

# Imatinib Mesylate Induced Erythroderma

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## Abstract

Imatinib, a specific tyrosine kinase inhibitor is a new anticancer agent, which has shown excellent efficacy in managing chronic myeloid leukemia. It is well tolerated with few side effects. Commonest adverse events are maculopapular eruptions and periorbital edema were reported. Severe adverse reactions are seen in 5% of patients. Exfoliative dermatitis has been very rarely reported with this drug. We report a case of a 55-year-old female who initially presented with a maculopapular rash and developed erythroderma on continuation of the drug.

## Introduction

Imatinib, a specific tyrosine kinase inhibitor has shown good efficacy in management of chronic myeloid leukemia (CML). There may be complete remission hematologically in the chronic phase of management of CML due to this drug.<sup>1</sup> It is mostly well tolerated. However, various dermatologic and also non-dermatologic adverse effects have been reported. Incidence of dermatological adverse effects with imatinib varies between 9.5% and 69%. Most frequently reported adverse events are maculopapular eruptions, periorbital edema, and the less frequently ones include Steven Johnson syndrome-Toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis, hypopigmentation, lichenoid reaction, pityriasis rosea, and Sweet's syndrome.<sup>2</sup>

## Case Report

A 55-year-old female presented to the oncology outpatient department with complaints of low grade fever and lump on the left side of abdomen since one month duration. Investigations revealed total leukocyte count of 1.2 lakhs/mm<sup>3</sup>. Bone marrow examination revealed 2% blast cells, serum lactate dehydrogenase was 1204 IU/L, and an ultrasound of the abdomen revealed splenomegaly with span of 20cm. Chromosomal studies revealed a bcr-abl gene rearrangement. The case was diagnosed as CML in chronic phase and patient was prescribed imatinib mesylate 400 mg once daily.

Seven days later, she developed redness and scaling involving dorsum of both hands which increased to

involve his entire body over a period of 15 days. The lesions were associated with severe itching. There was no history of any other drug intake, or history of fever, jaundice, chest pain, palpitation and dyspnoea on exertion. Imatinib was continued and the rash worsened.

When the patient was referred to us from oncologist, she had generalized skin rash of 21 days duration. General physical examination was unremarkable while systemic examination revealed splenomegaly, 3 cm below costal margin. Cutaneous examination revealed generalized involvement of the body in form of dusky, blanchable erythema, and diffuse fine scaling. At places erythematous plaques present (Figures 1-3). Angular cheilitis was present. Ophthalmological examination revealed periorbital edema with conjunctival congestion and loss of eyelashes. Nails showed transverse hyperpigmented bands at the same level in all nails. Investigations revealed hemoglobin of 14.5 gm%, total leukocyte count 11,500/mm<sup>3</sup>, and differential count was polymorphs-58, lymphocytes-9, monocytes- 3, and eosinophils 44. Urine examination, blood sugar, renal, and liver function tests were within normal limits.

Imatinib was immediately stopped and patient was prescribed on tablet prednisolone 40 mg/day, which was given full dose for two weeks, tapered by 10 mg/week, and stopped after a total of six weeks. Supportive measures like high protein diet, appropriate temperature control, fluid, and electrolyte balance were provided. Improvement was noticed with decreased erythema on 7 day

and significant reduction in scaling by day 12. The rash disappeared completely within 4 weeks. Imatinib was discontinued by the oncologist. The patient was changed to an alternative anti-CML medication (Cyclophosphamide based) and rechallenge or desensitization was not done, as erythroderma is considered a severe drug reaction.

## Discussion

Imatinib acts by inhibition of several tyrosine kinase enzymes, including Bcr-Abl tyrosine kinase.<sup>3</sup> It is the initial choice of treatment for most patients with CML. Milder skin reactions are more common (30-40%) than the severe forms (2-5%). Imatinib acts as a dose-dependent inducer of cutaneous adverse reactions with milder reactions to low or intermediate doses (200-600 mg/day), but severe reactions to high dose (600-1000 mg/day). Despite common occurrence of cutaneous adverse event with imatinib, severe adverse cutaneous drug reactions are uncommon and seen in 5% of cases.<sup>4</sup> Acute generalized exanthematous pustulosis, epidermal necrolysis, and Steven Johnson syndrome have been reported previously. Other rare reactions mentioned include mycosis fungoides like eruption, follicular mucinosis, porphyria cutanea tarda,<sup>4</sup> neutrophilic eccrine hidradenitis, eccrine squamous syringometaplasia, and panniculitis. Re-pigmentation of gray hair, hyperpigmentation of the nails and skin hypopigmentation have been reported.

There are very few cases of exfoliative dermatitis due to imatinib reported in literature.<sup>3-5</sup> Exfoliative dermatitis generally occurs 1-3 wks after starting treatment on initial exposure and within hours to days on rechallenge. Mechanism of development of rash after imatinib administration is not known,

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**Fig. 1: Multiple erythematous plaque on lower leg**

however, hypersensitivity reaction as a mechanism has been postulated. In this case causality assessment using Naranjo scale showed that imatinib was the probable cause for the ADRs (Score 7). A similar result was made with WHO-UMC causality categories.

Most of the rashes due to imatinib are self limiting and do not require discontinuation of treatment. Oral antihistaminics and topical steroids are required in most of these cases. In contrast, severe reactions require discontinuation of drug. Oral desensitization therapy can be used by administering increasing doses of drug in few cases of leukemia for milder reactions. For imatinib-intolerant patients, dasatinib and nilotinib are the alternative drugs.<sup>6</sup>



**Fig. 2: Multiple erythematous plaque on right leg**

Overall, the incidence of skin rash due to dasatinib and nilotinib is less in comparison with that due to imatinib. The reported incidence of maculopapular rash is 34% and 20% in patients on imatinib and nilotinib or dasatinib, respectively, But severe skin rash is 2% with imatinib therapy as compared to <1% with dasatinib and nilotinib. The incidence of cross-reactivity between imatinib and other tyrosine kinase inhibitors is very low.<sup>6</sup>

Thus, we report a rare case of imatinib-induced erythroderma, which required cessation of therapy. Dermatologists should be aware of imatinib as a cause of drug-induced erythroderma.



**Fig. 3: Multiple erythematous plaque associated with scaling on abdomen.**

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