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Hand-Foot Syndrome following Decitabine

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Abstract

We observed a case of Hand-Foot Syndrome (HFS) in a patient treated with decitabine. HFS has not previously been associated with decitabine, although it has been observed following treatment with the structurally similar pyrimidine analogue cytarabine.

Keywords

hand-foot syndrome; palmar-planter erythrodysesthesia; decitabine

The patient was a 61-year Caucasian male with AML (FAB-M1 with inversion 16) that had relapsed following induction with CLAM (cladribine, cytarabine, and mitoxantrone hydrochloride). The patient presented 6 months after his induction therapy with fatigue and weight loss. Labs showed CBC with 4% blasts. Bone marrow biopsy showed relapsed acute myeloid leukemia with 42% blasts. Given the patient's poor performance status, he was deemed inappropriate for further aggressive chemotherapy. On the third day of decitabine infusion (20 mg/m² daily for 5 days), the patient developed burning and tingling sensation in his palms. His symptoms didn't initially warrant discontinuation of the chemotherapeutic agent and he completed a 5-day course. However, in a few days, it progressed to symmetric well-defined swelling and erythema. The erythema was most prominent on the lateral aspects of the fingers and distal fat pads (Figure 1). No planter/nail involvement or other skin lesions were noted. This was evaluated as grade II HFS (WHO Classification) due to decitabine. The patient was not receiving any other medication that is known to cause HFS or interact with decitabine. Infectious causes were considered unlikely given the lack of systemic manifestations. The patient was treated symptomatically with pain control and high-potency topical corticosteroids. No progression to blistering, ulceration or desquamation was noted. Biopsy was deemed unnecessary given the typical clinical appearance. The rash and the pain improved, and gradually resolved over the next week.

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Unfortunately, the patient's functional status deteriorated due to recurrent pneumonia infection, which was unrelated to the rash, and the patient transitioned to supportive care.

Zeuhlke first described hand-Foot Syndrome (HFS) in 1974 associated with mitotane therapy for hypernephroma[1]. Subsequently, the condition was reported in the literature under a variety of terms (acral erythema, palmar-planter erythrodysesthesia, toxic erythema of the palms and soles, and Burgdorf's reaction). The skin changes of HFS are often painful and debilitating and can impair activities of daily function[2]. Hence, HFS is among the most common reasons for dose reduction and/or discontinuation of chemotherapeutic agents thus limiting the use of a potentially effective therapy. Rechallenge of patients with the causative chemotherapeutic agents using similar dosage schedules has lead to recurrence of the reaction in most but not all patients[3].

Diverse chemotherapeutics have been associated with HFS. Pegylated liposomal doxorubicin (PLD) and capecitabine have the highest reported HFS incidence at 40% to 60%. Other common causes of HFS include cytarabine (a pyrimidine analogue with structural similarities to decitabine), 5-fluorouracil (FU), and docetaxel[4]. HFS is also one of the most commonly reported adverse effects in patients taking the newer multitargeted tyrosine kinase inhibitors such as sorafenib, sunitinib, and others that target angiogenesis[5].

The risk of developing HFS appears to be dose-dependent. Drug formulation and administration schedules that result in sustained serum levels of cytotoxic agents are more likely to cause HFS. For example, PLD, the liposome-encapsulated form of doxorubicin which results in a smaller volume of distribution, greater AUC, and slower clearance of the drug, is associated with a higher HFS incidence than the non-encapsulated formulation[6]. Furthermore, while HFS is uncommon when 5-FU is administered as a bolus injection, it is often the dose-limiting toxicity with prolonged infusions[7].

Recent clinical attention has focused on evaluating decitabine (a DNA-hypomethylating agent used for the treatment of myelodysplastic syndromes) as frontline therapy for untreated high-risk elderly AML patients[8]. Decitabine is largely well tolerated, with cytopenias and infections being common. Dosing adjustment for hepatic and renal impairment hasn't been studied. Our patient didn't have or develop any renal or hepatic injury that suggests possible alterations in pharmacokinetics. HFS has never been reported as an adverse effect to decitabine, although many studies have listed non-specific rash as a side-effect [9].

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Figure 1. Grade II Hand-foot syndrome following therapy with decitabine: paresthesia followed by painful symmetric palmer edema and erythema most prominent over the fat pads of distal phalanges.