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LICHENOID DRUG ERUPTION INDUCED BY IMATINIB MESYLATE

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Abstract

Imatinib mesylate (IM) is an anticancer drug. Cutaneous reactions to IM have been reported to occur in varying number of patients in different case series. Non-lichenoid cutaneous reactions due to IM are the commonest non-hematologic adverse reactions associated with its use. Lichenoid drug eruption (LDE), also called drug-induced lichen planus, is an uncommon cutaneous adverse effect of IM. We report here a 52-year-old woman who presented with generalised lichen planus-like lesions due to the use of Imatinib mesylate for chronic myeloid leukaemia (CML). The skin lesions improved after discontinuation of Imatinib mesylate but re-administration of the drug at a lower dose provoked a mild recurrence. She could, however, continue to take the drug in same dose and her skin lesions were well-controlled by oral antihistaminic and topical corticosteroid treatment.

Introduction

Lichenoid eruption is an uncommon skin lesion which can be induced by many environmental agents, medications or industrial by-products such as inhaled particles. When a drug induces lichenoid eruption it can be called more specifically a lichenoid drug eruption. This rash can sometimes become difficult to distinguish from idiopathic lichen planus because of similarities in the clinical appearance and the pathology seen on skin biopsy [1]. It is characterized by a symmetric eruption of flat-topped, erythematous or violaceous papules resembling lichen planus on the trunk and extremities. The time interval between the initiation of the offending drug and the appearance of the cutaneous lesions varies from months to a year or more and depends upon the class of drug, dose, host reaction, and concurrent medications [2]. Several medications have been reported to cause LDE including NSAIDS, ACE inhibitors, some diuretics, carbamazapine, Phenytoin, ketoconazole, hydroxyurea, hydroxychloroquine, gold salts, sulfa drugs, tetracycline, some tumour necrosis factor antagonists, misoprostol etc [1].

Here we report a case where a female with chronic myeloid leukaemia developed LDE showing significant temporal association of occurrence of LDE with intake of Imatinib mesylate.

Case report

A 52 year, hindu, housewife, known patient of CML presented to our out-patient department with 25 days history of acute onset, raised, itchy, purple-colored fairly generalized skin lesions over her body. There was no history of discharge, blister formation or ulceration over the lesions. Initially small papular rash developed over face and trunk with low grade fever and mild bodyache but she did not bother it. Within a 7 days the rash increased and spread all over the body with itching. One month before the onset of the skin lesions the patient was put on monotherapy with IM (400 mg/day) for the treatment of CML and she had no history of any other drug intake or bone marrow transplantation. Then she consulted some local doctor who advised her to stop the IM and prescribed her some antihistaminic and asked her to go to some higher centre. Initially she responded well with antihistaminic but again

new crops of rash appeared, then she came to our department. Cutaneous examination revealed numerous, well-defined, violaceous, discrete and coalescing papules and plaques over the face, limbs, abdomen, chest, and the back. A few scattered hyperkeratotic papules were present on her palms. There was fine scaling but no vesiculation, oozing or crusting were present[Figures1 and 2]. The mucosae, the nails and hair were uninvolved. Her liver function test, renal function test, chest x-ray, routine urine examination was normal.

Based on the clinical presentation and regression of skin lesions after stopping IM, a diagnosis of generalized LDE associated with IM was made. The patient was treated with topical steroid cream application over the active skin lesions as well as oral antihistamines. Within a few weeks, almost all the lesions healed with residual post-inflammatory hyperpigmentation and new lesions stopped appearing.

Discussion

Imatinib mesylate is an anticancer drug which selectively inhibit certain protein tyrosinase kinase implicated in oncogenesis [3]. IM mainly used in treatment of CML, gastrointestinal stromal tumors (GIST), and dermatofibrosarcoma protuberans [3,4,5]. Cutaneous reactions to IM have been reported to occur in 9.5-69% of patients in different series [5]. IM causes several types of non-lichenoid cutaneous reactions which are well-documented in the literature and are the commonest non-hematologic adverse reactions associated with its use [6]. On the other hand, only a few reports of IM-associated lichenoid drug eruption have been described over the last decade[7]. It is important to keep in mind that IM can produce LDE and it can mimic idiopathic lichen planus but distinguishing features are LDE is extensive rash distributed symmetrically over the trunk and limbs predominantly in areas exposed to the sun, it may be scaly resembling eczema or psoriasis, wickham striae are usually absent, nail and mucous membrane involvement is uncommon and it is more likely to resolve leaving marked pigmentation [1]. Moreover, early recognition of the morphological pattern of such drug eruption is crucial to prevent the subsequent discontinuation of IM, which has radically changed the treatment and prognosis of CML and GIST.
Patients with LDE are often taking more than one medicine, which causes difficulty in recognition of ofending agent. Resolution of lesions on discontinuation of the offending drug favors the diagnosis of LDE [8]. There is no specific causes of imatinib induced skin lesions. The dose dependence of adverse reactions favors the assumption that imatinib related cutaneous reactions are mediated by changes in tyrosinase kinase signaling rather than immunologic mechanism as its molecular weight is very low [3].

Here we present the case where significant temporal association of IM with LDE was found in a woman who was treated with this medication for CML. The reaction appeared after the drug was introduced. There was no previous history of similar drug intake in the past .Significant clinical improvement was noted when the drug was discontinued. Since the type of the adverse cutaneous drug reaction was not life- threatening, IM was gradually re-introduced safely to achieve a dose of 400 mg/day by hematologists though initially few lesion appeared after rechallenging the drug but they subsided with topical steroid and the patient was advised regular follow-up. With thorough history taking, clinical examination and available laboratory investigations we could not found any other etiology for this constellation of symptoms. Due to lack of logistic support, detection of the drug concentration in the body fluid could not be carried out. Hence, according to Naranjo Casualty assessment scale the association of LDE due to IM in our case is probable [9]. The case is reported for its rarity in occurrence and associated significant morbidity if not diagnosed and treated immediately.

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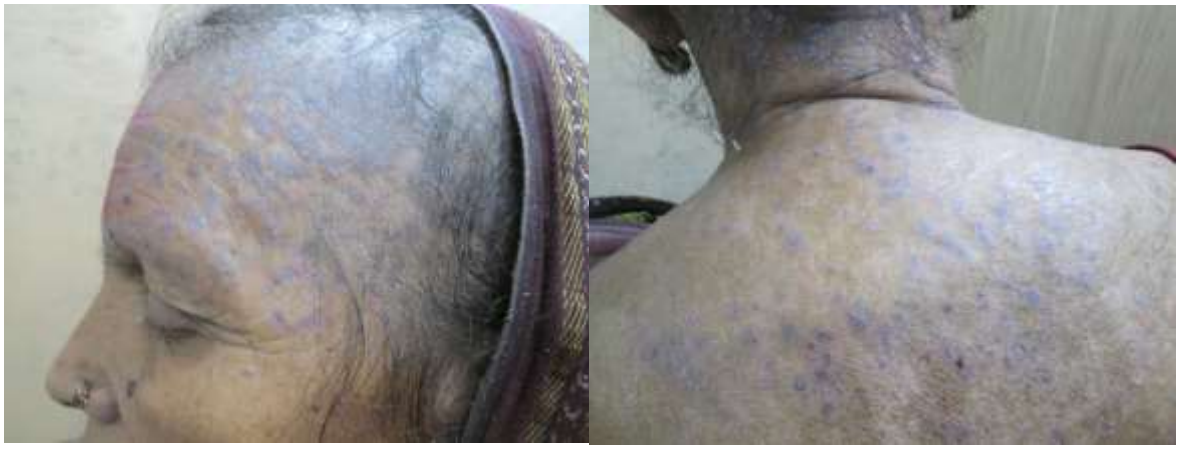

Figure 1:

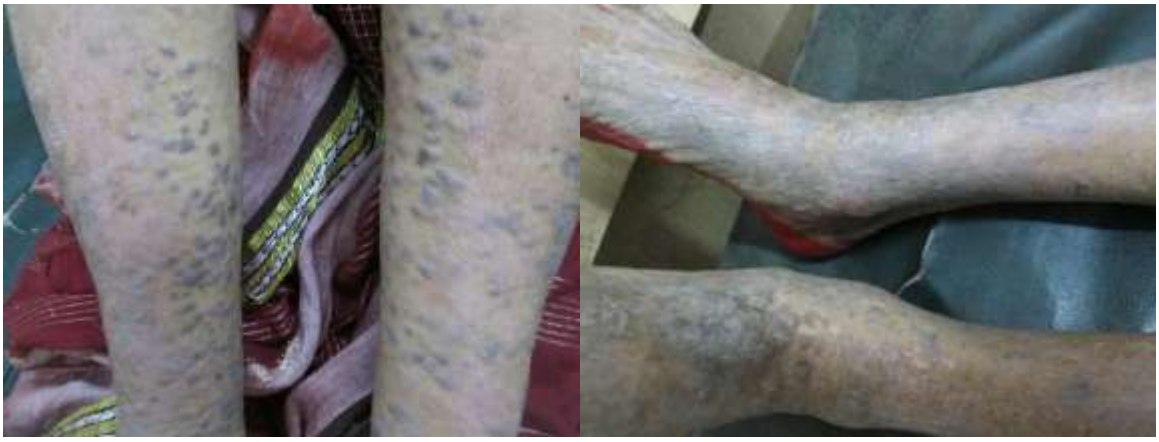

Figure 2:

Legend of pictures:

Legend of Figure 1: Numerous violaceous, coalescing papules and plaques with fine scaling.

Legend of Figure 2: Close-up showing purple-colored coalescing papules and plaques with fine scaling.