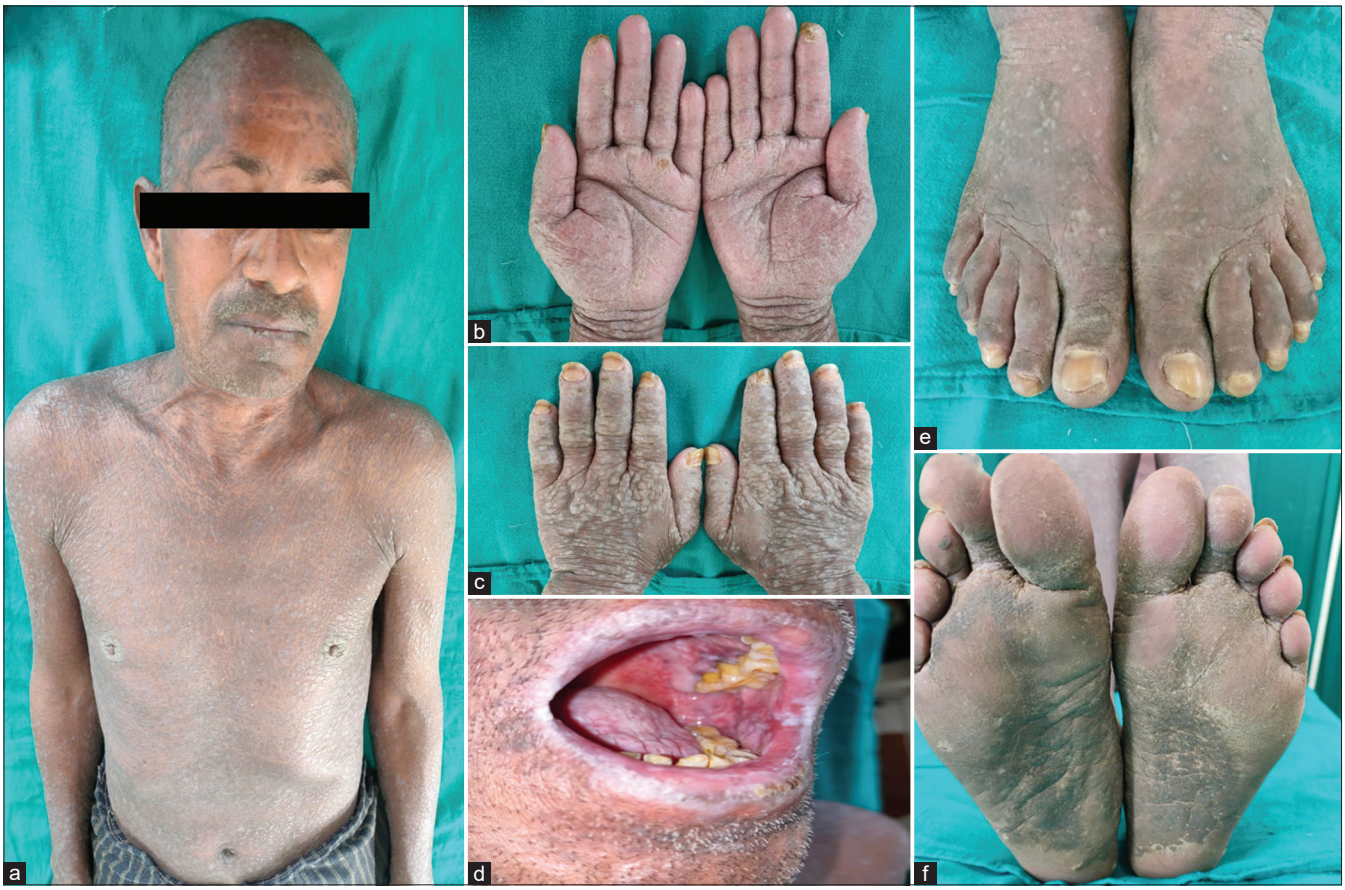

Figure 1: Bilaterally symmetrical, well-demarcated, violaceous, discrete plaques involving the whole body (a); Palms and soles showing confluent thickening (b, c, e, f); (d) Oral cavity showing white lacy plaques over bilateral buccal mucosa involving lips

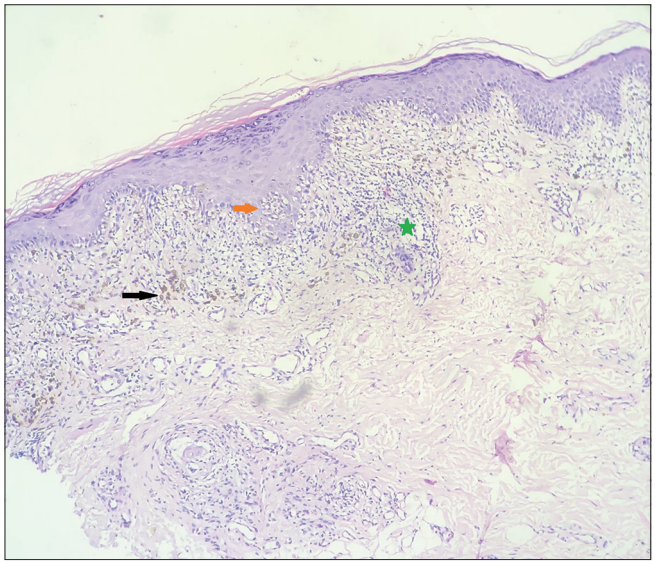

Figure 2: Orthokeratosis, wedge-shaped hypergranulosis, basal cell vacuolization (orange arrow), pigment incontinence (black arrow), and band-like lymphocytic infiltrate (marked with star) in upper dermis (H&E, 10x)

Patient was shifted on nilotinib 400 mg BD by hematology department; he developed similar lesions after 7 days of initiating it [Figure 4]. Nilotinib was immediately stopped. He was managed on short course of oral steroids, topical application of steroids, and symptomatic treatment.

Since the patient had two similar episodes of LDE and one episode of erythroderma after same group of drugs, cross-intolerance was suspected. Patient was shifted to other class of medications, that is, hydroxyurea after which no such episode was reported on follow-ups.

Discussion

Imatinib has been approved as the first-line therapy for CML. It has been indicated in treating various conditions including CML, gastrointestinal stromal tumors, and dermatofibrosarcoma protuberans.[3] Dermatological AEs to imatinib have been reported in 9.5–69% of patients.[4] The most frequently reported cutaneous AEs are xerosis, alopecia, facial puffiness, and photodermatitis while less common AEs include exfoliative dermatitis, LDE, nail disorders, psoriasis, Stevens–Johnson syndrome, erythema multiforme, and leucocytoclastic vasculitis.[2] LDE has been reported in 23 cases while LDE with oral involvement due to imatinib has been reported in very few cases.[5]

Nilotinib, a novel oral aminopyrimidine derivative TKI has a structural similarity to imatinib. Nilotinib is a second-generation TKI and 20–50 times more potent than

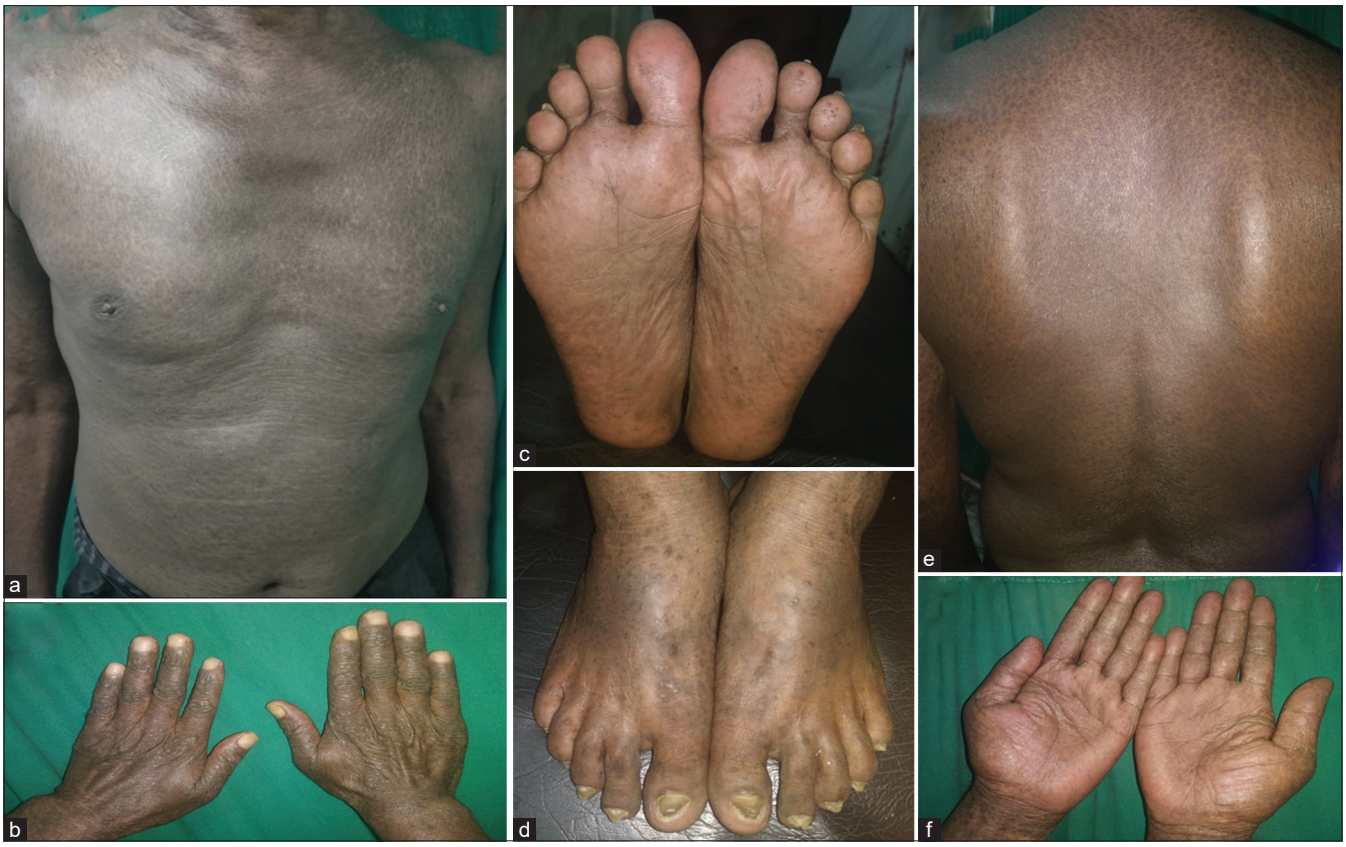

Figure 3: Resolution of lichenoid eruptions on trunk (a,e), dorsum of both hands and feet (b,d) and clearance of palmoplantar hyperkeratosis (c, f) after 2 weeks of stopping imatinib alongwith symptomatic treatment

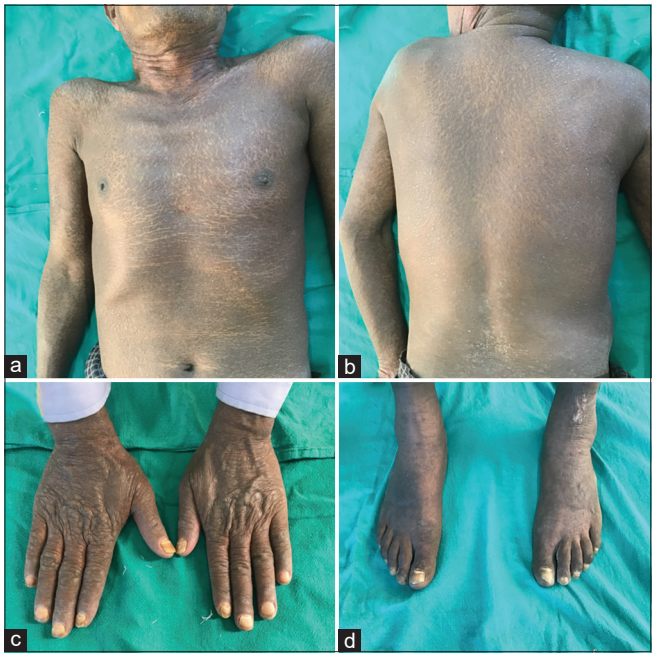

Figure 4: Occurrence of similar lichenoid eruption on trunk (a,b) with involvement of dorsum of both hands and feet alongwith nails involvement (c,d) after initiating nilotinib

imatinib in inhibiting bcr-abl, making it a wonder drug in imatinib-resistant cases and in patients intolerant to imatinib.[6]

Cutaneous AEs to TKIs, that is, imatinib and nilotinib, are the most commonly encountered, less severe, and not life-threatening sequelae. The mechanism for cutaneous AEs is not known but there are various theories proposed like immunogenicity, changes in TKI signaling, or dose-dependent.[7,8] However, nilotinib represents an effective therapy for patients who develop intractable or severe skin reactions with imatinib as there is minimal cross-reactivity reported between the different agents of TKIs in terms of cutaneous AEs.[9,10] A similar study by Cortes *et al*.[9] showed cross-intolerance between imatinib, nilotinib, and dasatinib in a patient diagnosed with CML.[9] But in our case, patient experienced LDE to both nilotinib and imatinib that may be explained on the basis of common mechanism for dermatological AEs.

Thus, our case may represent a unique occurrence of cross-reactivity between imatinib and nilotinib which should be borne in mind while selecting patients for initiating therapy and changes in treatment for CML.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that

his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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