Oral and Cutaneous Lichenoid Reaction Secondary to Standard Dose Imatinib: A Case Report and Literature Review

Standart Doz İmatinib'e Sekonder Oral Ve Kutanöz Likenoid Reaksiyon: Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT

Imatinib mesylate - Gleevec®, STI571- is an oral cancer drug that selectively inhibits several protein tyrosine kinases associated with human malignancy. The drug is used for the treatment of chronic myeloid leukemia, malignant gastrointestinal stromal tumors, and some other conditions. Treatment with imatinib is generally well tolerated but is not without the risk of adverse effects. Various types of skin eruptions have been reported. Cutaneous side effects with this treatment are common but a lichenoid drug eruption is rare. In this article, we report a 46-year-old woman who presented with lichen planus like lesions on the trunk and extremities, and oral mucosa due to the use of imatinib mesylate for the chronic myeloid leukemia. The literature on lichenoid drug eruption due to imatinib mesylate is reviewed.

Key Words: Imatinib, lichenoid reaction

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ÖZET

Imatinib mesilat- Gleevec® , (Novartis, USA) STI571- ağızdan alınan bir kanser ilacı olup malignitelerle ilişkili çok sayıda protein tirozin kinazı inhibe eder. Bu ilaç kronik myeloid lösemi, malign gastrointestinal stromal tümörler ve bazı diğer durumlarda kullanılır. İmatinib genellikle iyi tolere edilir, ancak yan etki riski vardır. Farklı tiplerde deri erüpsiyonları raporlanmıştır. Bu tedavi ile kutanöz yan etkiler sık görülürken likenoid ilaç erüpsiyonu nadirdir. Bu makalede, kronik miyeloid lösemi nedeniyle imatinib mesilat kullanımı sonucu gövde, ekstremiteler ve oral mukozada liken planus benzer lezyonlarla başvuran 46 yaşında kadın hasta sunulmakta ve imatinib mesilata bağlı likenoid ilaç erüpsiyonu ile ilişkili literatür gözden geçirilmiştir.

Anahtar Sözcükler: İmatinib, likenoid reaksiyon

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INTRODUCTION

Chronic myelogeneous leukemia (CML) is a clonal myeloproliferative disorder which is the first human malignancy to be associated with a specific genetic lesion, the Philadelphia chromosome, carrying BCR-ABL oncogene. Imatinib (Gleevec) is the first molecularly targeted drug developed for CML and has achieved a remarkable success (1-3). Few side effects are reported with imatinib consisting of mainly hematologic side effects such as neutropenia and thrombocytopenia. Cutaneous side effects with this treatment are common but a lichenoid drug eruption is rare (4).

CASE REPORT

A 46 year-old female with an approximately 15-month history of CML presented with grey-violaceous plaques with a reticular pattern on both cheek mucosal surfaces (Figure 1), and a disseminated purple, prurigenous papules on the trunk, legs, and arms (Figure 2). Dermatological findings were suggestive of lichen planus. She had splenomegaly other than the cutaneous eruption. She had been treated with Gleevec® (Novartis, USA) 400 mg daily for 3 months before onset of the rash. She stated that the eruption spread in the last three weeks.

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The punch biopsy taken from the trunk and oral mucosa revealed a lichenoid band of lymphocytes and histiocytes, hypergranulosis, and vacuolar degeneration in the basal layer (Figure 3). The histopathological findings were consistent with lichenoid eruption. The patient was given triamcinolone 0.1% cream topically and oral antihistaminic, which produced improvements in the lesions.

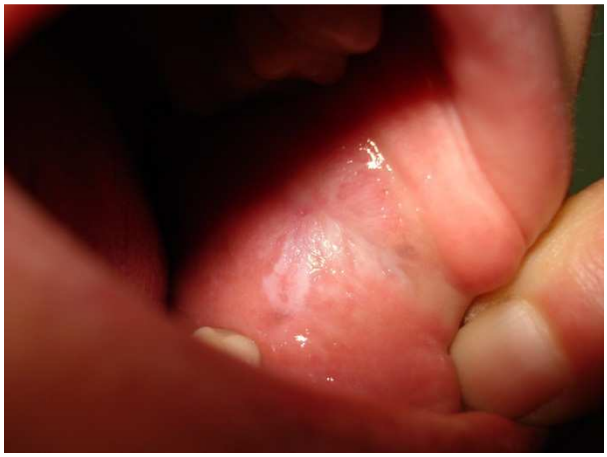

Figure 1. Grey-violaceous plaques with a reticular pattern on both cheek mucosal surfaces.

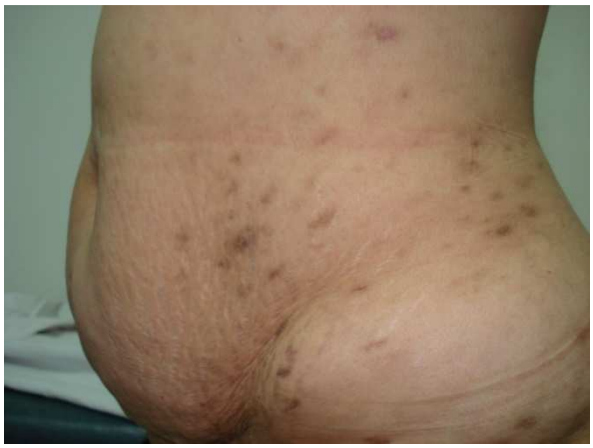

Figure 2. Disseminated purple, prurigenous papules on the trunk.

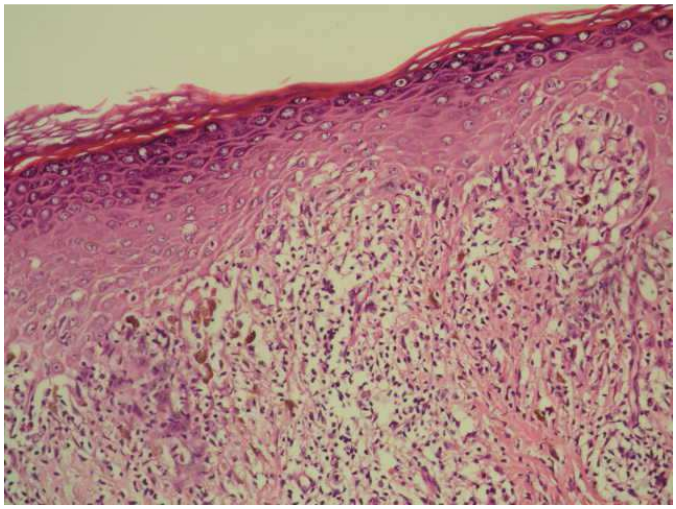

Figure 3. Lichenoid band of lymphocytes and histiocytes, hypergranulosis, and vacuolar degeneration in the basal layer.

DISCUSSION

Imatinib shows its effect by competitively inhibiting the adenosine triphosphate –binding site of the protein kinase enzyme, leading to the inhibition of tyrosine phosphorilation of proteins involved in BCR-ABL gene without affecting normal cells (1). Imatinib also shows its effect on the platelet derived growth factor and c-kit. Recently, it has been shown that imatinib has antifibrogenic effect on bone marrow fibrosis in CML (2). Except from CML, imatinib has also shown to be effective among idiopathic hypereosinophilic syndrome and gastrointestinal stromal tumors (1). There are few reports concerning the side effects of the drug. Hematologic alterations like leukopenia or thrombocytopenia, or trombocytosis and leukocytosis are all reported (3). Non-lichenoid cutaneous reactions secondary to imatinib have been well described and are the most common non-hematologic adverse events associated with its use. The most common cutaneous reactions include morbilliform eruptions and cutaneous edema, particularly, periorbital edema. Cases of severe generalized skin eruptions such as erythema multiforme, acute generalized exanthemous pustulosis, and toxic epidermal necrolysis have also been reported with imatinib use (4). Although skin reactions resulting from imatinib have been well-described, reports of an associated lichenoid dermatitis are rare. Since 2002, there have been twenty case reports of lichenoid eruptions, sixteen of which were in the context of CML treatment, and the others of GIST treatment (5-19). Twenty case reports, including our case, are summarized in Table 1. Three cases had oral involvement as the only manifestation (5-7) , seven had only cutaneous manifestations (8-14) , and the others presented with mucocutaneous involvement (15-19). Our patient presented with grey-violaceous plaques with a reticular on both cheek mucosal surfaces, and a disseminated cutaneous eruption composed of dark purple, prurigenous papules appeared on the trunk, legs and arms . The appeaerance of the majority of the lichenoid lesions was within 2-3 months (8-14). In some reported cases, the withdrawal of imatinib treatment was necessary (5,18). In other cases, dose adjustment and treatment with topical and/or corticosteroids allowed for the continuation of imatinib treatment (6-17,19). In two cases, oral acitretin improved the lesions (11). In our case, topical corticosteroids improved the lichenoid lesions.

Cutaneous reactions to imatinib appear to be dose-related, appearing more frequently and severely in patients on doses of 600 mg daily or greater. However lichenoid eruption may occur under the standard dose of Imatinib (400 mg/day) (1,7).

CONCLUSION

The early recognition and treatment of cutaneous adverse effects may allow for the continued administration of imanitib. With an increasing number of patients being treated with imatinib, clinicians should be aware of its side effect, even in the standard dose of the drug, and we anticipate further reports of lichenoid and other cutaneous reactions associated with its use.

Table 1. Reported cases of lichenoid drug eruption due to imatinib mesylate

Patient (ref)	Age (years/sex)	Disease	Imatinib dose (mg)	Duration (months)	Skin eruption	Mucosal lesions	Other treatments	Imatinib treatment
1 (5)	72/F	CML	ND	5	-	Erosion of the tongue		Discontinued
2 (8)	52/M	CML	400	2	Disseminated eruption	-		Tentative discontinuation
3 (6)	62/M	GIST	ND	12	-	Grey-vialaceus plaques on the cheeks	Oral CS	Continued
4 (9)	50/M	CML	400	6	Maculopapular lesions on the eyelids	-		Continued
5 (10)	69/F	CML	400	2	Pruritic papules and plaques	-		Tentative discontinuation
6 (10)	65/F	CML	400	3	Grey-vialaceous plaques on the trunk		Oral and topical CSs	Continued
7 (11)	76/M	CML	400	4	Erythema and lichenoid rash on the trunk and upper limbs	-		Discontinued
8 (11)	60/M	CML	400	2	Lichenoid eruption on the face, wrist and neck	Reddish macules and erosion	Oral CS	ND
9 (11)	75/M	GIST	400	1	Generalized eruption	-	Acitretin	Continued
10 (11)	50/M	CML	400	2	Generalized eruption on the face, chest and extremities	White reticulated macules on the buccal mucosa	Acitretin	Continued
11 (12)	56/M	CML	600	3	Vialaceous plaques and papules on the extremities and chest	-	Prednisolone and topical CS	Tentative discontinuation
12 (19)	31/M	CML	400	5	Generalized eruption on the face, chest and extremities, longitudinal ridging of nail	White plaques on the lips, buccal mucosa, tongue and genitalia	Topical CS	Continued
13 (7)	55/M	CML	ND	3	-	Erosions on the tongue, lower lip and buccal mucosa	Systemic CS	Continued
14 (7)	85/?	CML	400	ND	Skin eruption on the extremities	Ulcer on the lower lip	Prednisolone	Discontinued
15 (17)	57/M	CML	400	2	Lichenoid eruption on the extremities, palmoplantar keratosis	White streak with erosion on the buccal mucosa	Topical CS	Tentative discontinuation restarted with reduction of the dose
16 (14)	53/M	CML	400	2	Generalized vialaceous papules and plaques on the abdomen, upper extremities	-	Topical CS	Tentative discontinuation restarted with 400 mg
17 (18)	71/M	GIST	400	3	Lichenoid eruption on the flanks	Grey-violaceous erosive plaques on the tongue and labial mucosa	Topical CS	Discontinued
18 (13)	75/M	CML	400	4	-	Whitish plaques on the tongue	Oral CS	Discontinued, restarted with 400 mg
19 (16)	60/F	CML	400	12	Erythematous eruption on the arms, dorsum of the hands, face, neck, facial edema	White lesions on the oral mucosa and tongue	Prednisone, steroid mouthwashes	Discontinued, restarted with 400 mg
20 (15)	62/F	GIST	300	8	Grey-vialaceous,pigmented macules on the face, back	Grey-vialaceous,pigmented macules on the buccal mucosa	Topical CS	Continued
21 (present case)	46/F	CML	400	3	Disseminated vialaceous pigmented papules on the trunk, extremities	Whitish reticulated olaques on the buccal mucosa and cheeks	Topical CS	Continued

Conflict of Interest
No conflict of interest was declared by the authors.

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