Dermatology Practical & Conceptual

Significance of Clinical-Pathological Correlation in Ponatinib Reactions

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Introduction

The advent of molecular therapies targeting specific cellular pathways has significantly enhanced the prognosis for numerous cancer patients. However, these advancements often come with diverse cutaneous adverse drug reactions (CADR). These reactions can be serious, such as in Stevens-Johnson Syndrome (SJS), which has been reported as an adverse reaction induced by tyrosine kinase inhibitors (TKIs) like imatinib and masitinib. There have been no reports of SJS induced by ponatinib [1].

Ponatinib is a third-generation TKI specifically developed to target the gatekeeper T315I mutation. It is currently approved for the treatment of chronic myeloid leukemia in all phases of the disease, particularly for patients who have developed resistance to or cannot tolerate dasatinib or nilotinib, and for those with the T315I mutation for whom imatinib is no longer effective. Ponatinib is also indicated for Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) [2]. With over 10 years on the market, some CADR have been reported, including pityriasis rubra pilaris-like eruptions, ichthyosiform eruptions, and erythematous rash [3,4]. Recently, the term "ponatinib-induced desquamation" described sheet-like desquamation, symmetrical dermatitis, and lamellar ichthyosis-like. It was proposed because, regardless of its extensive total body surface area involvement, it is a benign, temporary condition that does not require discontinuing the medication [5].

Case Presentation

A 59-year-old woman was diagnosed with Ph+ ALL in 2022 and began treatment with imatinib. Upon detecting *T315I* mutation, the treatment was switched to ponatinib with a daily dosage of 45 mg. Twenty-seven days after initiating ponatinib, she developed a CADR that affected all body

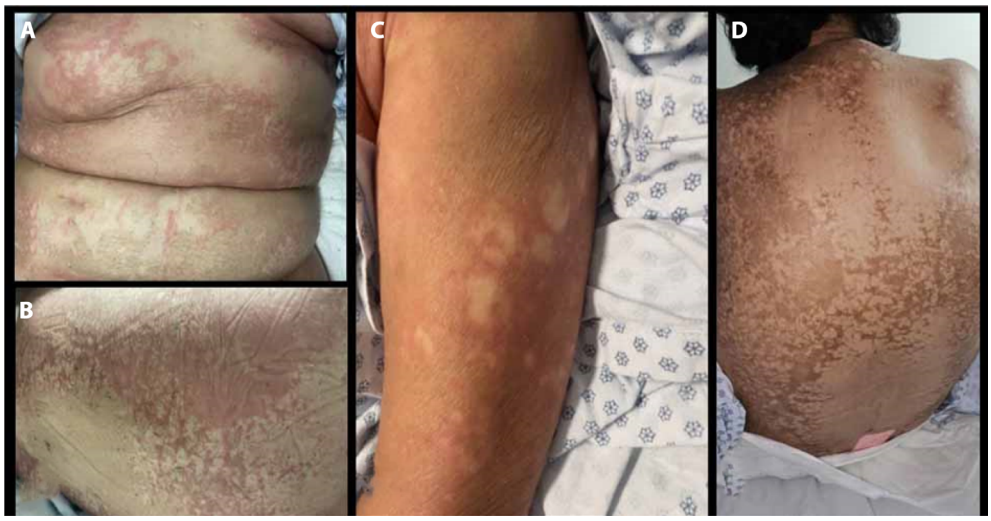

Figure 1. (A-C) Plaques with erythematous purpuric and ochre hues, arranged in a reticular pattern and surrounded by a halo of increased erythema. In some central areas of the lesions, there is evidence of fine adherent scaling. (D) Hypopigmented post-inflammatory patches with a reticulated appearance.

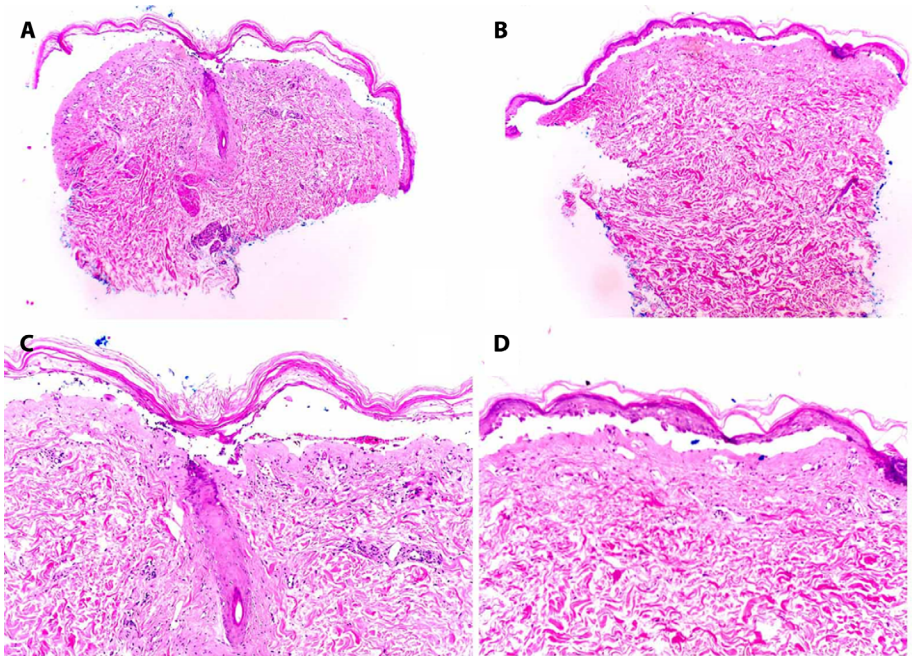

Figure 2. (A,B) Skin biopsy of the back show pauci-inflammatory subepidermal blistering dermatosis with multiple necrotic keratinocytes and lymphocytic and neutrophilic infiltration (H&E, x4). (C,D) Higher magnification (x40).

segments. The lesions were characterized by the presence of plaques with erythematous-purpuric and ochre hues, arranged in a reticular pattern with fine adherent scaling at the center, and surrounded by a halo of increased erythema. Over time, the lesions evolved with blood-tinged scaling. No involvement of mucous membranes was observed (Figure 1, A-C). Histopathologic examination showed pauci-inflammatory subepidermal blistering dermatosis with multiple necrotic keratinocytes and lymphocytic and neutrophilic infiltration (Figure 2, A-D). Although these histological features were consistent with findings described in SJS and other CADR, the clinical presentation of our patient, including the absence of other clinical features such as mucosal involvement, conjunctival inflammation, and absence of blisters, or the Nikolsky sign, led us to conclude that SJS was an unlikely diagnosis. Due to discrepancy between clinical

and pathological findings and the persistent cytopenias, it was decided to discontinue ponatinib treatment. Resolution of the initial lesions resulted in post-inflammatory hypopigmentation (Figure 1D).

Conclusions

We report a cutaneous reaction with an uncommon morphology currently known as Ponatinib-induced desquamation. Our patient exhibited skin lesions with a reticular pattern and peripheral erythema, even though the histopathological findings were consistent with SJS. We reported this case to highlight the significance of recording emerging cutaneous reactions linked to molecular therapies, emphasizing the importance of acting according to evolution in a patient instead of guiding our treatment based on only clinical or histopathological findings, especially when considering the implications for the patient's prognosis.

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