Imatinib-induced Lichen Planus Resolving with Depigmentation

Sir,

Imatinib mesylate (IM), a selective inhibitor of tyrosine kinase, has been used to treat Chronic Myeloid Leukemia (CML), gastrointestinal stromal tumors (GISTs), and dermatofibrosarcoma protuberans.\[^1\]\ Cutaneous reactions to imatinib have been reported to occur in 9.5%–69% of patients in different series.\[^1\]\ Lichenoid cutaneous reactions due to IM have been well documented in the literature; on the contrary, there are only a few case reports of IM-induced lichen planus (LP). In view of the fact that the clinical usage of IM is growing, one might expect an increasing number of similar patients in the future. It is thus important to realize the potential of IM to produce LP and to differentiate this entity from lichenoid drug rash.

A 44-year-old female, a case of CML on treatment with IM 400 mg OD for 6 months, presented with a 3-week history of acute onset, raised, itchy, and dark-coloured skin lesions all over her body. Cutaneous examination revealed bilaterally symmetrical, well defined, violaceous, discrete papules, few coalescing to form plaques over both wrists, dorsa of hands, and bilateral lower limbs, and discrete violaceous plaques over her bilateral eyelids. Well-demarcated scaly plaques were present on her palms and soles. The oral cavity revealed lacy white plaques over bilateral buccal mucosa. The nails, scalp, and genitals were uninvolved. The papules and plaques over bilateral palms and lower limbs resolved with depigmentation [Figure 1]. Histopathology from violaceous papule over dorsum of the hand revealed orthokeratosis, wedge-shaped hypergranulosus, acanthosis, lichenoid band-like infiltrate of lymphocytes at the dermoepidermal junction, and multiple colloid bodies.

Considering the clinical features, histopathological findings, and temporal association with imatinib, a diagnosis of imatinib-induced LP resolving with depigmentation was made. The patient was treated with topical clobetasol propionate (0.05%) cream application once daily over the active skin lesions as well as oral antihistamines. Since the type of the adverse cutaneous drug reaction was not life threatening, no change in her chemotherapeutic regimen was advised.

IM is a 2-phenylaminopyrimidine derivative which inhibits epidermal growth factor receptor tyrosine kinase activity. Its use in chronic myelogenous leukemia (CML), GISTs, dermatofibrosarcoma protuberans, and hypereosinophilic syndrome (HES) is supported by inhibition of the tyrosine kinase activities of BCR-ABL fusion protein, C-kit oncogene, platelet-derived growth factor receptor alpha, and the mutated genes involving in HES, respectively.\[^7\]

The common side effects of imatinib are nausea and myalgia. Cutaneous side effects of imatinib therapy include maculopapular eruption, edema, Stevens–Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, vasculitis, and mycosis fungoides-like eruption.\[^3\]\ Of these, incidence of rash is 66.7% and of edema is 65%.\[^1\]\ Other less commonly described side effects of imatinib include hypopigmentation, lichenoid drug eruption, pityriasis rosea, psoriasis, neutrophilic eccrine hidradenitis, Sweet’s syndrome, erythema nodosum, Epstein–Barr virus-positive cutaneous B-cell lymphoproliferative disease, follicular mucinosis, and pseudolymphoma-like drug eruptions.\[^4\]\

Imatinib-induced LP is rare, and so far two cases have been reported in literature till date.\[^3,5\]\ Imatinib-induced LP usually occurs between few weeks to months of initiation of imatinib.\[^5,6\]\ In our case, it appeared 6 months after imatinib was started. Clinically, LP is seen as a flexural distribution with mucosal and nail involvement whereas lichenoid drug reaction’s distribution is in a more generalized manner or in photodistributed areas with the absence of mucosal and nail involvement.\[^9\]\ Histopathology of LP reveals sawtooth rete ridges, vacuolar degeneration of basal cell layer, colloid bodies, band-like dermal infiltrate of lymphocytes with the absence of significant parakeratosis, spongiosis, or eosinophilic infiltrate which is seen in lichenoid drug reaction.\[^3\]\ Imatinib-induced LP has a self-remitting course with better prognosis while lichenoid drug reaction has a chronic relapsing course which takes several months to resolve.\[^9\]\ Specific causes of imatinib-induced LP remain unknown. Imatinib-associated LP seems to be a dose-dependent pharmacologic effect rather than hypersensitivity reaction.\[^2\]\ Furthermore, the previous literature of LP with imatinib shows that all patients were on IM in the dose of 400 mg or more.\[^1,3,5\]\ This dose dependence suggests that imatinib-related cutaneous reactions are mediated by changes in tyrosine kinase signal transduction mechanism rather than immunologic mechanism.\[^7\]\ It has been also proposed that the lesions in oral

Figure 1: Violaceous papules and plaques over palms and legs resolving with depigmentation (black arrow)
LP may be closely correlated with the altered expression of epidermal markers caused by imatinib.[4]

The resolving pattern of LP lesions with depigmentation over bilateral palms and lower limbs could be explained by the fact that IM leads to tyrosine kinase inhibition and inactivation of C-kit signaling pathway which has inhibitory effects on melanocyte survival, proliferation, and melanogenesis.[5]

This case is reported as very few cases of imatinib-induced LP resolving with depigmentation have been reported.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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