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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 10^9/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

Table.1 Clinical characteristics of patients with Stevens-Johnson syndrome following imatinib therapy

Author	Age/Sex	Indication & stage of disease	Dose/day	Comments
Sanchez-Gonzalez.et al[10]	72/F	ALL, Ph+	400 mg	No recurrence with re-challenge
Hsiao, et al[11]	42/M	CML, blast crisis, failed allogenic transplant	600 mg	Recurrence with re-challenge. Not restarted
Rule, et al[12]	66/F	CML, chronic phase	400 mg	Recurrence with re-challenge.Restarted with prednisolone, no recurrence
Vidal, et al[13]	58/M	CML, blast crisis	600 mg	No re-challenge
Present case	35/M	CML, chronic phase	400 mg	No recurrence with re-challenge

CML- chronic myeloid leukemia, ALL- acute lymphatic leukemia, Ph+ Philadelphia chromosome positive

these cases the lesions reappeared on re-challenge with imatinib.[11,12] However, our patient, as well as one of the reported cases[10] did not have any recurrence following re-challenge. Clinical characteristics of these patients are shown in Table 1. The etiology of Stevens-Johnson syndrome is not clear and drug-induced cases have been thought to be mediated by an immunological mechanism. Brouard and Saurat have shown that, the incidence of cutaneous reactions with imatinib increases with escalating doses of the drug.[14] Valeyrie et al have reported female sex and imatinib dosage as being independent risk factors for the development of rashes in a multivariate analysis.[1]

As the indications and use of imatinib are increasing, the incidence of adverse cutaneous reactions due to it is likely to increase proportionately. Imatinib induced Stevens-Johnson syndrome being a life threatening reaction, the physician should keep a high index of suspicion for early diagnosis, prompt withdrawal of the drug and institution of appropriate therapy.

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