Palmar-plantar erythrodysesthesia

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DESCRIPTION

A 59-year-old woman presented with pain, tingling and desquamation over bilateral palms and soles for 4 weeks, associated with inability to perform activities of daily living (ADL). She had received 5-fluorouracil, bevacizumab and irinotecan for metastatic colon cancer 6 weeks earlier. Examination revealed diffuse hyperpigmentation and blisters on palms and soles, and an ulcer over the right plantar surface (figures 1 and 2). A clinical diagnosis of grade 3 palmar-plantar erythrodysesthesia (PPE) was made, and she was treated with topical emollients. Chemotherapy was held and she ultimately opted for hospice care.

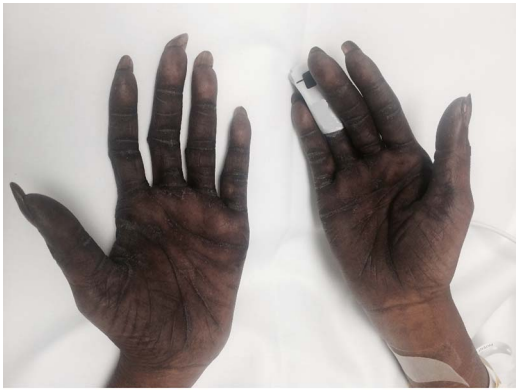

Figure 1 Volar aspect of bilateral palms demonstrating diffuse hyperpigmentation and skin peeling, and skin atrophy of the distal fingernails. The patient experienced pain and had difficulty performing activities of daily living.

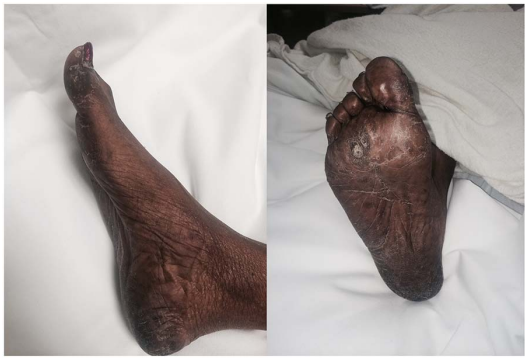

Figure 2 Medial and volar aspect of the right foot demonstrating dry desquamation, skin peeling, blistering and a 1 cm×1 cm ulceration.

This report is targeted for general practitioners, internists and emergency room physicians who may not encounter PPE often. PPE, or chemotherapy-associated acral erythema, is a cutaneous toxicity syndrome traditionally associated with cytotoxic chemotherapy agents (5-fluorouracil, docetaxel, cytarabine, liposomal doxorubicin, capecitabine); however, it is increasingly being associated with use of molecular agents (sorafenib, sunitinib, axitinib, pazopanib). Incidence, which was traditionally in the 10% range, has shot up and may be as high as 62% in patients treated with sorafenib.[1] Symptoms include dysesthesia and tingling, progressing to pain and swelling, blistering, desquamation and ulceration. Severity is graded per the Common Terminology Criteria for Adverse Events (CTCAE) V.4, with grade 3 reflecting severe skin changes and difficulty performing self-care ADL (table 1).[2] The pathogenesis is incompletely understood, but direct chemotherapy toxicity due to leakage into the capillary bed is a potential mechanism. Higher cumulative dose and sustained serum levels of cytotoxic drugs are more frequently associated with PPE occurrence.[3] Differential diagnoses include erythromelalgia, graft-versus-host disease and Raynaud's disease. Patients with grade 1 PPE are managed symptomatically and severe PPE (grade 2 or 3) needs dose reduction in chemotherapy or a switch to an alternative regimen (if available) to avoid recurrence. Preventive strategies include avoiding contact of hands and feet with heat (sunburn and saunas) and chemicals (household cleaning), and reducing frictional contact (occupational or recreational). Vigilance and reporting early symptoms may halt progression of the condition. There are no proven therapeutic treatments but emollients (urea), moisturisers, ice packs and cooling therapy, vitamin B6 supplementation and pain relief with non-steroidal anti-inflammatory drugs may provide symptomatic relief.

Table 1 CTCAE V.4, guidelines reflecting the severity of palmar- plantar erythrodysesthesia[2]*

Adverse event	Grade 0	Grade 1	Grade 2	Grade 3
Palmar-plantar erythrodysesthesia syndrome	No symptoms	Minimal skin changes or dermatitis (eg, erythema, oedema, or hyperkeratosis) without pain	Skin changes (eg, peeling, blisters, bleeding, oedema, or hyperkeratosis) with pain; limiting instrumental ADL	Severe skin changes (eg, peeling, blisters, bleeding, oedema, or hyperkeratosis) with pain; limiting self-care ADL

*Note there are no grade 4 or 5 CTCAE criteria for palmar-plantar erythrodysesthesia.
ADL, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events.

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Learning points

- Palmar-plantar erythrodysesthesia is a debilitating complication of some commonly used chemotherapeutic agents.
- Patients with grade 2 or 3 palmar-plantar erythrodysesthesia require dose reduction or an alternative chemotherapy regimen to avoid recurrence.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

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3 Webster-Gandy JD, How C, Harrold K. Palmar-plantar erythrodysesthesia (PPE): a literature review with commentary on experience in a cancer centre. *Eur J Oncol Nurs* 2007;11:238–46.