Capecitabine-induced palmo-plantar erythrodysesthesia (toxic erythema of chemotherapy)

Nidhi Pugalia, Riddhima Singh, Bhushan Madke, Kaveri Rusia, Sharwari Jaiswal

Affiliations: Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Higher Education and Research, Jawaharlal Nehru Medical College, Sawangi Meghe, Wardha, Maharashtra, India

Corresponding Author: Bhushan Madke, Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Higher Education and Research, Jawaharlal Nehru Medical College, Sawangi Meghe, Wardha, Maharashtra, India, Email address: drbhushan81@gmail.com

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To the Editor:

A 74-year-old woman presented with intense redness, discomfort, and peeling skin of both her the palms and soles. The patient had a history of modified radical mastectomy for stage IV adenocarcinoma of the breast six years prior. In the post-operative period, she received six cycles of chemotherapy and 25 sessions of radiation therapy. Recently she had presented with recurrence of her malignancy and metastasis to the spine. She was prescribed oral capecitabine (500mg every other day) a palliative chemotherapy. After three weeks of oral capecitabine use, she developed discomfort in her palms and soles followed by redness, swelling, and peeling of skin.

Cutaneous examination showed intense erythema, fissuring, swelling, and exfoliation of acral skin limited to palms and soles (**Figure 1**). She was prescribed oral gabapentin for pain relief, topical bland petrolatum, and super-potent topical corticosteroid ointment (clobetasol propionate 0.05%). She was asked to use ice cold compresses according to her tolerance. Our patient was advised to continue oral capecitabine therapy. On the basis of clinical findings and temporal association we diagnosed palmo-plantar erythrodysesthesia, a form of toxic erythema of chemotherapy (TEC).

Acral chemotherapy-related erythema is also known as palmar-plantar erythrodysesthesia, palmoplantar erythrodysesthesia, toxic erythema of the palms and soles, hand-foot syndrome (HFS), and Burgdorf reaction. It is an adverse event caused by many classic chemotherapeutic agents and newer molecular targeted therapies. Capecitabine is an oral fluoropyrimidine prodrug which was authorized by the U.S. Food and Drug Administration in 1998 [1]. Capecitabine alone or in combination with docetaxel is a common anti-cancer regimen [2,3]. Hand-foot syndrome was first described by Dr. Zuehlke in a patient receiving mitotane therapy [4]. Dysesthesia, tingling in the palms, fingers, and soles of the feet, and erythema are the first signs of HFS, which can quickly escalate to a severe and debilitating illness if not treated. Patients on capecitabine may experience impaired quality of life as a result of these symptoms [5,6]. Apoptotic keratinocytes, vacuolar degeneration of basal keratinocytes, dermal edema,

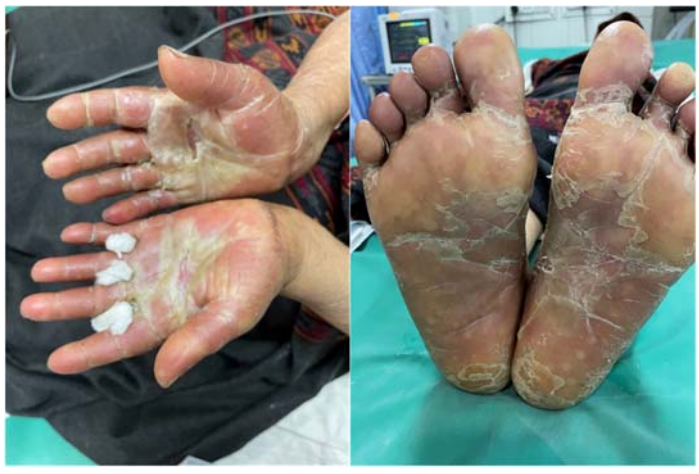

Figure 1. *Severe erythema, scaling, and peeling of acral skin of both **A)** the palms, and **B)** the soles*

and dermal perivascular lymphocytic infiltration are pathological changes of HFS [7]. Capecitabine is a more selective alternative to 5-fluorouracil (5FU) since it is transformed into the active form only in tumor cells, reducing the side effects of 5FU, such as neutropenia and stomatitis [1]. Despite this, a substantial number of capecitabine-treated individuals (almost 50%) are afflicted by HFS, with 17% of patients suffering from a severe form (grade 3), [6].

Hands are frequently afflicted more severely than the feet. Hand-foot syndrome has a prodrome of dysesthesia in the palms and soles, which is followed by painful, symmetric, well-defined erythema and edema in a few days [9,10] The median onset time is 79 days, with a range of 11 to 360 days. Skin regeneration usually takes one to two weeks after the withdrawal of the drug [10]. Apart from 5FU and capecitabine, other chemotherapeutic agents known to cause HFS include cytarabine, liposomal doxorubicin, hydroxyurea, mercaptopurine, cyclophosphamide, and docetaxel [10].

The core of HFS therapy are topical emollients, and corticosteroid creams and ointments. In extreme situations, the chemotherapeutic drug is stopped and then reintroduced at a reduced dose after the symptoms have subsided. Hand-foot syndrome typically resolves quickly and does not recur. If symptoms reappear, especially with a higher grade of involvement, the drug may need to be withheld. Topical wound care, limb elevation, and cold compresses are various supportive therapies that can help alleviate pain. Topical 99% dimethyl-sulfoxide, systemic corticosteroids, and oral pyridoxine have all been used with mixed results [11]. Lastly, we would like to emphasize that various descriptive terminology, e.g., acral erythema, acral erythrodysesthesia, chemotherapy-induced acral erythema, hand-foot syndrome, and palmar-plantar (palmoplantar) erythrodysesthesia should be avoided and a single entity named toxic erythema of chemotherapy may be preferred because of the wide variety of presentations [12].

Potential conflicts of interest

The authors declare no conflicts of interest.

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