Docetaxel-induced hand foot syndrome: "No dose is a safe dose"

Ankit Jain, Biswajit Dubashi

Department of Medical Oncology, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry 6, India

ABSTRACT

Docetaxel is an important chemotherapeutic agent used in the management of many solid tumors. The most important side effect of this drug is myelosupression. We report a case of carcinoma breast that developed severe hand-foot syndrome at 75 mg/m^2 doses of docetaxel. The exact mechanism of this side effect in not known. All the physicians using this drug must be aware of this side effect.

Key words: Acral erythema breast cancer, docetaxel, hand foot syndorme, palmo-plantar dysesthesia

INTRODUCTION

Hand-foot syndrome (HFS), acral erythema, or palmo plantar dysesthesia is a dermatological toxicity caused by many anticancer drugs.[1] The most common drugs implicated for this toxicity are capecitabine, liposomal doxorubicin, geftinib, and sunitinib. Docetaxel is also a common agent which causes HFS.[2] We report the clinical findings of docetaxel-induced HFS.

CASE REPORT

A 45-year-old female with breast cancer received adjuvant chemotherapy with three cycles of FEC100 regimen (5-flurouracil, epirubicin, and cyclophosphamide) followed by docetaxel 75 mg/m^2 four cycles. The premedications used prior to docetaxel infusion were ranitidine 50 mg, dexamethasone 16 mg, and ondansetron 8 mg. She developed painful erythema of both the hands when she came for follow-up after 10 days for the interim count. This was followed by desquamation of skin over the dorsum of hand and palms [Figures 1 and 2]. The patient was diagnosed as a case of Grade II HFS and was treated conservatively with emollients, and analgesics. The further cycles of docetaxel were continued at usual interval without further worsening of lesions and symptomatic treatment of HFS.

Access this article online	
Quick Response Code:	Website: www.jpharmacol.com
	DOI: 10.4103/0976-500X.95534

DISCUSSION

There are many case reports of docetaxel-induced HFS. In most of the case reports, the HFS is more common at higher doses of docetaxel such as 100 mg/m^2 or a dose-dense regimen. Our patient successfully completed all the four cycles of docetaxel. In a case series of five patients, all the patients developed HFS at doses of 100 mg/m^2 or if the docetaxel was given in a dose-dense manner.[2] The peculiarity of our case is the development of HFS at a dose of 75 mg/m^2, and she successfully completed all the cycles of chemotherapy. In a retrospective chart analysis of 2186 patients who received chemotherapy, 44 cases of acral erythema were identified. The most commonly implicated drugs were infusional 5-fluroruracil (5-FU) (22.7% of all cases of acral erthema), bolus 5-FU (13.6%), docetaxel (13.6%), liposomal doxorubicin (11.3%), and vinorelbine (9%).[3] Capecitabine has now become more common in view

Address for correspondence:
Ankit Jain, HIG 251, Thiruvikas Street, Lawspet Ashok Nagar, Puducherry 8, India. E-mail: ankitjaindm@gmail.com

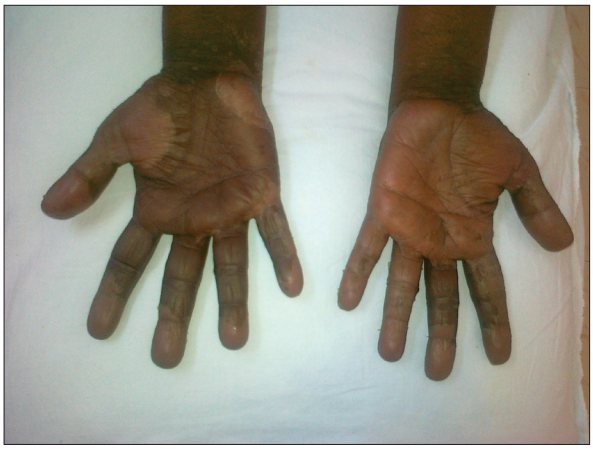

Figure 1: Palmar surface showing typical desquamated epithelium with redness characteristic of docetaxel-induced HFS

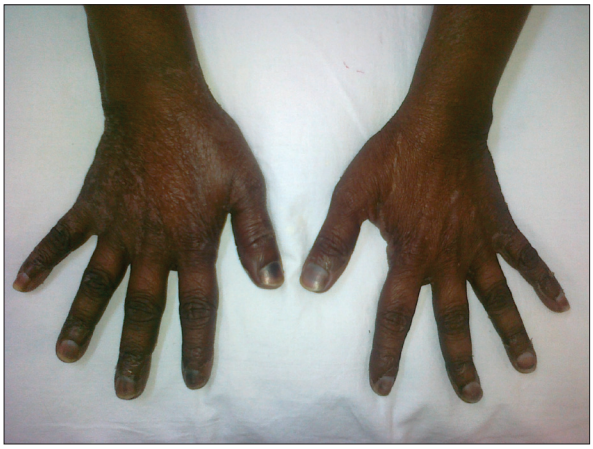

Figure 2: Dorsum of hand with desquamation, black discoloration as seen in established HFS

of more wider uses as compared to infusional 5-FU. The exact pathogenetic mechanism is not known for HFS, but the most commonly accepted effect is a direct toxic effect on epidermal cells.[3] In a retrospective observation analysis from Japan, the use of H2 blockers has been implicated as a cause of severe dermatological toxicity of HFS. This was seen in both univariate and multivariate analysis. This is because of inhibitory effects of H2 receptor blockers on CYP3A4 enzyme. The inhibition of this enzyme decreases the metabolism of docetaxel and therefore increases the toxicity such as myelosuppression and skin toxicity. The limitation of this study is retrospective nature, no pharmacokinetic data and doses used for H2 blockers were based on institutional policy and were not standardized.[4]

The management revolves around reduction in the dose, drug withdrawal, changing the administration intervals. These are the most successful methods in the management. Till now administration of pyridoxine was considered as a standard of care in the management of HFS. Recently, one randomized controlled trial has disproved this and no proven therapy is currently available for the management of HFS.[5]

In conclusion, docetaxel-induced HFS is a common toxicity and all physicians must be aware of this side effect. The important point of discussion is that it can occur at any dose of docetaxel, any schedule (dose dense or three weekly), not associated with concurrent administration of filgrastim. Correlation of HFS with docetaxel with premedications such as H2 blockers requires more prospective studies.

REFERENCES

1. Chu CY, Yang CH, Yang CY, Hsaio GH, Chiu HC. Fixed erythrodysaesthesia plaque due to intravenous injection of docetaxel. Br J Dermatol 2000;142:808-11.
2. Farhat HM, Nagi S, Saghir EL, Shamseddine AI. Hand foot syndrome with docetaxel: A five case series. Ann Saudi Med 2008;28:374-7.
3. Hueso L, Sanmartin O, Nagore E, Estrada RB, Requena C, Liombart B, *et al*. Chemotherapy induced acral erythema: A clinical and histopathological study of 44 cases. Actas Dermosifiliogr 2008;99:281-90.
4. Kawaguchi K, Ishiguro H, Morita S, Nakamura S, Ohno S, Masuda N, *et al*. Correlation between docetaxel induced skin toxicity and the use of steroids and H2 blockers: A multi-institution survey. Breast Cancer Res Treat 2011;130:1641-9.
5. Kang YK, Lee SS, Yoon DH, Lee SY, Chun YJ, Kim MS, *et al*. Pyridoxine is not effective to prevent hand-foot syndrome associated with capecitabine therapy: Results of a randomized, double-blind, placebo-controlled study. J Clin Oncol 2010;28:3824-9.

How to cite this article: Jain A, Dubashi B. Docetaxel-induced hand foot syndrome: "No dose is a safe dose". J Pharmacol Pharmacother 2012;3:200-1.

Source of Support: Nil, **Conflict of Interest:** None declared.