

Lichenoid eruption due to imatinib

Sir,

Imatinib mesylate is a tyrosine kinase inhibitor. It inhibits tyrosine kinases of bcr-abl, c-Kit and platelet derived growth factor receptors (PDGFRs). This drug has revolutionized the treatment of chronic myeloid leukemia (CML) and has been recently approved as first line treatment in CML patients. Most patients receiving imatinib experience hematological and non-hematological side effects. The common non-hematological side effects are nausea, musculoskeletal pain, superficial edema, skin rashes and muscular cramps. Skin changes are the most common non-hematological adverse effects.^[1] The prevalence and their relationship with the dose suggests that they are due to the direct pharmacological effect of imatinib.^[2] There are three reports of a lichenoid skin eruption due to imatinib.^[6-8]

A 50-year-old man presented with weakness and fatigue in November 2002. He had hepatomegaly of 4 cm and splenomegaly of 2 cm. Bone marrow aspiration was suggestive of chronic myeloproliferative disorder. Leukocyte alkaline phosphatase score was zero. His cytogenetic study was positive for Philadelphia chromosome positive. He received hydroxyurea and interferon 5 MIU/day, but there was no hematological remission and cytogenetically there was no response. He was started on imatinib 400 mg/day in May 2003. He achieved complete hematological response within two months. The cytogenetic response was partial at six months and complete at 12 months.

Six months after imatinib was started, he noticed hyperpigmented skin lesions on the eyelids [Figure 1], which slowly spread to involve the neck, chest, and limbs. The lesions were maculopapular, brownish black in color and non-pruritic. He refused a skin biopsy of the pigmented lesions. The patient was continued on imatinib and is doing well.



Figure 1: Hyperpigmented macules and lichenoid erythematous papules on the eyelids

The common cutaneous adverse effects of imatinib are superficial skin edema, rashes, hypopigmentation and pruritus.^[1] Rarely does it lead to severe epidermal necrolysis, acute generalized exanthematous pustulosis, hyperpigmentation or a lichenoid eruption.^{[3],[4],[5],[6]} Reports of pigmentary changes due to imatinib are from ethnically pigmented patients, with 40.9% having hypopigmentation.^[3] The molecular mechanism for the skin changes is not clear. In one report, all seven patients having depigmentation had a skin rash, suggesting a common etiology, but in another report, only 5.4% patients of patients with pigmentary changes had a skin rash, indicating a complex molecular interaction.^{[2],[3]}

Two of the three reported cases of lichenoid eruption due to imatinib had involvement of the buccal mucosa, and one had skin involvement.^[6-8] The eruption started 12 weeks after imatinib was first administered in two patients, and after eight weeks in the third. Our patient developed a skin eruption six months after imatinib was started. This case illustrates that a lichenoid eruption can occur in patients receiving imatinib. The eruption may be mild or extensive. The mild form may not need discontinuation of imatinib as in our patients. If it is extensive, then temporary discontinuation might be needed.



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Imatinib induced Stevens-Johnson syndrome: Lack of recurrence following re-challenge with a lower dose

Sir,

Imatinib mesylate (STI-571) is a selective and potent small-molecule inhibitor of tyrosine kinases, including BCR-ABL fusion protein, c-Kit and platelet-derived growth factor receptor. It is the most active agent for the treatment of chronic myeloid leukemia (CML), and

gastrointestinal stromal tumors. Cutaneous reactions to imatinib therapy are increasingly being recognized, with 5% of these reactions being severe. Though a variety of dermatological manifestations have been described, occurrence of Stevens-Johnson syndrome is rare.

A 35-year-old man was diagnosed as having Philadelphia-positive chronic myeloid leukemia in the chronic phase. He was started on imatinib 400 mg daily, which was the only medication given. His initial hemogram revealed: hemoglobin, 12.8 g/dl; white blood cell count, 248 x 10⁹/l; and platelet count, 440x 10⁹/l. Complete hematologic remission was achieved with imatinib in two weeks. On the 14th day of treatment, the patient developed an itchy macular eruption mainly over the trunk. Atypical target lesions were observed without areas of necrosis. In addition to the skin lesions, the mucosae were involved with ulcerative lesions. A clinical diagnosis of Stevens-Johnson syndrome was made.

Imatinib was stopped immediately and the patient was given fexofenadine and prednisolone. Healing started within a few days and in one week the lesions cleared. One week following the complete clearance of the rash imatinib was restarted at a dosage of 100 mg daily. This re-challenge at a lower initial dose did not produce any adverse cutaneous reaction. The dose of imatinib was gradually escalated to 400 mg which was continued. Presently, he is in hematologic remission without any untoward side effect.

A variety of adverse cutaneous reactions have been described with imatinib. Of these, rash and edema occur most commonly, the incidence being 66.7% and 65% respectively.^[1] Severe and life threatening reactions occur in 5% cases. Reports of cutaneous adverse reactions other than maculo-papular eruptions are rare with imatinib. However, it may cause acute generalized exanthematous pustulosis,^[2] oral lichenoid eruption,^[3] vasculitis,^[4] pseudolymphoma,^[5] epidermal necrolysis,^[6] hypopigmentation,^[7] erythema nodosum,^[8] exfoliative dermatitis,^[9] and Stevens-Johnson syndrome.^[10-13] Of the four cases of Stevens-Johnson syndrome due to imatinib reported previously, two were males and two females. All these patients, except one, had CML.^[10] In two of

