Flagellate Dermatitis due to Bleomycin Intake

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ABSTRACT Flagellate dermatitis is a rare cutaneous manifestation in which long, striated erythematous lesion appear on the patient's skin. It is most frequently associated with bleomycin treatment or Shiitake mushroom intake, but it may also be attributed to many other possible causes. Herein we present a case of striated, hyperpigmented lesions which occurred after bleomycin intake. The typical flagellate lesions appeared for the first time on the patient's back and shoulders after the first course of chemotherapy for seminoma (bleomycin, etoposide, and cisplatin). The active lesions disappeared with the discontinuation of chemotherapy. Clinicians should be aware of flagellate pattern of dermatitis which may accompany different clinical situations.

KEY WORDS: flagellate dermatitis, testicular cancer, bleomycin, chemotherapy, drug eruption, adverse drug reaction
Conflict of interest:

INTRODUCTION

Flagellate dermatitis, also called flagellate erythema, is a term specific for a drug eruption which was firstly described by Moulin *et al*. (1) in 1970 as bleomycin-induced linear hyperpigmentation. Though the disease was initially associated with the use of bleomycin, more possible causes have been found since then that include Shitake mushrooms intake, chemotherapeutics (peplomycin, docetaxel), hypereosinophilic syndrome, mechanical causes (torture), and rheumatological disorders (2). Flagellate dermatitis is often described as a dose-dependent reaction, which usually occurs with total doses above 100 U of bleomycin, but the lesions may also appear with very low, scintigraphy doses of 15 U (3,4).

CASE REPORT

A 33-year-old Caucasian man was referred to our Department due to multiple skin lesion affecting his back and shoulders. The patient reported that he had been treated for to testicular cancer (seminoma). Other than a history of neoplasm, he did not have any comorbidities and appeared to be in good general health. The patient was diagnosed with testicular cancer in July 2019, underwent radical orchiectomy, and was treated with chemotherapy (bleomycin, cisplatin, and etoposide regimen) for lymph nodes and pulmonary metastases. Before the second course of chemotherapy (September 2019), red lesions appeared on the patient's back and shoulders, with associated xerosis. Their number increased with the next courses of the therapy. The patient did not report any itch nor pain. After completion of chemotherapy (November 2019), the lesions stopped spreading, gradually changed their color to brown, and persisted unchanged to date. On admission, physical examination revealed multiple, linear hyperpigmented

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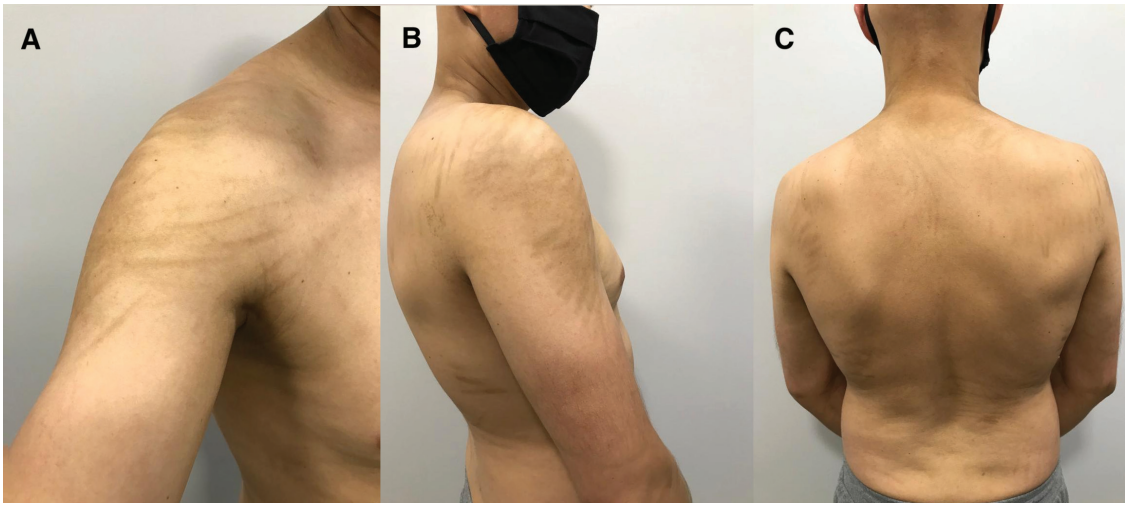

Figure 1. Lesions on the patient's shoulder (A and B) and back (C).

lesions (Figure 1) located on the shoulders and on the back. There was no evidence of mucosal or systemic involvement. The patient did not report any pathological sensation in the affected area. Flagellate dermatitis was diagnosed on the basis of the clinical picture and medical history. Nevertheless, due to the lack of subjective symptoms and no ongoing treatment with bleomycin, no treatment was prescribed.

DISCUSSION

Bleomycin is an antineoplastic agent which belongs to a subfamily of glycopeptide antibiotics. It is frequently used as a part of cytotoxic chemotherapy regimens. Since its approval it has been used for Hodgkin's lymphoma, squamous cell carcinoma, and testicular cancer. The primary mechanism of action is its ability to damage DNA. This breakdown of DNA and subsequent production of thymine causes cells to stop the cycle at the G2 phase (5). The adverse effects of the therapy are mostly visible in tissues with relatively low levels of bleomycin hydrolase enzyme (lungs or skin) and are believed to be effects of drug accumulation (5). Drug-related skin manifestations are observed in the majority of patients (50-88%) and are in most cases reversible (3). Among the possible symptoms, the literature mentions alopecia, stomatitis, painful and inflamed nodules or fingers, affectation of nails, and flagellated erythematous infiltrates frequently associated with intense itch (3).

The pathophysiology is yet to be fully discovered; however, local accumulations of bleomycin may play an important role in its development. A study by Takeda *et al*. (6) showed that bleomycin hydrolase is localized only in the subcorneal layers of the epidermis, and the drug thus cannot be fully degraded at the dermal levels. Moreover, bleomycin-induced skin changes often appear on the extremities and over bony prominences, and it is believed that trauma-related blood flow increases the accumulation of the drug (3).

The lesions vary and may appear as striated erythematous, urticarial, but also papular and vesicular skin changes, which tend to heal with subsequent hyperpigmentation (3). Although the lesions are often pruritic, our patient did not report any pathological sensation at any point of the therapy or after its completion. The time of development varies greatly, and in some cases it may start several hours after the drug introduction while in others it may take up to two months (3).

The diagnosis is established mostly based on the clinical picture. The association of skin manifestations with drug administration and hyperpigmentation after drug suspension is typical (7). Although it has been reported that histopathological findings in flagellate dermatitis are similar to fixed drug eruptions (8), recent studies have indicated that the histological picture is neither specific nor uniform (3). The differential diagnosis mostly includes other causes of flagellate dermatitis, including Shitake mushroom intake (9).

There is no specific treatment available. Normally, lesions clear in 6-8 months after the suspension of bleomycin. In some patients the chemotherapy may be continued without bleomycin, but this decision has to be made on the basis of risk-benefit analysis (10). The treatment of the associated pruritus may include topical and systemic corticosteroids as well as oral antihistamine drugs. These have been reported to be beneficial to relieving pruritus and decreasing skin trauma (10).

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Flagellate dermatitis is an uncommon skin manifestation of bleomycin therapy. We believe that all clinicians should be aware of this manifestation in order to act appropriately against this adverse reaction.

References:

1. Moulin G, Fière B, Beyvin A. Pigmentation cutanée par la bléomycine [Cutaneous pigmentation caused by bleomycin]. Bull Soc Fr Dermatol Syphiligr. 1970;77:293-6.
2. Bhushan P, Manjul P, Baliyan V. Flagellate dermatoses. Indian J Dermatol Venereol Leprol. 2014;80:149-52.
3. Ziemer M, Goetze S, Juhasz K, Elsner P. Flagellate dermatitis as a bleomycin-specific adverse effect of cytostatic therapy: a clinical-histopathologic correlation. Am J Clin Dermatol. 2011;12:68-76.
4. Perrot H, Ortonne JP. Hyperpigmentation after bleomycin therapy. Archives of Dermatological Research. 1978;261:245-52.
5. Brandt JP, Gerriets V. Bleomycin. StatPearls [Internet]: Treasure Island (FL): StatPearls Publishing; 2020 Jan.
6. Takeda A, Nonaka M, Ishikawa A, Higuchi D. Immunohistochemical localization of the neutral cysteine protease bleomycin hydrolase in human skin. Arch Dermatol Res. 1999;291:238-40.
7. Grynszpan R, Niemeyer-Corbellini JP, Lopes MS, Ramos-e-Silva M. Bleomycin-induced flagellate dermatitis. BMJ Case Rep. 2013;2013:bcr2013009764.
8. Mowad CM, Nguyen TV, Elenitsas R, Leyden JJ. Bleomycin-induced flagellate dermatitis: a clinical and histopathological review. Br J Dermatol. 1994;131:700-2.
9. Baran W, Batycka-Baran A, Maj J, Szepietowski JC. Shiitake dermatitis - now also in Poland. Acta Derm Venereol. 2015;95:102-3.
10. Jones RH, Vasey PA. Part II: testicular cancer--management of advanced disease. Lancet Oncol. 2003;4:738-47.