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REGORAFENİB-INDUCED HAND–FOOT SKİN REACTİON: A CASE REPORT

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Dear Editor

Hand–foot syndrome (HFS) and hand–foot skin reaction (HFSR) are well-recognized dermatologic adverse effects associated with several cytotoxic chemotherapeutic agents and molecularly targeted multikinase inhibitors (MKIs). HFSR typically occurs shortly after the initiation of MKIs and is characterized by painful erythematous lesions on the palms and soles, which may later progress to blistering or hyperkeratotic plaques. Regorafenib, sorafenib, dabrafenib, and cabozantinib are among the most frequently implicated agents.[1-3]

Herein, we report a case of regorafenib-induced HFSR in a patient with metastatic colon cancer.

CASE PRESENTATİON

A 64-year-old male patient presented to our dermatology clinic with painful erythematous lesions on his hands and feet that had developed over the previous two months. His medical history revealed that he had undergone surgery for colon carcinoma two years earlier and had been followed for liver metastases since then. He had been receiving oral regorafenib therapy (4 tablets daily) for approximately four months. The skin lesions appeared during the third month of treatment.

Dermatological examination revealed bilateral erosive superficial ulcers measuring approximately 2 × 2 cm on erythematous bases on both the palmar and plantar surfaces. The peripheral erythema was more pronounced around the lesions (Figure 1). Laboratory investigations, including complete blood count and routine biochemical parameters, were within normal limits. According to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, the lesions were consistent with grade 2 hand–foot skin reaction, characterized by painful hyperkeratotic plaques on pressure areas that interfered with daily activities. The causal relationship between regorafenib and the dermatologic findings was assessed using the Naranjo Adverse Drug Reaction Probability Scale, yielding a score of 6, indicating a probable adverse drug reaction.

After consultation with the medical oncology department, the regorafenib dose was reduced from four tablets daily to two tablets daily. Topical treatment consisting of 2% boric acid ointment, topical steroid cream twice daily, and epithelializing and moisturizing agents was initiated. The patient showed clinical improvement within three days. However, the lesions recurred while continuing regorafenib at the reduced dose, and therefore the medication was discontinued. No recurrence was observed during one month of follow-up.

Figure 1: Symmetrical hyperkeratotic plaques with erythematous halos on the palmar surfaces, targetoid hyperkeratotic lesion on the palm and hyperkeratotic plaques localized to pressure areas of the sole.

DİSCUSSİON

Although the exact pathogenesis of HFSR remains unclear, several mechanisms have been proposed. Damage to epidermal keratinocytes and eccrine sweat glands during drug excretion may play an important role. Platelet-derived growth factor receptor (PDGFR) and c-KIT are expressed in eccrine glands, and their inhibition by MKIs may contribute to eccrine gland dysfunction and subsequent skin toxicity.[3,4]

In addition, inhibition of angiogenesis pathways by MKIs may disrupt endothelial repair mechanisms and microvascular integrity, particularly in areas subjected to mechanical stress such as the palms, soles, and elbows. This vascular impairment may compromise tissue repair, predisposing these regions to localized skin damage.

Clinically, HFSR most commonly affects the fingertips, interdigital spaces, heels, and lateral aspects of the feet. Lesions may appear as erythematous plaques, focal hyperkeratotic lesions, or bullae. Although HFSR does not directly affect survival, it may significantly impair patients' quality of life and frequently necessitates dose reduction or discontinuation of anticancer therapy.[5-7]

Management is mainly symptomatic because the underlying mechanisms are not fully understood. Current strategies include high-potency topical corticosteroids, keratolytic agents such as urea-based creams, analgesics, and dose modification of the causative drug. Some studies have also suggested potential benefits from treatments such as acitretin in refractory cases.[2]

Hand–foot skin reaction associated with multikinase inhibitors differs from classical chemotherapy-induced hand–foot syndrome by the presence of localized hyperkeratotic plaques on pressure areas rather than diffuse erythema. This pattern was clearly observed in our patient.

In conclusion, clinicians should be aware of regorafenib-associated HFSR as an important dermatologic adverse effect. Early recognition and appropriate management are crucial to maintain treatment adherence and improve patient quality of life.

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