

**Imatinib Induced Psoriasis in Two Patients with Chronic Myeloid Leukemia**

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**Abstract:** Imatinib or Glivec® is a tyrosine kinase receptor inhibitor that has revolutionized the prognosis of chronic myeloid leukemia and gastrointestinal stromal tumors. This molecule is not devoid of cutaneous adverse effects. We report two cases of Imatinib-induced psoriasis, successfully managed by topical steroids. The aim of this work was to highlight the main features of Imatinib induced Psoriasis, through a systematic review of cases published in the medical literature, to enable rapid diagnosis and appropriate management of this adverse effect.

**Keywords:** Imatinib, psoriasis, tyrosine kinase inhibitor, chronic myeloid leukemia.

**INTRODUCTION**

Imatinib mesylate is an oral chemotherapy anticancer agent, was found to potently inhibit Bcr-Abl family tyrosine kinases implicated in oncogenesis [1], and was used in the treatment of multiple cancers, especially for Philadelphia chromosome positive (Ph+) chronic/myeloid leukemia (CML) for first-line treatment [2], indicated also for treatment of gastrointestinal tumors (GIST) [3], and dermato-fibrosarcoma protuberans [4]. Since its use, imatinib has caused different types of side effects, notably nausea, edema, cardiotoxicity, and 30% of patients who were treated with imatinib present a cutaneous toxicity [5].

It is increasingly important to recognize adverse cutaneous manifestations associated with imatinib and to be aware of their management and outcomes to avoid unnecessarily discontinuing a potentially lifesaving medication.

In the current case, we report two cases of imatinib-induced psoriasis, a rare cutaneous side effect of imatinib use, along with a review of the literature.

**CASE REPORT**

A 52-year-old woman was diagnosed with CML in the chronic phase. Imatinib mesylate was started at a daily dose of 400 mg. The patient achieved a complete hematological response within 3 months. Three months after her CML diagnosis and imatinib use, she developed multiple erythematous and pruritic papuloplaques with silver scales on the trunk and extremities (Psoriasis Area and Severity Index score: 7,8 ) (Figures 1, 2). She had no previous history of psoriasis and had not taken any drugs except for imatinib, nor did she had any relatives with a history of psoriasis. The patient underwent a skin biopsy, which revealed a neutrophilic scale crust and loss of the granular cell layer, which are most consistent with

psoriasis (Figure 3). The discontinuation of imatinib treatment wasn't necessary, and the skin lesions had been well controlled with systemic antihistamine and topical corticosteroid. So far, the patient had not complained of any cutaneous side effects, and she achieved a complete cytogenetic response at 6 months and remains clinically well.

The second case was about a 45-year-old man with no previous history of psoriasis, who was treated by Imatinib 400mg / day for CML, who developed, 4 months later, erythematous-scaly patches of both knees (Figure 3). Physical examination revealed onycholysis, beau lines and pitting, which are typical features of psoriatic nail dystrophy. Imatinib was continued and combined with topical corticosteroid, with a good improvement. The lesions improved during the 8-week follow-up, without recurrence or other cutaneous side effects.



**Fig-1: Erythematous and pruritic papuloplaques with silver scales on the trunk and extremities**



**Fig-2: Erythematous papulosquamous lesions on the lower extremities**



**Fig-3: Erythemato-scaly patches of the knee**

## DISCUSSION

It is now proposed that psoriasis is a complex, multifactorial disease appearing to be influenced by genetic and immune-mediated components, which is induced or exacerbated by various environmental factors, such as drugs, infections, emotions, and stress. Drugs that have been associated with the precipitation or exacerbation of psoriasis include  $\beta$ -blockers, lithium, synthetic antimalarial drugs, nonsteroidal anti-inflammatory drugs, and tetracyclines [5].

Mild skin reactions are relatively frequent, ranging from 7% to 21% of patients treated with Imatinib [6]. In a recent report from Italy [7], the percentage was relatively higher (25%), likely because of close monitoring of patients, with an increase in the incidence rate. The psoriasis induced by imatinib occurred at a mean period of 3-8 weeks of imatinib administration, with variability in the morphologies including plaque, pustular or guttate type flaring up of psoriasis, and nail dystrophy.

In the review of the literature, numerous studies have shown that the interaction of the cellular immune system with T cells and cytokines plays an important role in the pathogenesis of psoriasis [8, 9]. Furthermore, imatinib has been thought to ameliorate psoriasis through the inhibition of c-Kit and PDGFR, which may reduce the production of tumor necrosis factor and other proinflammatory cytokines involved in psoriasis and suppress the proliferation of keratinocytes. Miyagawa *et al.* [10] reported a case with intractable chronic psoriasis that showed a significant improvement while the patient was undergoing imatinib treatment for metastatic gastrointestinal stromal tumor. However, both in our case and most of the report studies, imatinib has aggravated or induced psoriasis. There are several possible explanations for this.  $CD4^+$ ,  $CD25^+$ ,  $FoxP3^+$ , regulatory T cells (Treg) has recently been found in psoriatic skin lesions, and functional defects to restrain effector T cell proliferation have been observed in Treg cells from both psoriatic dermal and peripheral blood origin of patients with psoriasis, indicating that Treg cells play an important role in the pathogenesis of psoriasis [11, 12]. The balance between the regulatory

and effector T cells is important for maintaining adequate immune responses [13]. Imatinib has been shown to interfere with this balance by blocking intracellular signaling [14].

It is thought that cutaneous reactions to imatinib are dose-dependent, as these adverse effects are rarely observed at lower doses of the drug (25-140mg daily) and are much more common at doses of 400-800mg daily. Improvement in the psoriasis upon dose reduction or discontinuation of imatinib has been reported, as well as recurrence following imatinib re-initiation [15].

Topical corticosteroids, oral acitretin, and phototherapy UVB may be reasonable treatment options if discontinuing imatinib is not possible in a symptomatic patient. If these therapies fail and the eruption is extensive or intolerable, dosage adjustment is another option to consider before discontinuation of imatinib. Second-generation TKIs, including dasatinib and nilotinib, may be considered as an alternative treatment in patients who are unable to tolerate imatinib-induced eruptions.

## CONCLUSION

Imatinib represents a major advance in the treatment BCR-ABL-positive leukemias. Psoriasis is a rare side effect of Imatinib that should not lead to a drug withdrawal. Imatinib-induced psoriasis is typically successfully managed with standard psoriasis treatments such as topical corticosteroids and vitamin D analogues. Psoriasis is a highly treatable cutaneous condition and development of imatinib induced psoriasis or similar eruptions should not automatically preclude continued therapy with these effective medications.

## CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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