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Case Report

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Itraconazole-Associated Purpuric Drug Eruption: A Rare Adverse Effect of a Commonly Prescribed Drug

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Abstract

Purpuric drug eruption (PDE) is a rare drug reaction characterized by purpuric macules, papules, and confluent plaques predominantly on the lower extremities. The drugs reported to induce purpuric drug eruption are epidermal growth factor receptor inhibitors, ketoconazole, acetylsalicylic acid, penicillin, sulfonamides, indomethacin, lenalidomide, linezolid, vancomycin and itraconazole. Drug induced thrombocytopenia, platelet dysfunction and direct toxic effect of the drug on capillary wall leading to increased capillary fragility are the proposed etiology. There is only a single report of itraconazole-induced purpuric drug eruption in the literature till date.We hereby present a case of 57-year-old female with PDE due to itraconazole.

Keywords: Purpuric Drug Eruption, Itraconazole, Purpura

1. Introduction

Purpuric drug eruption (PDE) is a rare drug reaction characterized by purpuric macules, papules, and confluent plaques predominantly on the lower extremities [1]. Itraconazole, despite being one of the most common systemic antifungals used, rarely cause cutaneous reactions [2]. There is only a single report of itraconazole-induced purpuric drug eruption in the literature till date [3]. We hereby report a case of purpuric drug eruption associated with itraconazole due to its rarity.

2. Case Presentation

A 57-year-old female presented with multiple, asymptomatic petechial and purpuric macules over bilateral axilla, lower abdomen, groin, and bilateral thigh for 4 days (Figure 1a). She denies any systemic symptoms, and there is no history of similar cutaneous lesions in the past. She took oral itraconazole 100 mg twice daily for tinea cruris for 3 days which preceded the skin lesions. Mucosae examination revealed normal findings.

Routine blood investigations performed were normal except for eosinophilia. Skin biopsy from the right thigh revealed mild perivascular and superficial lymphocytic infiltrates and extravasated red blood cells (Figure 2 a, b). A probable adverse drug reaction to itraconazole was suspected as the Naranjo adverse drug reaction probability scale was 6. Similarly, the reaction was graded probable as per the WHO-UMC causality assessment scale. Patient denied consent for an oral rechallenge test. Patient was counselled regarding the probable drug reaction to itraconazole and advised to avoid triggering medication. The skin lesions regressed leaving few hyperpigmented macules on the 10-day follow-up visit (Figure 1b).

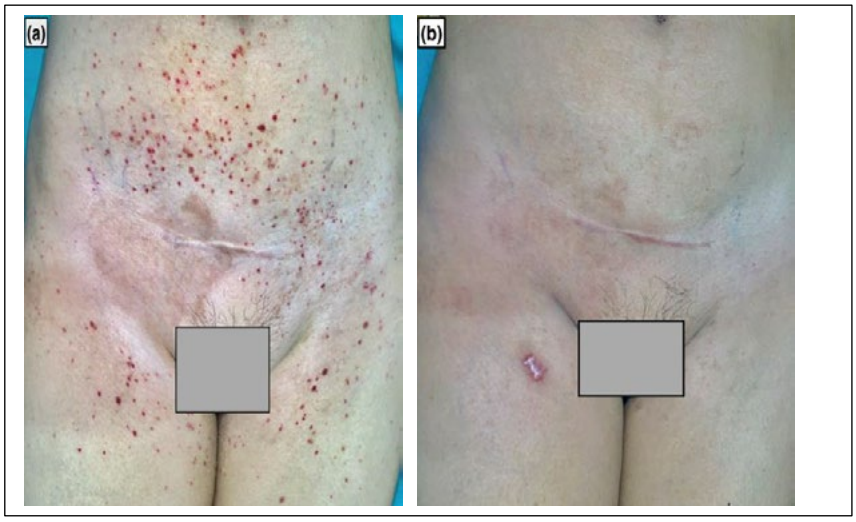

Figure 1: Multiple petechiae and purpura present over lower abdomen, groin and bilateral thighs (a). On follow-up after 10 days, the rash regressed completely leaving few hyperpigmented macules (b).

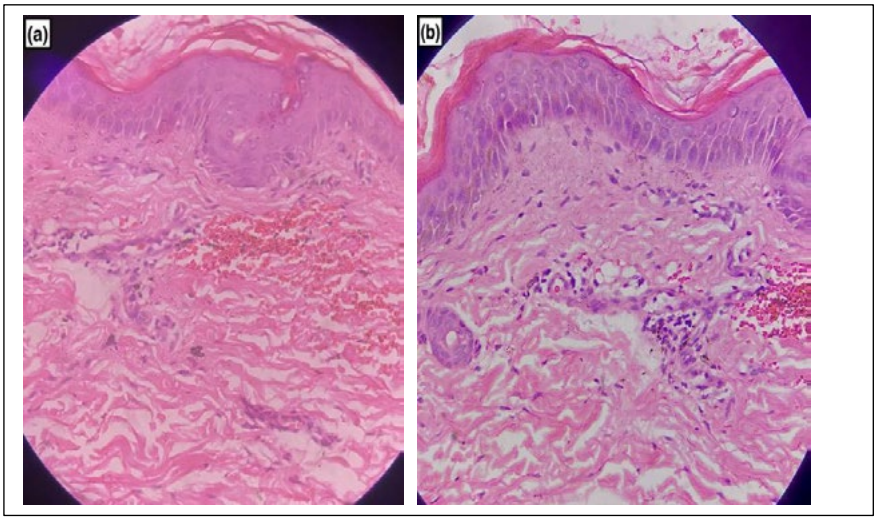

Figure 2: (Figure 2a and Figure 2b) Haematoxylin and eosin stain (40x) revealed, mild superficial perivascular lymphocytic infiltrates and extravasated red blood cells.

3. Discussion

Purpuric drug eruption is relatively rare and accounts approximately 1.17% of drug eruptions [4]. The drugs reported to induce purpuric drug eruption are epidermal growth factor receptor inhibitors, ketoconazole, acetylsalicylic acid, penicillin, sulfonamides, indomethacin, lenalidomide, linezolid, vancomycin and itraconazole [1,3,5]. Drug induced thrombocytopenia, platelet dysfunction and direct toxic effect of the drug on capillary wall leading to increased capillary fragility are the proposed etiology [4]. As the blood investigations were unremarkable except for eosinophilia, direct toxic effect of itraconazole on the capillaries might be the cause for the PDE seen in our case. Itraconazole, a triazole antifungal agent, inhibits fungal cytochrome P-450 dependent enzyme which disrupt the ergosterol synthesis in the fungal cell membrane.6 Cutaneous adverse drug reactions have been described with itraconazole in 2% of cases and include maculopapular drug eruption, urticaria, angioedema, Stevens-Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), vasculitis, symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) and fixed drug eruption (FDE). Purpuric drug eruption induced by itraconazole is extremely rare and to the best of our knowledge only one case has been reported in the literature so far [2,3,6,7]. Differential diagnoses include maculopapular exanthem and leukocytoclastic vasculitis which were excluded by clinical presentation and histopathology.

PDE can be diagnosed on clinical grounds, however, skin biopsy, drug lymphocyte stimulation test and systemic rechallenge helps in diagnostic confirmation [5]. Histopathologically, PDE is characterized by vacuolar interface dermatitis, a sparse superficial perivascular lymphoid cell infiltrate with rare eosinophils, and extravasated red blood cells as described in our case [3,4]. Treatment is mainly symptomatic with topical and systemic corticosteroids, antihistamines and avoidance of

offending drug is of paramount importance [3,4].

4. Conclusion

Awareness of unusual drug reactions is crucial, as the association between skin eruptions and drug exposure can often be overlooked or misdiagnosed. PDE due to itraconazole is extremely rare, so this case is being reported to enlighten the clinicians with an uncommon rash induced by a commonly prescribed drug, which will aid in early diagnosis and management.

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