DOI: 10.7860/JCDR/2026/82939.23893

Case Report

Dermatology Section

A Case Report on Cabozantinib-induced Hand-Foot Skin Reaction

BHAKTI JAIPRAKASH SARDA[1], BHUSHAN MADKE[2], ASHISH VAIDYA[3], NAGA NITYA VANGALA[4]

ABSTRACT

Cabozantinib is a multi-targeted tyrosine kinase inhibitor that targets Vascular Endothelial Growth Factor Receptor (VEGFR) 2, c-MET, and RET. It exhibits antiangiogenic and antitumorigenic effects and has the potential to treat a variety of malignancies. Palmar-Plantar Erythrodysesthesia (PPE), one of the most common side-effects of tyrosine kinase inhibitors, can have a considerable impact on patients' quality of life and medication adherence, making it a key therapeutic obstacle in maximising the efficacy of targeted cancer therapy. We describe a rare early-onset bullous type of PPE that developed within 15 days of starting cabozantinib in a 32-year-old woman with papillary renal cell carcinoma. The patient developed severe bullous and hyperpigmented acral lesions, which hampered everyday activities. The response followed a dosage-dependent pattern, with partial improvement and relapse after dose adjustment and full resolution after additional dose reduction and topical treatment. This case emphasises the need to identify unusual and early signs of PPE to provide prompt care while maintaining oncologic therapy.

Keywords: Adverse reactions, Acral dermatoses, Antineoplastic agents, Drug-related side effects, Skin toxicity, Tyrosine kinase inhibitors

CASE REPORT

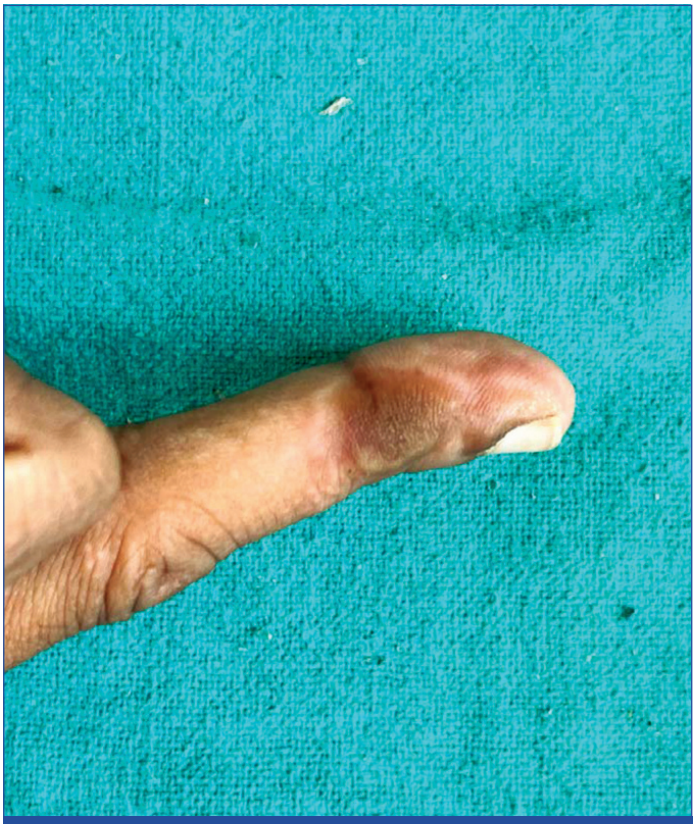
A 32-year-old female presented to the dermatology outpatient department with painful, pruritic lesions over the fingers and feet, significantly interfering with activities of daily living. She was a known case of left papillary renal cell carcinoma with sarcomatoid differentiation, status post-left radical nephrectomy. The lesions appeared fifteen days after initiation of oral cabozantinib 60 mg once daily.

She had no history of diabetes mellitus, peripheral vascular disease, autoimmune disorders, or prior dermatological illness. There was no history of chemotherapy or radiotherapy, and she was not receiving any other medications known to cause PPE. Baseline haematological and biochemical investigations, including liver and renal function tests, were within normal limits.

Cutaneous examination revealed a tender, tense bulla on the medial aspect of the right third digit [Table/Fig-1] and well-defined, circular, hyperpigmented, tender plaques on the plantar surfaces of both great toes [Table/Fig-2]. Based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, the patient was diagnosed with Grade 3 PPE, as the lesions were painful and restricted routine daily activities [1].

A skin biopsy was deferred since the temporal association with drug initiation, characteristic acral distribution, dose-dependent course, and clinical response to dose modification were sufficient for diagnosis. Histopathological evaluation would not have altered management, as supported by previous literature [2]. Bullous fixed drug eruption and erythema multiforme were considered in the differential diagnosis but excluded due to absence of mucosal involvement, lack of target lesions, and no recurrence at the same sites after dosage stabilisation.

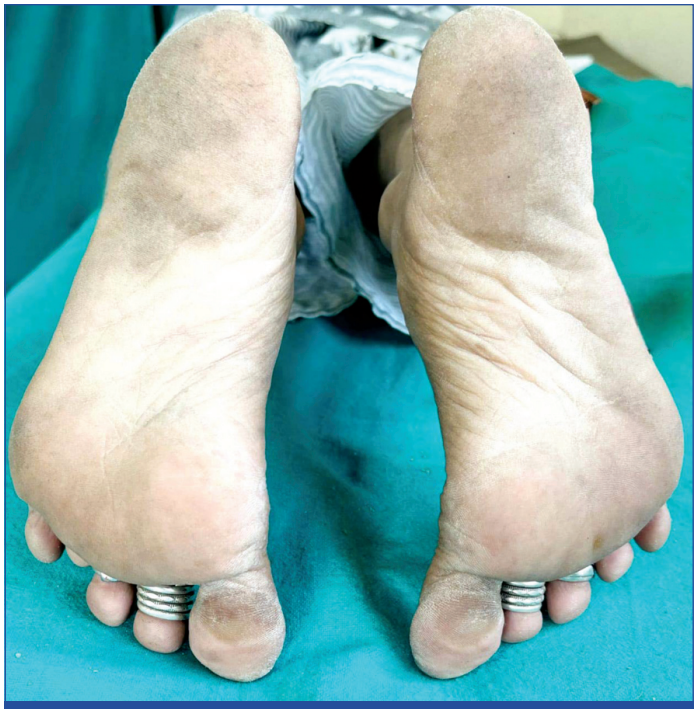
Cabozantinib dose was reduced to 40 mg daily, resulting in partial improvement after seven days. However, lesions recurred within five days. The patient was then treated with topical clobetasol propionate 0.05% ointment twice daily for ten days, along with an emollient cream containing glycerin and white soft paraffin thrice daily. Systemic analgesics were prescribed for pain relief. Complete resolution of lesions was achieved within ten days. Subsequently, cabozantinib was further reduced to 20 mg daily, with no recurrence observed. The patient was followed up monthly for three months and remained in remission.



[Table/Fig-1]: Tense bulla on the medial aspect of the right third digit in a patient receiving cabozantinib therapy.

DISCUSSION

The PPE, often known as hand-foot syndrome, is a common dermatologic complication linked with several cytotoxic and targeted anticancer drugs, including multikinase inhibitors like cabozantinib [3]. Previous research has shown that PPE occurs in 9-62% of patients on multikinase inhibitors [2].



[Table/Fig-2]: Well-defined, hyperpigmented, tender plaques on the plantar surfaces of both great toes consistent with palmar–plantar erythrodysesthesia.

Although the actual mechanism of PPE is not entirely understood, several contributing aspects have been proposed, including direct cytotoxic damage to keratinocytes, eccrine-mediated drug clearance, and frequent mechanical stress over pressure-prone acral regions [4]. Hand-foot syndrome, or chemotherapy-associated acral erythema, is a cutaneous toxicity syndrome that has traditionally been associated with cytotoxic chemotherapy agents (5-fluorouracil, capecitabine, cytarabine, docetaxel, liposomal doxorubicin); however, it is now being linked to the use of molecular agents (cabozantinib, sorafenib, axitinib, sunitinib, pazopanib) [5].

Cabozantinib affects vascular repair and epidermal homeostasis through inhibition of VEGFR-mediated signalling pathways, rendering acral skin more susceptible to injury [2,6].

Acral skin is especially sensitive because of its significant eccrine gland population, absence of pilosebaceous units, rapid epidermal renewal, constant exposure to frictional forces, and specific vascular features [4]. Clinically, PPE often presents as sensory abnormalities or erythema of the palms and soles, which can progress to blistering, scaling, fissuring, ulceration, and oedema in the absence of prompt management [7].

Severity evaluation of PPE is frequently undertaken using the CTCAE, which provides a standardised framework for classifying cutaneous toxicities [1]. In this instance, the early onset and bullous morphology indicate an increased acral vulnerability to cabozantinib-induced vascular and epidermal damage. The dose-dependent recurrence provides additional evidence for a causal link.

Therapeutic options for PPE are determined by severity, with mild cases responding well to conservative therapies such as emollients, keratolytic drugs, and adjustment of aggravating mechanical or environmental factors [5]. Preventive methods such as patient education, early emollient use, and friction avoidance were reinforced after the initial episode in this patient, and they most likely led to long-term remission after dose reduction.

Hand-Foot Skin Reaction (HFSR) is a recognised class effect of VEGFR-targeting multikinase inhibitors, with previously reported cases of sorafenib and sunitinib describing early onset (within 2-6 weeks) of painful, well-demarcated hyperkeratotic plaques over pressure-bearing areas, commonly corresponding to CTCAE grade 2 severity and occasionally requiring dose modification [2]. Our patient developed similarly localised, tender hyperkeratotic lesions shortly after initiating cabozantinib, reflecting a comparable mechanical distribution and presumed VEGFR inhibition-mediated microvascular injury. Consistent with earlier reports, symptoms improved with topical corticosteroids, keratolytics, and supportive care, allowing continuation of anticancer therapy, thereby highlighting the shared toxicity profile and the importance of early dermatologic intervention [7]. Belum VR et al. conducted a meta-analysis evaluating cabozantinib-associated HFSR in patients with solid malignancies. The study demonstrated that both the incidence and risk of developing HFSR with cabozantinib were considerably high. The authors emphasised that timely recognition of this dose-limiting adverse event is essential to guide supportive care, ensure appropriate patient counselling, and implement preventive or therapeutic interventions [8]. Similar to our case, Growcott S et al. reported a case of 67-year-old man with metastatic renal cell carcinoma who developed a bullous skin reaction confined to both hands after two weeks of cabozantinib 40 mg daily, initiated as third-line therapy. The lesions were painful, pruritic, and functionally disabling, leading to difficulty with basic activities such as feeding and personal hygiene. Examination revealed tense bullae with erythematous borders on the fingers, thumbs, and palmar surfaces, accompanied by sensory deficits. Cabozantinib was discontinued, and supportive management with emollients and potent topical steroids was instituted, resulting in complete resolution within two weeks. The drug was successfully reintroduced at a reduced dose of 20 mg daily without recurrence [9]. The current case stands out for its early onset, bullous morphology, and clear dose-response relationship, highlighting a distinct clinical presentation.

CONCLUSION(S)

This case describes an uncommon early-onset bullous manifestation of cabozantinib-induced PPE with a distinct dose-dependent history. Early detection of PPE and timely therapeutic action, including topical therapy and dosage reduction, were crucial in avoiding development and enabling continuous oncologic treatment. Recognising such unusual appearances is critical for optimising patient care and increasing treatment adherence.

REFERENCES

[1] National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. 2017. Available at: https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf, Last accessed on 12/01/2026.

[2] Lacouture ME, Wu S, Robert C, Atkins MB, Kong HH, Guitart J, et al. Evolving strategies for the management of hand-foot skin reaction associated with the multitargeted kinase inhibitors sorafenib and sunitinib. Oncologist. 2008;13(9):1001-11. Doi: 10.1634/theoncologist.2008-0131. Epub 2008 Sep 8. PMID: 18779536.

[3] Rathi N, Maughan BL, Agarwal N, Swami U. Cabozantinib in the treatment of advanced renal cell carcinoma and hepatocellular carcinoma. Cancer Manag Res. 2020;12:3741-49.

[4] Farr KP, Safwat A. Palmar-plantar erythrodysesthesia associated with chemotherapy and its treatment. Case Rep Oncol. 2011;4(1):229-35.

[5] Gupta A, Mehta A, Khanna S. Palmar–plantar erythrodysesthesia. BMJ Case Rep. 2015;2015:bcr2015212434.

[6] Zuo RC, Apolo AB, DiGiovanna JJ, Parnes HL, Keen CM, Nanda S, Dahut WL, Cowen EW. Cutaneous adverse effects associated with the tyrosine-kinase inhibitor cabozantinib. JAMA Dermatol. 2015;151(2):170-77. Doi: 10.1001/jamadermatol.2014.2734. PMID: 25427282; PMCID: PMC6776420.

[7] Webster-Gandy JD, How C, Harrold K. Palmar-plantar erythrodysesthesia: A literature review. Eur J Oncol Nurs. 2007;11(3):238-46.

[8] Belum VR, Serna-Tamayo C, Wu S, Lacouture ME. Incidence and risk of hand-foot skin reaction with cabozantinib, a novel multikinase inhibitor: A meta-analysis. Clin Exp Dermatol. 2016;41(1):8-15. Doi: 10.1111/ced.12694. Epub 2015 May 25. PMID: 26009777; PMCID: PMC5066302.

[9] Growcott S, Banner A, Bray A, Hilman S. A rare cutaneous adverse effect secondary to cabozantinib therapy. Oxford Medical Case Reports. 2018;2018:omy105. Available from: https://doi.org/10.1093/omcr/omy105.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
2. Professor, Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
3. Professor, Department of Medical Oncology, Siddharth Gupta Memorial Cancer Hospital, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
4. Junior Resident, Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Bhakti Jaiprakash Sarda,
Sawangi (Meghe), Wardha, Maharashtra, India.
E-mail: bhaktisarda99@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 11, 2025
- Manual Googling: Apr 04, 2026
- iThenticate Software: Apr 06, 2026 (2%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Aug 26, 2025**
Date of Peer Review: **Dec 27, 2025**
Date of Acceptance: **Apr 08, 2026**
Date of Publishing: **Jul 01, 2026**