LETTER TO THE EDITOR
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Fingertip Fissures Associated with Ibrutinib in an Elderly Patient with Mantle Cell Lymphoma

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To the Editor,

Ibrutinib is an oral, irreversible inhibitor of Bruton's tyrosine kinase (BTK), which plays an important role in signaling in the B-cell receptor pathway and significantly affects B-cell maturation and survival processes (1). Since it was approved for use, ibrutinib has become a key treatment option for several B-cell cancers, including chronic lymphocytic leukemia (CLL), Waldenström's macroglobulinemia, and mantle cell lymphoma (MCL)(2). MCL is a rare and aggressive subtype of non-Hodgkin lymphoma characterized by the malignant transformation of B lymphocytes within the mantle zone of lymphoid follicles (3). This disease mainly affects older adults, and, usually, patients present with lymphadenopathy, splenomegaly, and bone marrow involvement at an advanced stage (4). Although initial treatment responses can be favorable, MCL often relapses, and long-term prognosis remains poor, prompting the need for targeted therapies such as BTK inhibitors (5)

Although the clinical efficacy of ibrutinib in MCL is clearly documented, its adverse event profile includes a broad array of hematologic, cardiovascular, gastrointestinal, and dermatologic toxicities (6). Dermatologic side effects are frequently underestimated and underreported, yet they may significantly impair quality of life and treatment adherence, particularly in elderly patients (7, 8). Herein, we report a rare cutaneous adverse reaction painful fingertip fissures associated with prolonged ibrutinib therapy in an elderly patient with relapsed MCL.

A 72-year-old woman with relapsed MCL was started on ibrutinib at a dose of 560 mg/day. She had no prior dermatologic history, and baseline skin examination was unremarkable. Within one year of treatment initiation, she developed painful fissures on the fingertips of both hands. These lesions appeared as linear, dry, superficial cracks localized to the distal phalanges, without signs of infection or systemic involvement (Figure 1).

Although xerosis and rash are recognized cutaneous toxicities of ibrutinib, painful fingertip fissures have rarely been reported. According to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, this presentation corresponds to Grade 2 dermatologic toxicity due to localized pain and functional discomfort. The Naranjo Adverse Drug Reaction Probability Score was calculated as 6, indicating a probable causal relationship between ibrutinib and the observed skin lesions (9).

There was no recent history of new topical exposures, or environmental changes. Laboratory tests, including complete blood count, liver, renal function panels, and inflammatory markers, were within normal ranges. Dermatologic evaluation supported a diagnosis of drug-induced xerosis with secondary fissuring, likely attributable to ibrutinib.

Conservative management using emollients, barrier creams, and topical corticosteroids was initiated and ibrutinib was continued. Improvement was noted in about two weeks, and at the end of one month, there were no signs of the condition, and no scarring remained (Figure 2). There was no need for dose reduction, and fissures did not recur during the follow-up. The precise mechanism of fingertip fissures created by ibrutinib is not clearly elucidated. However, it might work with off-target effects as well. In addition to its primary action on BTK, ibrutinib exhibits weak inhibitory activity against the epidermal growth factor receptor (EGFR), particularly at higher doses (10). EGFR plays a pivotal role in keratinocyte homeostasis and maintenance of the epidermal barrier; its inhibition has been linked to xerosis and impaired wound healing (10). The absence of confounding factors and the temporal association with drug initiation support a causal link in this case.

The favorable outcome with conservative therapy highlights the importance of early recognition and appropriate supportive skin care. Routine use of emollients and topical corticosteroids allowed symptom resolution without

compromising systemic therapy. Clinicians should maintain a high index of suspicion for such underreported adverse effects, especially in elderly patients receiving long-term ibrutinib.
This case illustrates a potentially underrecognized cutaneous toxicity of Ibrutinib and underscores the need for dermatologic and supportive care in susceptible populations.

References

1. Brown JR. Ibrutinib in chronic lymphocytic leukemia and B cell malignancies. Leuk Lymphoma. 2014;55(2):263-9.
2. Mouhssine S, Maher N, Matti BF, Alwan AF, Gaidano G. Targeting BTK in B Cell Malignancies: From Mode of Action to Resistance Mechanisms. International Journal of Molecular Sciences. 2024;25(6):3234.
3. Armitage JO, Longo DL. Mantle-Cell Lymphoma. New England Journal of Medicine. 2022;386(26):2495-506.
4. Jain P, Wang ML. Mantle cell lymphoma in 2022-A comprehensive update on molecular pathogenesis, risk stratification, clinical approach, and current and novel treatments. American journal of hematology. 2022;97(5):638-56.
5. Wang ML, Rule S, Martin P, Goy A, Auer R, Kahl BS, et al. Targeting BTK with Ibrutinib in Relapsed or Refractory Mantle-Cell Lymphoma. New England Journal of Medicine. 2013;369(6):507-16.
6. Roufarshbaf M, Javeri M, Akbari V, Matin PH, Farrokhi P, Sadeghi E, et al. Efficacy and safety of ibrutinib in mantle cell lymphoma: A systematic review and meta-analysis. Daru : journal of Faculty of Pharmacy, Tehran University of Medical Sciences. 2022;30(2):367-78.
7. Sibaud V, Beylot-Barry M, Protin C, Vigarios E, Recher C, Ysebaert L. Dermatological Toxicities of Bruton's Tyrosine Kinase Inhibitors. Am J Clin Dermatol. 2020;21(6):799-812.
8. Sollena P, Mannino M, Laurenti L, De Simone C, Peris K. Ibrutinib-associated palmo-plantar fissures in a patient with Chronic Lymphocytic Leukaemia: a novel cutaneous adverse event. Journal of the European Academy of Dermatology and Venereology. 2019;33(9):e342-e4.
9. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical Pharmacology & Therapeutics. 1981;30(2):239-45.
10. Singer S, Tan SY, Dewan AK, Davids M, LaCasce AS, Treon SP, et al. Cutaneous eruptions from ibrutinib resembling epidermal growth factor receptor inhibitor-induced dermatologic adverse events. Journal of the American Academy of Dermatology. 2023;88(6):1271-81.

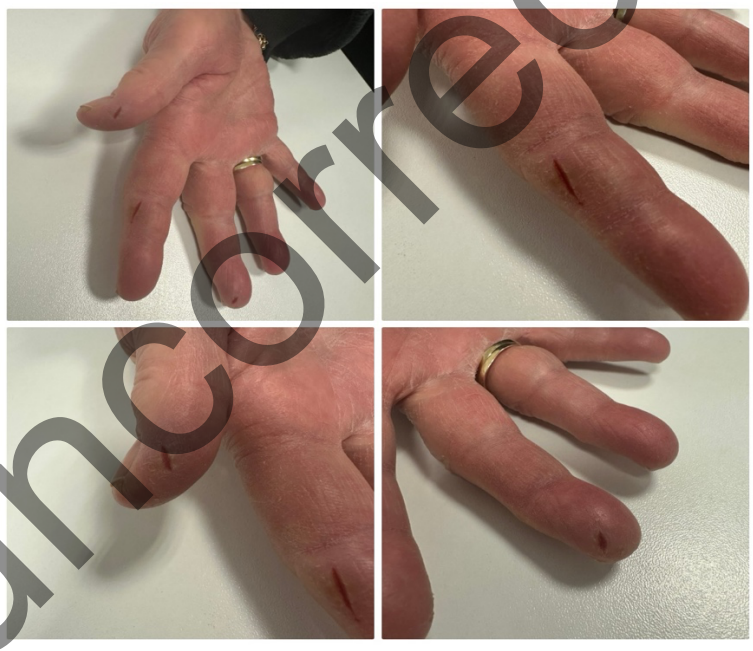

Figure 1 Palmor fissures after 1 year of ibrutinib therapy

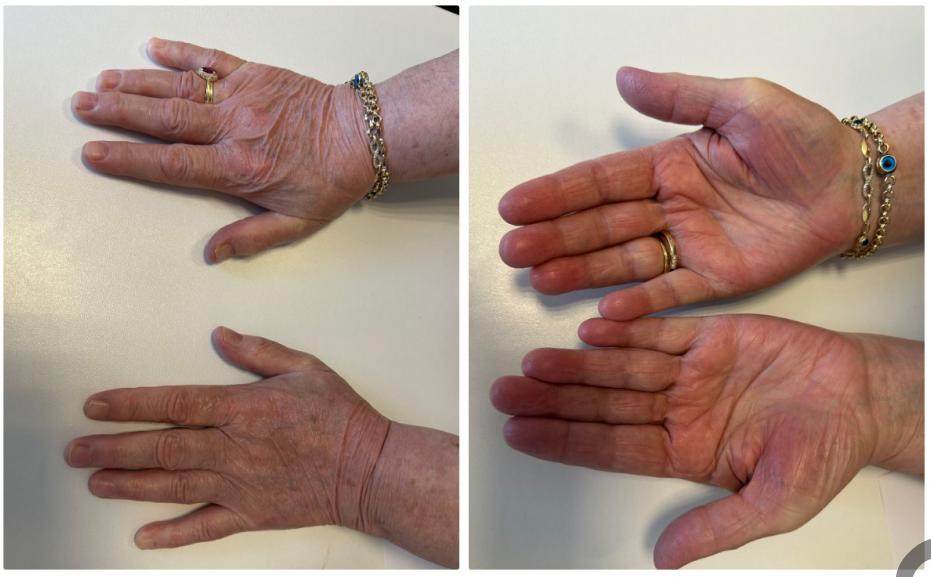

Figure 2 Resolution of palmar fissures after treatment