Paclitaxel-induced dorsal hand-foot syndrome

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Abstract

Hand-foot syndrome (HFS), also known as palmoplantar erythrodysesthesia or acral erythema, is a known adverse effect of chemotherapeutic agents that most commonly presents as palmoplantar dysesthesia and erythematous plaques localized to the palms and soles. Paclitaxel is an uncommon cause of HFS and is notable for its unique presentation on the dorsal hands and feet. We present an unusual case of paclitaxel-induced HFS localized to the dorsal hands of a 66-year-old man with metastatic angiosarcoma. Early identification and management of HFS is critical to allow for continuation of chemotherapy while improving patient quality of life.

Keywords: acral erythema, chemotherapy, hand-foot, paclitaxel, palmoplantar erythrodysesthesia, toxic erythema

Introduction

Hand-foot syndrome (HFS), also known as palmoplantar erythrodysesthesia or acral erythema, is a known adverse effect of chemotherapeutic agents and is characterized by palmoplantar dysesthesia and well-demarcated erythematous plaques most commonly involving the palms and soles. The incidence of HFS ranges from 6% to 64% and is most frequently associated with pegylated liposomal doxorubicin, capecitabine, 5-fluorouracil, cytarabine, and docetaxel [1]. Paclitaxel is an uncommon cause of HFS. We report a 66-year-old man with metastatic angiosarcoma treated with paclitaxel who developed HFS localized only to the dorsal hands.

Case Synopsis

A 66-year-old man with a history of multifocal hepatic angiosarcoma was initiated on single-agent paclitaxel. One week after completing six weekly doses of paclitaxel, he developed a rash on his bilateral dorsal hands. The patient reported paresthesia and numbness localized to the area of the rash and at his fingertips. The patient did not notice improvement with application of OTC topical hydrocortisone.

Physical examination showed erythematous scaly plaques symmetrically distributed on the medial and lateral aspects of the bilateral dorsal hands (**Figure 1**). Numbness was present within the plaques, but sensation was intact in the skin directly adjacent to the plaques. The palms and feet were clear of rash. This presentation was consistent with grade two severity of HFS according to the National Cancer Institute Common Terminology Criteria for Adverse Events. Histopathologic examination demonstrated areas of parakeratosis with hypergranulosis, occasional dyskeratotic keratinocytes in the basilar cell layer and superficial aspects of the eccrine ducts, and papillary dermal extravasation of red blood cells (**Figure 2**). The diagnosis of hand-foot syndrome was made. The patient significantly improved with clobetasol 0.05% cream and was then transitioned to 10% urea cream for preventive maintenance. The patient was continued on paclitaxel.

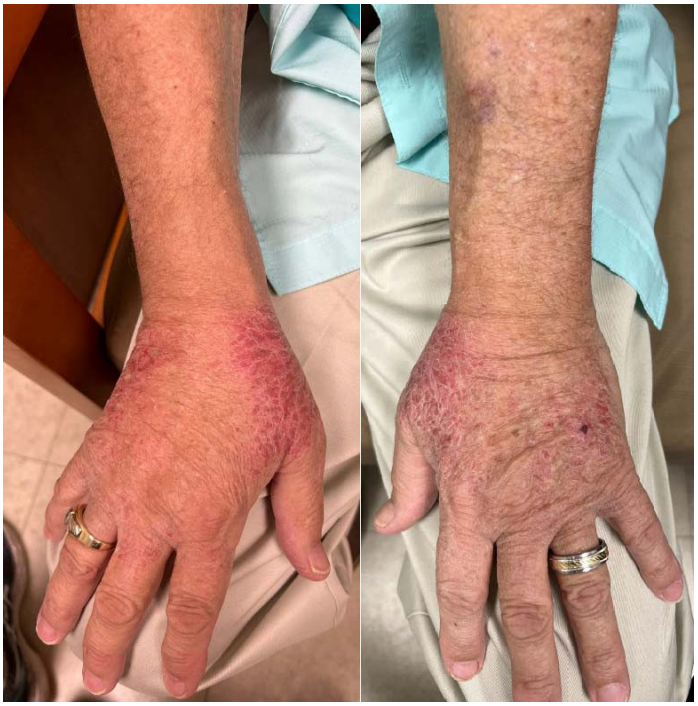

Figure 1. *Erythematous scaly plaques symmetrically distributed on the medial and lateral aspects of the bilateral dorsal hands.*

Case Discussion

Hand-foot syndrome is a well-documented adverse effect of chemotherapeutic agents. It classically presents with well-demarcated erythematous plaques and edema of the palms and soles accompanied by palmoplantar dysesthesia, such as tingling and burning pain [2]. Erythema can progress to blistering, erosion, or ulcerations [1]. These symptoms can oftentimes significantly impact quality of life and may necessitate discontinuation of treatment.

The incidence of HFS may be as high as 50% to 60% for certain chemotherapeutic agents, such as capecitabine and pegylated liposomal doxorubicin [1]. Hand-foot syndrome occurs in 5-10% of patients treated with taxanes and even more rarely occurs with paclitaxel when compared to docetaxel [3]. Taxanes are cytotoxic anti-microtubule agents that ultimately arrest mitosis [4]. They are a preferred treatment for angiosarcoma [5]. Dermatologic adverse events are common, although the true incidence is not known. They include HFS, flexural and intertriginous rashes, morbilliform rashes, pustular eruptions, drug-induced lupus erythematosus, scleroderma-like changes, radiation

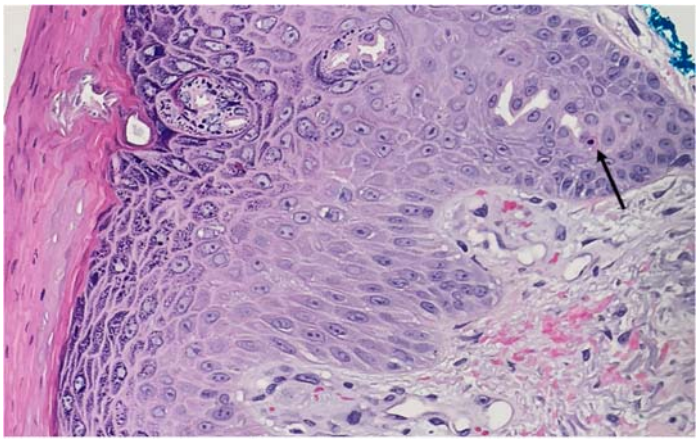

Figure 2. *Parakeratosis with coarse hypergranulosis, occasional dyskeratotic keratinocyte (indicated by black arrow) in the superficial aspect of the eccrine duct, and papillary dermal extravasation of red blood cells.*

and UV recall, pigmentary changes such as reticulate hyperpigmentation, edema, alopecia, subungual pyogenic granulomas, onycholysis, and mucositis [3,6-8]. Taxane-induced HFS is particularly notable for its unique presentation involving the dorsal hands and feet [3]. There are several case reports of paclitaxel-induced HFS. They are most notable for varying distributions of scaly erythematous plaques including involvement of the entire dorsal surfaces of the bilateral hands [9], both the dorsal hands and the soles [10], both the palms and the dorsal feet [11], the dorsal hands and palms as well as the soles [12], only the lateral surfaces of the dorsal feet [13], in a dermatomyositis-like distribution on the metacarpalphalangeal joints and interphalangeal joints [14], and on sun-exposed areas [15].

The pathophysiology of HFS is poorly understood, but it is believed to occur due to direct cytotoxic effect on keratinocytes with preferential secretion of chemotherapeutic agents by the eccrine ducts leading to predominant involvement of the palms and soles [1]. Other suggested mechanisms include increased trauma, rich capillary networks, and keratinocyte turnover of the palms and soles [1]. As these hypotheses do not explain the dorsal localization of HFS seen with paclitaxel, sun exposure may likely be a contributing factor [3].

Paclitaxel-induced photosensitive dermatoses include photo-distributed erythema multiforme, photo-onycholysis, UV recall phenomenon, and

subacute cutaneous lupus erythematosus [16,17]. There are also several reported cases of paclitaxel-induced photosensitivity [17,18]. One case demonstrated elevated urinary and erythrocyte porphyrins in a patient with metastatic breast cancer who was treated with paclitaxel and trastuzumab and developed photo-distributed erythema multiforme and onycholysis. Discontinuation of paclitaxel led to resolution of the rash and normalization of porphyrin levels [19]. A case series demonstrated aberrant porphyrin biosynthesis in several patients treated with paclitaxel; however, photosensitivity was not seen in all patients with elevated porphyrins [20]. It remains unclear whether the aberrations in porphyrin biosynthesis is causative or an epiphenomenon in the development of paclitaxel-induced photosensitivity.

Management of HFS is case dependent. Grade one HFS may be managed symptomatically, whereas more severe cases may require dose reduction, treatment interruption, or an alternative chemotherapeutic regimen; symptoms usually improve within one to two weeks. Avoidance of sun exposure, hot water, friction, and trauma may be helpful in preventing HFS [1]. Treatment is largely supportive and includes use of high-potency topical corticosteroids, urea-based creams, regional cooling, wound care, and pain control [1].

Conclusion

We presented a case of paclitaxel-induced HFS localized to the dorsal hands. Clinicians should be aware of paclitaxel as an uncommon cause of HFS and its unique presentation on the dorsal hands and feet. Early identification and management of paclitaxel-induced HFS can minimize interruptions in chemotherapy, while maintaining patient quality of life, as in our case.

Potential conflicts of interest

The authors declare no conflicts of interest.

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