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PALMAR-PLANTAR ERYTHRODYSESTHESIA (HAND-FOOT SYNDROME) IN A PACLITAXEL-TREATED LUNG CANCER PATIENT: A RARE CASE REPORT WITH LITERATURE REVIEW

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ABSTRACT

Palmar-plantar erythrodysesthesia (PPE), commonly termed Hand-Foot Syndrome (HFS), is a dose-dependent cutaneous toxicity associated with certain chemotherapeutic agents. While it is well-established with capecitabine, 5-fluorouracil, and liposomal doxorubicin, its occurrence with paclitaxel is uncommon. We report the case of a 26-year-old male with metastatic carcinoma of the left lung who developed Grade 2 PPE following six cycles of carboplatin and paclitaxel chemotherapy. The syndrome manifested during the fourth chemotherapy cycle as tingling, burning, dryness, peeling, cracking, and dark discoloration of the palms. Concurrent adverse drug reactions (ADRs) included Grade 1 monocytopenia, Grade 3 neutropenia, and reduced serum creatinine, classified per Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Management with pyridoxine (vitamin B6) and emollients, along with paclitaxel dose adjustment in the sixth cycle, led to symptomatic improvement. This case underscores the importance of recognizing paclitaxel-associated PPE and implementing timely pharmacovigilance measures.

KEYWORDS: Palmar-plantar erythrodysesthesia; Hand-Foot Syndrome; Paclitaxel; Carboplatin; Chemotherapy toxicity; Adverse drug reactions; CTCAE; Lung carcinoma.

1. INTRODUCTION

Chemotherapy-induced dermatological toxicities represent a clinically significant group of adverse drug reactions that can severely impair a patient's quality of life (QoL) and necessitate dose interruptions or treatment discontinuation. Among these, palmar-plantar erythrodysesthesia (PPE), also known as Hand-Foot Syndrome (HFS), is a well-characterized cutaneous reaction predominantly associated with fluoropyrimidines (capecitabine, 5-fluorouracil), liposomal doxorubicin, and targeted therapies such as sorafenib and sunitinib.[1,2]

PPE is characterized by erythema, swelling, tenderness, and dysesthesia affecting the palms and soles anatomical sites subjected to repetitive mechanical stress and possessing a high density of eccrine sweat glands. The pathophysiology centers on the extravasation of cytotoxic agents into the dermal capillaries of these high-friction areas, triggering local inflammation, oxidative stress, and progressive epidermal damage.[3] The syndrome follows a dose-dependent trajectory and is graded according to the Common Terminology Criteria for Adverse Events (CTCAE): Grade 1 (mild erythema/dysesthesia, no functional impairment), Grade 2 (moderate changes with pain limiting instrumental ADLs), and Grade 3 (severe changes limiting self-care).[4]

While paclitaxel, a taxane-class antimitotic agent, is a cornerstone of therapy in lung, breast, and ovarian cancers, its association with PPE is uncommon and infrequently reported in the literature. The rarity of paclitaxel-induced PPE means it may be under-recognized, leading to delayed management and potentially compromised treatment outcomes.[5,6] Here, we present a case of Grade 2 PPE in a young male with metastatic lung carcinoma treated with carboplatin-paclitaxel and provide a focused review of the literature on this rare phenomenon.

2. Literature Review

2.1 Epidemiology and Implicated Agents

PPE was first described by Zuehlke in 1974 and has since been documented with a broad range of systemic therapies. The highest incidence is reported with capecitabine (45–68%), pegylated liposomal doxorubicin (up to 40%), and continuous infusion of 5-fluorouracil

(34%). Multikinase inhibitors such as sorafenib and sunitinib are also frequently implicated, with incidence rates of 30–45% and 9–21%, respectively.1,2

In contrast, paclitaxel-associated PPE is rare, with only isolated case reports in the published literature. Wahab et al. (2020) described a case of Grade 2 palmar-plantar erythrodysesthesia in a patient receiving weekly paclitaxel for breast cancer, while Ben Abdallah et al. (2021) documented a severe case in a patient on three-weekly paclitaxel.[5,6] Assi et al. (2013) further reviewed management strategies in paclitaxel-induced HFS, noting the need for dose reduction and supportive care.[7]

2.2 Pathophysiology

The precise mechanism underlying paclitaxel-induced PPE remains incompletely elucidated. The prevailing hypothesis attributes PPE to leakage of drug from capillaries in mechanically stressed, high-pressure areas of the palms and soles. The resulting local drug accumulation causes direct cytotoxic damage to basal keratinocytes and eccrine gland epithelium.[3]

Paclitaxel, by stabilizing microtubules and inhibiting mitotic spindle depolymerization, disrupts the rapid cellular turnover of basal epidermal cells. This, combined with eccrine gland-mediated drug secretion onto the skin surface, is postulated to generate focal inflammatory and cytotoxic effects. Oxidative stress pathways, prostaglandin E2 release, and cyclooxygenase activation may further amplify tissue inflammation in the affected areas.[3,8]

2.3 Clinical Features and Grading

PPE typically manifests 2–12 weeks after initiation of the offending agent, although earlier onset has been reported with weekly dosing schedules. Prodromal symptoms include tingling, burning, and paresthesia of the palms and soles, followed by erythema, edema, blistering, desquamation, and potentially ulceration. Hyperpigmentation is a recognized feature, particularly in patients with darker skin phototypes and following repeated cycles.[1,4]

CTCAE v5.0 grades PPE as follows: Grade 1 minimal skin changes or dermatitis without pain; Grade 2 skin changes with pain, limiting instrumental activities of daily living (ADLs); Grade 3 severe skin changes with pain limiting self-care ADLs. The grading directly informs clinical decision-making: Grade 1 warrants supportive care; Grade 2 requires treatment hold and dose reduction upon rechallenge; Grade 3 mandates treatment discontinuation.[4]

2.4 Management

No universally standardized protocol exists for PPE prevention or treatment. Preventive measures include the use of thick emollients (urea-based creams, petroleum jelly), avoidance of friction-generating activities, and cool water soaks. Pyridoxine (vitamin B6) at doses of 50–200 mg/day has been used empirically and may provide symptomatic relief through a proposed anti-inflammatory mechanism, though high-quality randomized evidence remains limited.[9]

Pharmacological interventions include topical corticosteroids to reduce inflammation, topical analgesics (e.g., lidocaine gel) for pain, and oral celecoxib for refractory cases. Dose modification of the implicated chemotherapeutic agent remains the definitive intervention. Lorusso et al. (2007) have emphasized that early recognition and graded management are central to preventing dose interruptions and preserving QoL.[9]

3. CASE REPORT

A 26-year-old male, previously healthy, presented to the oncology department with a chief complaint of a left-sided neck mass. Fine needle aspiration cytology (FNAC) of the left cervical lymph node revealed atypical cells consistent with metastatic carcinoma. Subsequent imaging and histopathological evaluation confirmed a diagnosis of metastatic carcinoma of the left lung, involving the upper lobe and lingular segments with nodal metastasis.

The patient was initiated on a standard chemotherapy regimen comprising carboplatin and paclitaxel, administered every 21 days. He completed six cycles of this regimen. The skin changes documented in this case were noted beginning with the fourth cycle onward and are characteristic of PPE rather than drug-induced hyperpigmentation alone (see Figure 1), with bilateral, symmetrical involvement of the palms, characterized by erythema, darkening, and early peeling, consistent with palmar-plantar erythrodysesthesia.

During the fourth cycle, the patient reported progressive tingling and burning sensations in his palms and soles, accompanied by dryness, peeling, cracking, and mild dark discoloration. There was no blistering or ulceration. The findings were bilaterally symmetrical, predominantly palmar, and spared the dorsal aspects. On clinical grading per CTCAE v5.0, these findings were consistent with Grade 2 Palmar-Plantar Erythrodysesthesia skin changes with associated pain, causing discomfort but not limiting basic self-care activities.

Management was initiated with oral pyridoxine (vitamin B6) 100 mg/day and application of a thick emollient (urea-based cream) twice daily. In the sixth cycle, the oncologist reduced the paclitaxel dose to limit cumulative dermatologic toxicity. The patient demonstrated progressive symptomatic improvement with these measures, and chemotherapy was completed without further treatment interruption. Additional subjective ADRs included anorexia, alopecia, weight loss, and diarrhea.

Figure 1: Initial signs of Grade 2 palmar-plantar erythrodysesthesia during cycle 4.

Table 1: Adverse Drug Reactions (ADRs) Classified per CTCAE v5.0.

ADR	Onset	Observed Finding	CTCAE Grade	Clinical Significance / Action Taken
Palmar-Plantar Erythrodysesthesia (PPE/HFS)	Cycle 4 (Day ~21)	Tingling, burning, dryness, peeling, cracking, dark discoloration of palms (bilateral)	**Grade 2**	Pyridoxine 100 mg/day, emollients; paclitaxel dose reduction in Cycle 6
Monocytopenia	During chemotherapy cycles	Absolute monocyte count below lower limit of normal	**Grade 1**	Monitored; no dose change required
Neutropenia	During chemotherapy cycles	ANC significantly reduced; severe neutropenia	**Grade 3**	G-CSF prophylaxis / supportive care; dose monitoring
Decreased Serum Creatinine	During chemotherapy cycles	Serum creatinine below reference range (possible muscle mass loss / dilution)	**Grade 1**	Renal function monitored; no dose adjustment required

Anorexia	During treatment	Reduced appetite and food intake	**Grade 1–2 (subjective)**	Nutritional counselling; symptomatic management
Alopecia	During treatment	Hair loss (expected taxane effect)	**Grade 2**	Reversible; patient counselled
Weight Loss	During treatment	Clinically observed unintentional weight loss	**Grade 1–2 (subjective)**	Dietary support; nutritional assessment
Diarrhoea	During treatment	Increased stool frequency	**Grade 1 (subjective)**	Oral hydration; loperamide if needed

CTCAE: Common Terminology Criteria for Adverse Events v5.0; ANC: Absolute Neutrophil Count; ADL: Activities of Daily Living; G-CSF: Granulocyte-Colony Stimulating Factor; HFS: Hand-Foot Syndrome; PPE: Palmar-Plantar Erythrodysesthesia.

4. DISCUSSION

This case presents a rare but clinically important manifestation of Grade 2 PPE in a young patient receiving carboplatin-paclitaxel for metastatic lung carcinoma. Several features of this case warrant discussion in the context of existing literature.

First, the clinical designation as PPE (palmar-plantar erythrodysesthesia) is appropriate for this presentation. Both PPE and HFS describe the same syndrome; however, the term *PPE* is preferred in the context of chemotherapy-induced toxicity, particularly when associated with antimitotic agents like paclitaxel, as it more specifically denotes the dysesthetic component. The bilateral, symmetrical palmar involvement with erythema, peeling, and dysesthesia observed from cycle 4 onward is characteristic of chemotherapy-induced PPE rather than simple drug hyperpigmentation.

The onset at cycle 4 is consistent with the cumulative dose-dependent nature of PPE, as reported by Ben Abdallah et al. (2021) and Wahab et al. (2020), who similarly documented PPE emergence after multiple cycles of paclitaxel.[5,6] The bilateral symmetrical palmar involvement with dysesthesia from cycle 4 onward is consistent with the cumulative dose-dependent pattern reported in paclitaxel-associated PPE.

The concomitant ADR profile is clinically important. Grade 3 neutropenia is a serious toxicity requiring prompt management and highlights the myelosuppressive potential of carboplatin-paclitaxel. Grade 1 monocytopenia and a reduced serum creatinine (potentially reflecting sarcopenic muscle loss from cachexia) add to the comprehensive toxicity burden.

These findings collectively emphasize the need for systematic ADR monitoring in patients receiving carboplatin-paclitaxel, with particular attention to both hematological and dermatological toxicities.

Management with pyridoxine and emollients, alongside a sixth-cycle paclitaxel dose reduction, aligns with established practice guidelines. While the efficacy of pyridoxine in preventing capecitabine-induced PPE is controversial in randomized trials, its empirical use in paclitaxel-associated PPE has been supported by case reports.[7,9] The dose reduction strategy allowed chemotherapy completion without discontinuation, reflecting a successful balance between oncological efficacy and toxicity management.

5. CONCLUSION

This case highlights palmar-plantar erythrodysesthesia as a rare but clinically significant adverse effect of paclitaxel-based chemotherapy in a young patient with metastatic lung carcinoma. The occurrence of Grade 2 PPE following six cycles of carboplatin-paclitaxel, with progressive worsening from cycle 4 onward, underscores the importance of recognizing this toxicity beyond its commonly implicated agents. A comprehensive ADR profile, including Grade 3 neutropenia, Grade 1 monocytopenia, and decreased serum creatinine, further emphasizes the need for multisystem pharmacovigilance in this setting. Early identification, CTCAE-guided grading, and prompt supportive management are essential to ensure treatment adherence and protect patient quality of life.

INFORMED CONSENT: Written informed consent was obtained from the patient for publication of this case report and accompanying clinical images.

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