International Journal of Scientific Reports
Metin N et al. Int J Sci Rep. 2026 Sep;12(9):311-313
https://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164
DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20262821

Case Report

Atypical bullous erythrodysesthesia mimicking fixed drug eruption during cabozantinib therapy: a case report

Nurcan Metin*, Hatice Korkmaz

Department of Dermatology and Venereology, Health Sciences University Erzurum City Hospital, Erzurum, Republic of Turkey

Received: 02 July 2026
Accepted: 07 August 2026

***Correspondence:**
Dr. Nurcan Metin,
E-mail: drnurcanmetin@hotmail.com

ABSTRACT

Cabozantinib is a multi-targeted tyrosine kinase inhibitor used in the treatment of advanced renal cell carcinoma. Palmar-plantar erythrodysesthesia (PPES) is a well-recognized cutaneous adverse effect of tyrosine kinase inhibitors; however, atypical bullous presentations are extremely rare. We report a 79-year-old man who developed painful, pruritic, well-demarcated bullous lesions on the distal fingers of both hands and the left heel three weeks after initiating cabozantinib therapy. Unlike classic PPES, the lesions consisted of tense bullae without hyperkeratosis and closely resembled bullous fixed drug eruption. This case highlights a rare presentation of cabozantinib-induced bullous erythrodysesthesia that mimics fixed drug eruption. Awareness of this uncommon adverse reaction is important for accurate diagnosis, appropriate treatment modification, and avoidance of unnecessary diagnostic procedures.

Keywords: Cabozantinib, Renal cell carcinoma, Bullous erythrodysesthesia, Fixed drug eruption

INTRODUCTION

Tyrosine kinase inhibitors (TKIs) are used as personalized anticancer agents targeting specific gene products.[1] Cabozantinib is a small molecule multi-targeted inhibitor that acts on tyrosine kinase receptors, including vascular endothelial growth factor receptors (VEGFR) 1, 2 and 3.[2] It was approved by the National Institute for Health and Care Excellence (NICE) in August 2017 for the treatment of advanced renal cell carcinoma in adults who have previously received VEGF-targeted therapy.[3]

Palmar-plantar erythrodysesthesia (PPES), also known as hand-foot syndrome, is characterized by acral erythema associated with chemotherapy. It is a common adverse effect of conventional chemotherapy agents and typically resolves upon drug withdrawal.[4]

Various cytotoxic drugs have been implicated in PPES, most commonly 5-fluorouracil, pegylated liposomal doxorubicin, docetaxel, capecitabine, vinorelbine, gemcitabine, and sorafenib.[5] Although typical palmar-plantar dysesthesia due to TKIs is frequently reported, atypical fixed drug reaction-like bullous erythro-dysesthesia is very rare.[6,7] In this report, we present a rare case of bullous drug reaction resembling a fixed drug eruption caused by cabozantinib.

CASE REPORT

A 79-year-old male patient was consulted to our department from the adult palliative care unit with a 3-week history of painful and pruritic lesions on the fingers of both hands and the left heel. Cabozantinib 40 mg/day had been initiated two months earlier for metastatic renal cell carcinoma. The lesions developed approximately three weeks after the start of treatment.

Dermatological examination revealed tense bullae with erythematous, well-demarcated borders on the distal palmar surfaces of the fingers (Figure 1) and a similar bullous lesion on the left heel (Figure 2). The lesions were painful and tender. There was no mucosal involvement, systemic symptoms, or fever.

The patient's medical history included hypertension, chronic obstructive pulmonary disease, congestive heart failure, hypothyroidism, diabetes mellitus, right nephrectomy, and bone metastases due to renal cell carcinoma. His regular medications included apixaban, metoclopramide, calcium, magnesium, vitamin D3, fluticasone, salmeterol, metoprolol, pantoprazole, losartan, hydrochlorothiazide, sertraline, and levothyroxine. One week prior to presentation, he had taken nitrofurantoin and ciprofloxacin for a urinary tract infection, but the lesions had appeared before these drugs.

Laboratory findings revealed normal complete blood count. Liver function tests, bilirubin, alkaline phosphatase, and C-reactive protein were mildly to moderately elevated. A diagnosis of atypical fixed drug reaction-like bullous erythrodysesthesia induced by cabozantinib was made. The patient was treated with topical fusidic acid 20 mg/g and betamethasone valerate 1 mg/g cream, along with hamamelis virginiana ointment, applied twice daily for 10 days. Lesions improved one month after discontinuation of cabozantinib. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

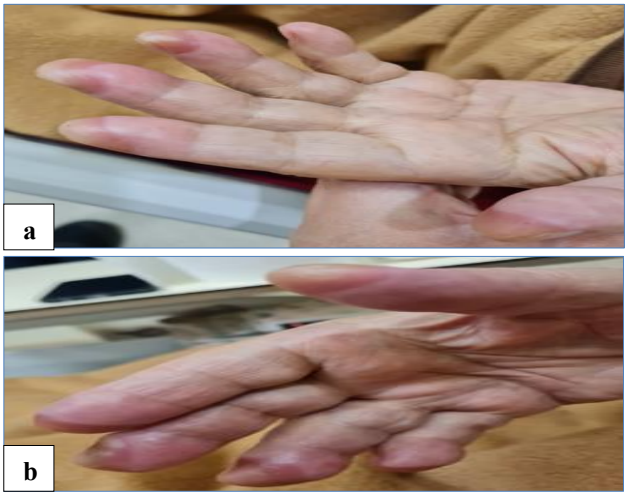

Figure 1 (a and b): Left hand palmar surface: erythematous, sharply demarcated, bullous lesion on the distal part of the fingers.

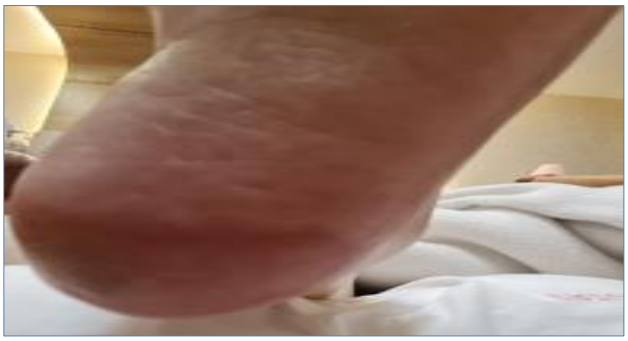

Figure 2: Right heel: erythematous, sharply demarcated bullous lesion.

DISCUSSION

Classic chemotherapy-induced PPES is characterized by dysesthesia and tingling on the dorsal surfaces of the hands and feet, palmar-plantar, and intertriginous areas. Over time, dryness, cracking, desquamation, edema, and ulceration may occur on the erythematous base. Notably, the erythema is typically diffuse with poorly defined borders. Lesions are most prominent at pressure points on the palms and soles but may also affect the lateral surfaces of the hands and feet, interdigital areas, and periungual skin under mechanical stress.[2,5] In a study involving 41 patients on cabozantinib, PPES was observed in 54%, characterized by painful, bilateral, localized callus-like hyperkeratosis and surrounding edema and erythema affecting the palmoplantar surfaces.[2] Although erythrodysesthesia is a well-known side effect of TKIs, bullous erythrodysesthesia is unusual and rare.[6] In our case, the presentation differed from classic PPES by featuring sharply demarcated bullous lesions without hyperkeratosis.

The pathogenesis of PPES is not fully understood. Hypotheses include high local drug concentrations in eccrine glands, drug leakage into surrounding tissues due to capillary microtrauma in areas under mechanical stress, and accumulation of drug metabolites in specific skin regions.[2] Histopathology typically shows keratinocyte vacuolization, hyperkeratosis, parakeratosis, inflammatory infiltrates, telangiectasia, and acanthosis.[7] A biopsy was planned but could not be performed due to the patient's refusal. Diagnosis was based on clinical presentation and history. The lesions emerged during the third week of cabozantinib therapy and regressed after discontinuation, further supporting a drug-related reaction.

Another differential diagnosis considered was bullous fixed drug eruption (FDE), a form of delayed-type hypersensitivity. FDE typically appears 1-2 weeks after initial exposure and recurs quickly upon re-exposure. Post-inflammatory hyperpigmentation may persist for months. Although not uncommon, bullous FDE on hands and feet is rare and usually involves few lesions.[8] In our case, the patient had bullous erythema on almost all distal finger surfaces, differing significantly from classic FDE. A similar case of cabozantinib-induced atypical bullous erythrodysesthesia was reported in the literature, with clinical features closely resembling ours.[6] That report also considered FDE in the differential diagnosis. Given the sharply demarcated lesions and their atypical nature, we classified the case as fixed drug reaction-like bullous erythrodysesthesia.

Current treatment recommendations for PPE are mainly based on case reports and series due to lack of clinical trial data. Dose reduction or discontinuation of the drug often leads to rapid improvement of painful lesions. Topical corticosteroids (e.g., clobetasol) may be beneficial for erythematous and inflammatory lesions. Limited data exist on systemic therapies such as vitamin E and pyridoxine

(vitamin B6).[2] The U.S. Food and Drug administration advises withholding cabozantinib until symptoms resolve or reduce to grade 1 toxicity.[9] If treatment must be continued, it should be reintroduced at a lower dose with caution. Growcott et al. reported a similar case in which lesions regressed two weeks after drug discontinuation and topical steroid use.[6]

CONCLUSION

In conclusion, cabozantinib-induced bullous erythrodysesthesia is a rare and atypical presentation of PPES that may clinically mimic bullous fixed drug eruption. Recognition of its characteristic sharply demarcated bullous lesions and temporal relationship with cabozantinib is important for accurate diagnosis and appropriate management. Early drug withdrawal can lead to complete clinical improvement.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Hasan AA, Masuo Y, Fujita KI, Shimada K, Iida N, Wakayama T, et al. Discrimination of hand-foot skin reaction caused by tyrosine kinase inhibitors based on direct keratinocyte toxicity and vascular endothelial growth factor receptor-2 inhibition. Biochem Pharmacol. 2022;197:114914.
2. Zuo RC, Apolo AB, DiGiovanna JJ, Parnes HL, Keen CM, Nanda S, et al. Cutaneous adverse effects associated with the tyrosine-kinase inhibitor cabozantinib. JAMA Dermatol. 2015;151(2):170-7.
3. National Institute for Health and Care Excellence (NICE). Cabozantinib for previously treated advanced renal cell carcinoma. NICE Technology Appraisal Guidance [TA463]. London: NICE; 2018.
4. Nagore E, Insa A, Sanmartín O. Antineoplastic therapy-induced palmar plantar erythrodysesthesia ("hand-foot") syndrome: incidence, recognition and management. Am J Clin Dermatol. 2000;1(4):225-34.
5. Webster-Gandy JD, How C, Harrold K. Palmar-plantar erythrodysesthesia (PPE): a literature review with commentary on experience in a cancer centre. Eur J Oncol Nurs. 2007;11(3):238-46.
6. Growcott S, Banner A, Bray A, Hilman S. A rare cutaneous adverse effect secondary to cabozantinib therapy. Oxf Med Case Rep. 2018;2018(12):omy105.
7. Yang CH, Lin WC, Chuang CK, Chang YC, Pang ST, Lin YC, et al. Hand-foot skin reaction in patients treated with sorafenib: a clinicopathological study of cutaneous manifestations due to multitargeted kinase inhibitor therapy. Br J Dermatol. 2008;158(3):592-6.
8. Lee AY. Fixed drug eruptions: incidence, recognition, and avoidance. Am J Clin Dermatol. 2000;1(5):277-85.
9. U.S. Food and Drug Administration. CABOMETYX™ (Cabozantinib) tablets, for oral use: Prescribing information. Silver Spring (MD): FDA; 2021.

Cite this article as: Metin N, Korkmaz H. Atypical bullous erythrodysesthesia mimicking fixed drug eruption during cabozantinib therapy: a case report. Int J Sci Rep 2026;12(9):311-3.