

Case Report

Hand and foot syndrome secondary to capecitabine

Murali Narasimhan, Abhishek Kumar, Ramachandran Ramakrishnan*

Department of Dermatology Venereology Leprology, SRM Medical College Hospital and Research Centre, Potheri, Tamil Nadu, India

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***Correspondence:**

Dr. Ramachandran Ramakrishnan,
E-mail: drram.srkn@gmail.com

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ABSTRACT

Hand and foot syndrome are an adverse effect often seen with chemotherapy or with the use of biologics. It is characterised by painful erythema and edema, dry or moist desquamation of palms and soles in mild to moderate case. Severe cases usually present with cracking, peeling, blister, ulcer and severe pain. Here we report a 65-year-old woman with breast carcinoma who was on treatment with capecitabine and presented with fissuring and bleeding over palms and soles, with progressive burning sensation. On examination, hyperpigmentation and scaling were also noted over both palms and soles. She was diagnosed with hand and foot syndrome and was treated with emollients, antibiotics and topical steroids.

Keywords: Capecitabine, Chemotherapy, Hand and foot syndrome

INTRODUCTION

Hand and foot syndrome (HFS) also known as acral erythema, palmar - plantar erythrodysesthesia, Burgdorf's reaction or toxic erythema of the palms and soles, is an adverse effect of acute onset, usually noted with chemotherapeutic agents (5-Fluorouracil, cytarabine and doxorubicin), multikinase inhibitors (e.g. sorafenib, sunitinib and regorafenib) and BRAF inhibitors (e.g. vemurafenib and dabrafenib).^{1,2}

Cases of capecitabine, methotrexate and etoposide causing Hand and foot syndrome have also been reported.³⁻⁵ When not treated in early stage, HFS can progress from a mild cutaneous reaction to an immensely painful and crippling condition with substantial effect on a patient's quality of life.

CASE REPORT

A 65 year old lady with carcinoma breast was operated and started on chemotherapy with letrozol and capecitabine.

Ten days later, she developed burning sensation over hands and feet, pain and tenderness on holding objects, followed by fissuring, bleeding and difficulty in daily activities. On dermatological examination, hyperpigmentation and scaling were present over both palms and soles.

Fissuring and bleeding were noted over both palms and soles. Patient was diagnosed clinically as Hand and foot syndrome following capecitabine therapy. Patient was treated with oral antibiotics, liquid paraffin and topical steroids under occlusion and lesions resolved well with the treatment (Figure 1).



Figure 1: (A and B) Scaling, hyperpigmentation, fissuring and bleeding with crusted lesions noted over both palms and soles; (C and D) lesions over palms and soles started resolving with treatment.

DISCUSSION

Capecitabine, a fluoropyrimidine carbamate derivative is an oral prodrug of 5-fluorouracil.⁶ It is used as tumor selective cytotoxic drug in the treatment of colorectal and breast carcinomas, which are recalcitrant to standard chemotherapies. Hand and foot syndrome are well known adverse effect of capecitabine. HFS was first described by Lokich and Moore in 1984, reported in case treated with 5-fluorouracil.⁷ HFS is a dose-dependent adverse effect. The pathogenesis of HFS is by accumulation of drug in the stratum corneum of the palms and soles, which is rich in eccrine glands and deficient in sebaceous gland, reaching toxic quantities and causing local injury. Other proposed mechanisms include stimulation of melanogenesis by elevating levels of melanocyte stimulating hormone, reduction of levels of tyrosinase inhibitors and stable drug-melanin complex formation, increased photosensitivity, and increased enzyme activity resulting in higher concentration of active metabolite in these areas.^{8,9} Initially, HFS manifests as dysesthesia, paresthesia and an increasing discomfort over hands and feet. Later, patients may develop burning sensation, pain and tenderness while holding objects and difficulty in standing or walking, followed by a progressive, symmetric edema and erythema starting over the thenar and hypothenar eminences. At this stage, patient may complain severe pain even at rest. Blisters may develop in very severe cases followed by ulceration and bleeding. The condition heals over a few weeks with desquamation over the hands and feet. Grading can be done by WHO classification systems (Table 1).¹⁰

Table 1: Various proposed classification of HFS.¹⁰

Grades	WHO classification system
Grade 1	Erythema and dysesthesia
Grade 2	Erythema, edema and pain when grasping objects or walking
Grade 3	Periungual compromise and fissures
Grade 4	Blisters, ulcers, and severe pain, making walking or use of hands difficult.

Skin biopsy and histopathological examination shows vacuolar degeneration of basal keratinocytes, apoptotic keratinocytes, dermal edema and dermal perivascular lymphocytic infiltration. The management of Hand and Foot syndrome differ according to the grades. Grade 1 and 2 patients can be treated symptomatically with emollients, cold compresses, wet dressings, topical corticosteroids and antibiotics (to prevent secondary infection). In patients with grade 3 HFS, drug should be stopped or given in reduced (25-50% of) dose, along with intensive topical care. In patients with grade 4 HFS, drug should be completely stopped to avoid recurrences or worsening of the existing condition.¹¹ Avoidance of sunlight, heat and elevation of hands and feet may provide symptomatic relief. Oral vitamin B6 (pyridoxine) may be beneficial in few cases. Our patient had grade 3 HFS and she was treated with intense topical care while continuing the drug, and she improved well.

CONCLUSION

Hand and foot syndrome can impair physical and psychosocial condition in patients undergoing treatment for cancer. Early intervention is essential to prevent high grade complications of cutaneous toxicity and consequent anti-cancer treatment disruption.

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