IMAGES

Dry Dressing for Epidermal Sloughing after Subcutaneous Azacitidine Injection in a Myelodysplastic Syndrome

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The myelodysplastic syndromes can be characterized by the conditions from which myeloid malignancy arises due to ineffective hemopoiesis resulting in several possible forms of progressive cytopenia and occasionally, in acute myeloid leukemia. To date, the myelodysplastic syndromes have been known to have poor prognoses even with allogeneic hematopoietic stem cell transplantation, which can only modify the progression of disease and rarely achieve a complete cure. Age accounts for the difficulty with allogeneic hematopoietic stem cell transplantation in most patients, and azacitidine is known to show a significant improvement in survival over other conventional care regimens such as supportive care, low-dose cytarabine, and intensive chemotherapy [1].

A 76-year-old male patient, who had gout and hypothyroidism, had been diagnosed with a myelodysplastic syndrome seven months before presentation to our department. He received a first cycle of 75 mg/m^2/day of azacitidine subcutaneously for 7 days, and no additional cycles were administered. Redness was observed at the injection site 10 days after finishing the first cycle of azacitidine injection (Fig. 1A). The lesion was progressively extending to the adjacent area, and profuse discharge with skin sloughing and hemorrhagic bullae developed 19 days after the injection (Fig. 1B). No mucosal lesions were noted. A biopsy showed marked inflammatory cell infiltration with eosinophils and subepidermal bullae (Fig. 2). The wound failed to heal after treatment with a 9-day course of glucocorticoids, antihistamines, antibiotics, and moisture polyurethane foam dressing. Dry dressing was started 29 days after injection. We applied a meshed silicone sheet (Mepitel One, Mölnlycke Health Care, Göteborg, Sweden) on the raw surface to conserve the exposed dermis and covered the sheet with an alginate dressing (SeaSorb, Coloplast, Peterborough, United Kingdom) to increase discharge absorption. Thereafter, the discharge decreased gradually. The wound had mostly healed 37 days after injection without any surgical intervention (Fig. 1C). At a 4-month follow-up visit, the wound had completely healed with hyperpigmentation (Fig. 1D).

Azacitidine has been the treatment of choice for patients with high-risk myelodysplastic syndromes [1]. Some adverse cutaneous reactions associated with azacitidine, such as erythema on the injection site, rash, pruritus, pyoderma gangrenosum, and Sweet's syndrome, have been reported [2]. Injection-

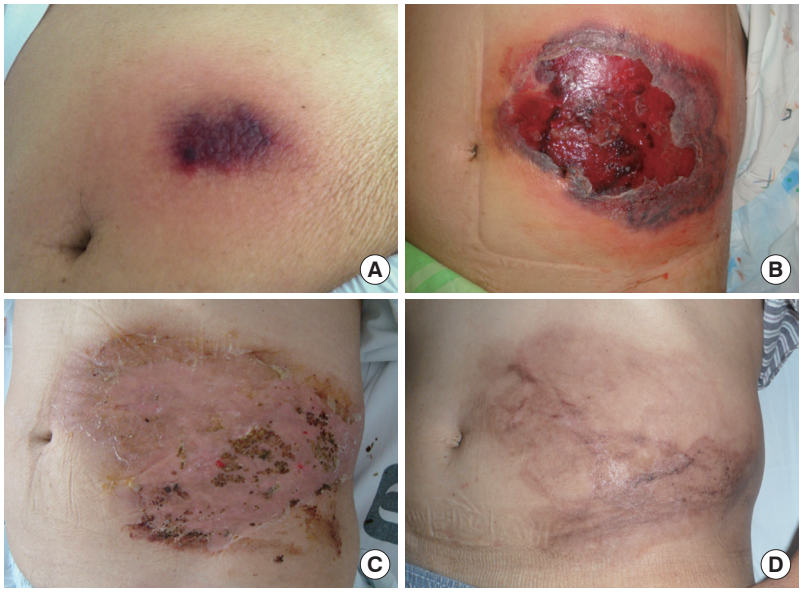

Fig. 1.
Evolution of azacitidine-induced erythema multiforme. (A) First presentation of the skin lesion 10 days after injection. (B) Expansion of hemorrhagic skin sloughing 19 days after injection. (C) Resolution of the skin lesion 37 days after injection, and (D) 4-month follow-up view.

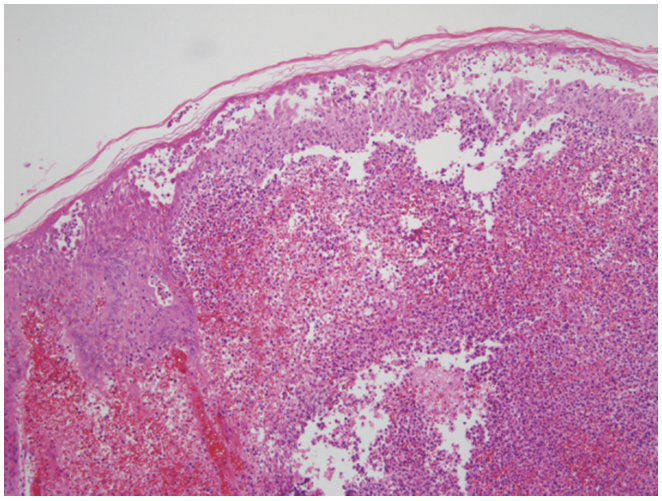

Fig. 2.
Skin punch biopsy specimen from the abdominal wound. The epidermis shows lytic changes with subepidermal bullae. Marked inflammatory cell infiltration with eosinophils can be seen (H&E, × 100).

site skin reactions after azacitidine injection are common, occurring in 46% to 72% of patients, with a mean duration of 12 days. The majority of these reactions are resolved during treatment, but a minority (< 12%) of injection-site reactions have been reported to require treatment with concomitant corticosteroids and/or antihistamines [3].

The presenting pathologic findings suggest drug-induced erythema multiforme, which characteristically shows infiltration with a large number of eosinophils [4]. However, the skin lesions typical of erythema multiforme, that is, round, erythematous papules that appear with symmetrical distribution on the acral extremity, were not found in the present case, while the more severe conditions of skin lesions accompanied by epithelial detachment and progressive hemorrhagic bullae in the injection site can be seen (Fig. 2). The authors suspected that the skin lesion was an exaggerated form of injection site reaction because no skin eruption or other side effects were found after two months when the route of administration of azacitidine was changed from a subcutaneous to intravenous route.

The management of this type of epidermal sloughing skin lesion should be focused on the preservation of the exposed dermis because the dermis can be re-epithelialized without surgical intervention as long as the causative agents are resolved and the exposed dermis is preserved without necrosis. These wounds are usually managed by a moist occlusive wound dressing such as hydrocolloid or polyurethane foam. A moist wound environment enhances wound re-epithelialization; however, excessive wound moisture can cause wound maceration and can result in a delay in wound healing. In our case, a 9-day course of glucocorticoids, antihistamines, and antibiotics did not improve the condition of the wound; however, the refractory wound then improved after changing to dry dressing. Moist desquamation after radiation therapy also shows similar histological features to our case, and it has been reported that moist wound dressing with hydrogel delays wound healing relative to dry dressing in cases of moist desquamation after radiation therapy [5].

When any adverse skin reaction occurs after anticancer drug administration, stopping the inducing drug and thoroughly evaluating the patient is most important. However, proper skin wound management is also important to avoid unnecessary surgical intervention in a cancer chemotherapy patient who may take a long time to heal.

The case presented here shows that subcutaneously injected azacitidine may cause severe epidermal sloughing. Proper skin wound management should be started early, and if there is no response with conventional occlusive dressing, switching to dry dressing should be considered.

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