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A case of bleomycin-induced flagellate dermatitis: A case report

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Abstract

The article description and significance to dermatologists: bleomycin flagellate dermatitis is a rare cutaneous manifestation, believed to be due to the lack of bleomycin hydrolase enzyme in the skin, which inactivates bleomycin, resulting in its accumulation. This is thought to be a dose-dependent reaction, and doses over 200 U and higher may increase risk. This case describes a male developing a pruritic, erythematous linear flagellated dermatitis to the lower back after his third cycle of bleomycin, etoposide and cisplatin for a stage 3 seminoma. Pruritis resolved and erythema improved with the treatment of bilastine and desoximetasone cream. It is important to recognize this condition because untreated pruritis may lead to increased impairment of the skin barrier in already immunocompromised patient populations. This may also give further evidence to having ongoing and continuing collaboration between Dermatology and Medical Oncology for any patients presenting with a new rash undergoing chemotherapy treatments.

Keywords

Flagellate, dermatitis, erythema, bleomycin

Introduction

Bleomycin is a glycopeptide antineoplastic antibiotic agent, that inhibits DNA synthesis, by causing single-stranded breaks and inhibiting thymidine from being incorporated into DNA. Bleomycin is commonly used in chemotherapy treatment of malignancies such as testicular tumours, germ cell tumours, Hodgkin's lymphoma and squamous cell carcinoma. Cutaneous reactions such as erythema, flagellate dermatitis are reported between 8% and 20% in patients being treated with bleomycin.[1,2]

Case report

A 32-year-old man with stage 3 seminoma, undergoing treatment with bleomycin, etoposide and cisplatin (BEP) chemotherapy with curative intent. Upon presenting to dermatology, he endorsed a history of initial symptoms that began 9 weeks prior to the visit, during the third cycle of BEP, that included a pruritic linear rash on his back, with similar appearing rash subsequently developing to the abdomen and both arms during this time period. Diphenhydramine and hydroxyzine provided no symptomatic relief. Upon examination, there was an erythematous linear flagellated dermatitis, to the lower mid back (Figure 1). These findings were consistent with bleomycin-induced flagellate dermatitis. Hydroxyzine was discontinued and he was started on bilastine 40 mg and desoximetasone 0.25% cream. Upon follow-up 6 weeks later, he noted both improvement of the pruritus and the rash with the topical treatment, new antihistamine and completion of his testicular cancer treatments with BEP. Follow-up examination demonstrated post-inflammatory hyperpigmentation to the mid lower back (Figure 2).

Discussion

The differential diagnosis of flagellate erythema includes bleomycin flagellate dermatitis, dermatomyositis, shiitake mushroom dermatitis, adult-onset Still's disease and infection with human immunodeficiency virus.[3] Although the exact mechanism is still unclear, the proposed pathophysiologic mechanism regarding the cutaneous manifestations is thought to be due to the lack of bleomycin hydrolase enzyme in the skin, which inactivates bleomycin, resulting in an accumulation of bleomycin in the skin.[1,2,4] Furthermore, the pruritis that manifests from these changes may lead to excoriations, causing abrasions and

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microtrauma, leading to vasodilation and further bleomycin accumulation, which may explain the Koebner phenomenon that has been reported, but the evidence is conflicting.[4,5] Other proposed mechanisms causing cutaneous inflammation and pigmentation are that bleomycin damages endothelial cells by upregulating TGF-β (tumour necrosis factor beta), inducing keratinocytes apoptosis and a cytotoxic effect on melanocytes.[3,4] This is thought to be a dose-dependent reaction, and doses over 200 U and higher may demonstrate cutaneous manifestations.[4] Other risk factors include patients with decreased bleomycin hydrolase in conditions such as atopic dermatitis, due to a filaggrin gene mutation, and interestingly, one study presented a potential link between patients with atopy and developing bleomycin pulmonary toxicity.[6,7] This is in contrast to shiitake mushroom dermatitis in which the triggers are thought to be due to the polysaccharide lentinan causing inflammation by stimulating interleukin-1,[5] and interestingly, shiitake mushrooms contain a sulphur compound with a similar structure to bleomycin.[5] The main treatment is to discontinue the inciting agent if possible. Symptomatic treatment includes bilastine, which is more effective than first-generation antihistamines in the treatment of pruritis and urticaria, due to its high affinity for peripheral H1-receptors, as it inhibits inflammatory mediators. Furthermore, there is evidence that increasing the dosage to 40 or 80 mg enhances the anti-inflammatory properties, without any sedating effects as it does not cross the blood–brain barrier.[8,9] Desoximetasone 0.25% cream was effective in the treatment of the hyperpigmentation and pruritis due to its anti-inflammatory, vasoconstrictive and immunosuppressive effects, which were further increased because it is a potent class 2 steroid.[8] The mechanism is due to the induction of lipocortins which suppress phospholipase A_2, and therefore, blunting endogenous chemical inflammatory mediators.[10]

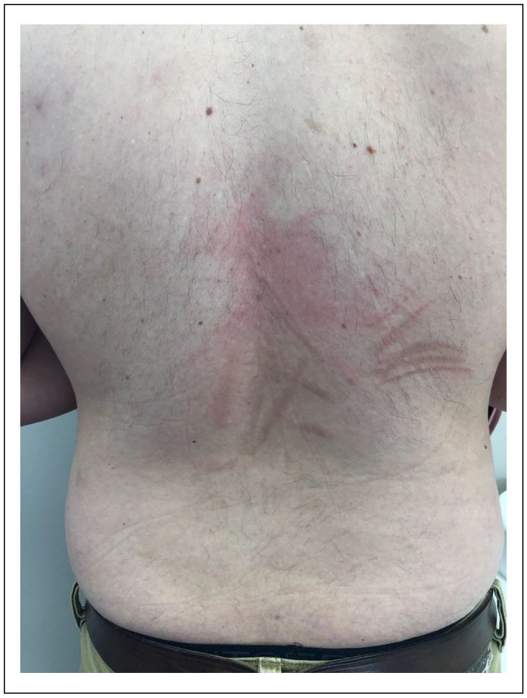

Figure 1. Bleomycin-induced flagellate dermatitis. Classic whip-like flagellate linear erythema to the back, due to bleomycin.

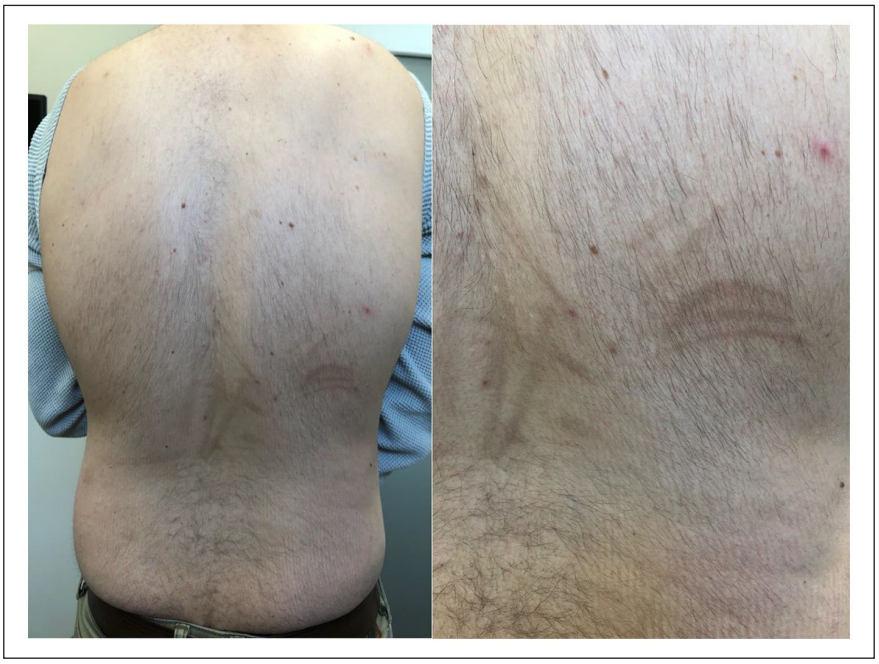

Figure 2. Bleomycin-induced flagellate dermatitis. Resulting post-inflammatory hyperpigmentation after discontinuation of BEP and topical corticosteroid use.

The above findings may be of importance for oncologists and family physicians to recognize this condition in their bleomycin patients and to initiate treatment. If the diagnosis is uncertain or there is worsening of the cutaneous lesions, a referral to a dermatologist is appropriate. It is also important to be aware of the heat-induced recall phenomenon, which is when flagellate erythema is induced by heat to a previously affected area.[3,4] Counselling patients to avoid heat on previously affected areas, as well as cooling prior to chemotherapy and trying to use the minimum effective dose of bleomycin may aid in the prevention of heat-induced recall.[3,4]

Prolonged pruritis if untreated may lead to increased risk of infections, due to chronic scratching and impairment of the skin barrier in already immunocompromised patient populations. Unmanaged pruritis has shown to have negative effects on mental health and can decrease patients' quality of life.[11] Regarding hyperpigmentation, patients may become self-conscious and withdraw from daily activities.[11] This may also give further evidence to using a potent class 2 or super potent class 1 steroid with bilastine as a treatment regime for these patients.

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Informed consent

The patient provided signed consent for publication of the case report.

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