Case Report

What mind does not know eyes cannot see!! – A case of bleomycin-induced flagellate hyperpigmentation

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ABSTRACT

Recognition of cutaneous side effects of bleomycin, a commonly used chemotherapeutic agent, is important to avoid unnecessary discontinuation of therapy. Here, we present the case of a 15-year-old boy who was undergoing treatment with standard BEP (bleomycin, etoposide, and cisplatin) regime, presented with flagellate hyperpigmented lesions in the back, arm, and thighs.

Key words: Bleomycin, Dermatitis, Flagellate pigmentation

Flagellate dermatoses are uncommon figurate dermatoses characterized by parallel linear or curvilinear arrangement simulating the marks of whiplashes. The term flagellate dermatitis was first introduced for bleomycin-induced dermatitis. Bleomycin-induced flagellate erythema was first reported in 1970 by Moulin *et al*. [1] Over the course of time, other causes for this pattern have emerged. However, with the declining use of bleomycin, this unique adverse effect has become infrequent in common clinical practice [2].

We herein provide an overview of the clinical presentation and treatment options of this skin toxicity by citing the case of a 15-year-old Indian boy with germ cell tumor of the central nervous system (CNS) developing flagellate dermatitis following his two cycles of chemotherapy with bleomycin, etoposide, and cisplatin (BEP) regimen.

CASE REPORT

A 15-year-old boy presented to the dermatology outpatient department (OPD) with complaints of generalized pruritus and the appearance of linear black-colored lesions over the back and thighs for 2 weeks.

On enquiry, he was found to have a biopsy-proven germ cell tumor of the CNS and he had received combination chemotherapy with standard BEP regime postoperatively, comprising intravenous administration of cisplatin 30 mg and etoposide 130 mg from day 1 to day 5. Bleomycin was also administered in the dose of 30 IU intravenously on day 1, day 8, and day 15. This cycle was repeated every 3 weeks. After two cycles of the BEP regime, the patient was referred to the dermatology OPD.

Cutaneous examination revealed near total scalp alopecia, multiple linear hyperpigmented lesions (flagellate pigmentation) of various sizes on the back (Fig. 1a), arms, and thighs (Fig. 1b); largest being 3 cm × 2 cm. The lesions were painless. The nails also showed streaks of hyperpigmentation. Mucosa, palms and soles were normal. The routine blood investigations and pulmonary function test did not reveal any abnormality. The patient completed four cycles of chemotherapy. No progression of the skin lesion was noted. The patient was managed conservatively with oral antihistamines and topical capsaicin cream.

DISCUSSION

Bleomycin is an antitumor antibiotic. It has a plethora of indications, for example, Hodgkin's and non-Hodgkin's lymphoma, germ cell tumor, head-and-neck cancer, etc. Bleomycin is rapidly inactivated by enzyme hydrolase in every organ except skin and lungs which accounts for its side effects. The toxic cutaneous concentration of bleomycin might be the most probable explanation for this skin eruption [3]. It is further speculated that linear pigmentation may be caused by scratching, which induces subclinical local vasodilatation by a dermographic mechanism resulting in excessive local accumulation of bleomycin [4].

Cutaneous side effects are many, for example, painful inflammatory nodules on fingers, digital gangrene, erythema multiforme, infiltrated violaceous plaques, sclerodermoid changes,

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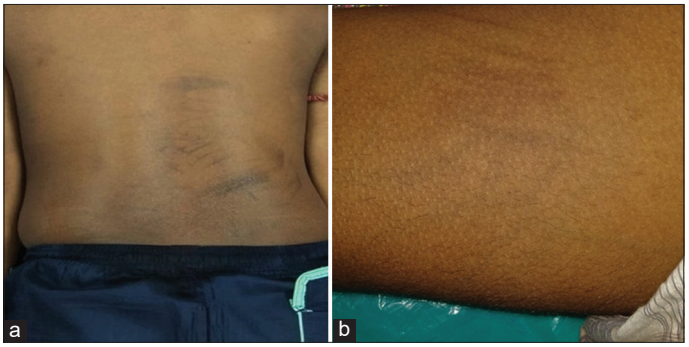

Figure 1: Linear hyperpigmented lesions on the (a) back and (b) thigh

and a variety of hyperpigmentary changes. Bleomycin-associated hyperpigmentation can be diffuse, patchy, or linear. The linear type is characterized by band-like or "flagellate" hyperpigmentation in trauma prone areas mainly involving the trunk and proximal extremities [2]. Erythematous, linear, and intermingled streaks are formed by rows of adjoining firm papules [5]. Although the majority of cases seem to be preceded by a prodrome of generalized pruritus, there are few reports describing the lesions as non-pruritic [6]. There might be evidence of punctuating hemorrhage and pustules [5]. There is no characteristic distribution as the lesions can be located in the face, trunk, and extremities [5]. However, there have been some reports highlighting the predominance of lesions over a bony prominence [1].

Dermatographia is present to a limited extent and the role of scratching in producing the linear shape of the lesion is debated [5]. As the rash becomes less erythematous, affected areas become deeply pigmented. These hyperpigmented areas may persist for up to 6 months [7,8]. The incidence of bleomycin-induced flagellate dermatitis is around 8–20% [2]. Cutaneous adverse effects of bleomycin are a relatively late manifestation, usually developing in the 2nd and 3rd week of treatment, after a cumulative dose of 150–200 units; although may occur even after the first dose [9]. There is no specific treatment. It may resolve after discontinuation of bleomycin.

Typical flagellate hyperpigmentation was noted in our patient receiving bleomycin. It appeared after a cumulative dose of 150 mg and after 6 weeks of therapy. It was associated with generalized pruritus, alopecia, and pigmentation of few nails. Oral mucosa was spared. As there were no other systemic complaints or alteration of pulmonary function, symptomatic management for pruritus was given and bleomycin was continued. Pruritus improved significantly after completion of bleomycin but flagellate pigmentation persisted.

Flagellate dermatitis has also been reported in patients receiving other chemotherapeutic agents such as peplomycin, a bleomycin derivative, and docetaxel [9,10]. Flagellate dermatitis can also occur in association with consumption of shiitake mushroom, dermatomyositis, adult-onset Still's disease, and infection with human immunodeficiency virus [5,11]. Both bleomycin and consumption of shiitake mushroom may cause flagellate dermatitis at a low dose. However, there is no long-standing post-inflammatory hyperpigmentation or systemic effect associated with the latter [5].

CONCLUSION

Increased use of various chemotherapeutic agents to match the upsurge of cancer in the present era has led to a rise in the incidence of cutaneous side effects, thus worsening of the quality of life of patients. Proper counseling of patients and their family members before initiation of chemotherapy is, therefore, necessary to reduce psychological trauma. Coordination between oncologists and dermatologists to promptly identify the rare but benign cutaneous side effects of chemotherapeutic agents like bleomycin is, therefore, necessary to avoid undue avoidance of drugs.

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