

## Do you know this syndrome? Hand-foot syndrome\*

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### CASE REPORT

We report a 73-year-old woman under post-surgical chemotherapy (breast ductal carcinoma) who presented with transudation and pain on the lower limbs 20 days after the first cycle with doxorubicin and cyclophosphamide and no improvement with furosemide.

Due to treatment failure after four cycles of adjuvant regimen, the patient was started on herceptin and paclitaxel. From the 45<sup>th</sup> day of this new regimen, we observed the development of an edema and considerable erythema on the hands, wrists, legs, and feet. We also observed desquamation, ulceration, vesicopustules, and intense burning sensation. Little improvement was observed after analgesia, topical corticosteroids and cephalixin (Figures 1 and 2).



**Figure 1:** Erythema and acral edema on the lower limbs, with flaking and areas of ulceration

Laboratory tests were normal. Histopathological examination showed areas of epidermal necrosis with small clefts, keratinocyte apoptosis, parakeratosis foci, and basal vacuolar degeneration with extensive involvement of the acrosyringium without squamous syringometaplasia.

We opted for hospitalization, suspension of chemotherapy, and administration of opioids, prednisone (0.5 mg/kg), potassium permanganate compresses, and application of occlusive dressing with fludrocortide. The patient was discharged five days later with significant improvement in pain and lesions.

### DISCUSSION

Hand-foot syndrome (HFS) – or palmar-plantar erythrodysesthesia, acral erythema, or Burgdorf reaction – is an adverse event of many chemotherapeutic agents, especially liposomal doxorubicin, capecitabine, 5-fluorouracil, cytarabine, docetaxel, sorafenib,



**Figure 2:** Detail of scaly erythematous lesions of the posterior region of the ankles with areas of ulceration and vesicopustules

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**Chart 1:** Clinical description of severity for hand-foot syndrome according to NCI-CTCAE (National Cancer Institute - Common Terminology Criteria for Adverse Events) and WHO (World Health Organization) and associated histologic findings

Grade	NCI-CTCAE (version 4.03)	WHO	Histological findings
1	minimal skin changes OR dermatitis (e.g. erythema, edema, or hyperkeratosis) NO pain	Dysesthesia/paresthesia, tingling in hands and feet	Dilated vessels in the superficial dermal plexus
2	Cutaneous lesions (e.g. flaking, blistering, bleeding, swelling, and hyperkeratosis) WITH pain, but with minimum limitation	Discomfort when holding objects and walking, painless swelling, or erythema	
3	Ulcerative dermatitis or serious painful cutaneous lesions (e.g. flaking, blistering, bleeding, swelling, and hyperkeratosis) interfering with function and self-care	Painful erythema and swelling of the palms and soles; erythema and periungual swelling	Isolated keratinocytes necrosis in the outer layers of the epidermis
4		Desquamation, ulceration, blistering, and severe pain	Complete epidermal necrosis

sunitinib, cyclophosphamide, etoposide, vinorelbine, methotrexate, hydroxyurea, tegafur, mercaptopurine, and paclitaxel.<sup>1,2</sup>

After alopecia and mucositis, HFS is the most common adverse dermatologic reaction to chemotherapy, with an incidence of 3%-64%. The highest incidences occur with doxorubicin (40%-50%) and capecitabine (50%-60%). The risk of HFS seems to be dose-dependent: formulations that prolong the serum level or that concentrate the drug at the affected sites have the highest association rates.<sup>1</sup>

The pathogenesis of HFS is not known. It is believed to be a toxic reaction due to the local accumulation of the drug with consequent degeneration and necrosis of the sweat glands. That is because its microscopic features resemble squamous eccrine syringometaplasia and neutrophilic eccrine hidradenitis patterns.<sup>2,3</sup>

HFS presents with prodromal dysesthesia and palmar-plantar tingling. Within days, the reaction progresses to burning pain, well-defined edema and erythema with a tendency to symmetry and flaking, and limitation of daily activities. Extreme cases involve ulceration and blisters, palmoplantar keratoderma, nail dystrophy, inflammation of actinic keratoses, and may affect the folds of the skin (axillary, inguinal, perineal, and inframammary).<sup>1,2,4-6</sup>

Different classifications grade the severity of HFS. The two most commonly used criteria are provided by the World Health Organization and by the National Cancer Institute (Chart 1).<sup>7</sup>

There are no longitudinal studies that explore specific treatments. Suggestive therapy include reducing chemotherapy dosage, increasing the interval between cycles, or even stopping chemotherapy, which would lead to remission of the picture in up to two weeks. Dressings, rigorous analgesia, emollients, cold compresses, and potent topical corticosteroids associated with emollients or systemic corticosteroids are reported as efficient. Cooling of the hands and feet and use of emollients and antiperspirants (aluminum chloride hydroxide) during infusions can prevent the reaction. Oral pyridoxine showed no preventive efficacy in HFS.<sup>2,8-10</sup>

With an aging population and greater access to health care and oncological diagnosis, cutaneous reactions to chemotherapy should become more frequent. Prevention, identification, and early intervention is essential for clinicians in cases of HFS. □

**Abstract:** Hand-foot syndrome is a common cutaneous adverse effect associated with certain systemic chemotherapy drugs. It is characterized by erythema, edema, and burning sensation, especially over palmoplantar surfaces. We report the case of an elderly patient undergoing chemotherapy after a breast cancer surgery who developed symptoms two months after the start of the regimen. There are no studies that explore specific therapies. Suggestive therapy include reducing agent dosage, increasing the interval between cycles, or even stopping chemotherapy. Emollients, analgesics, and cold packs are described as effective. After alopecia and mucositis, hand-foot syndrome is the most common adverse dermatologic reaction to chemotherapeutic agents.

**Keywords:** Adjuvant chemotherapy; Chemotherapy; Drug eruption; Hand-foot syndrome

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