

Flagellate Erythema Secondary to Bleomycin for Non-Seminomatous Testis Tumor

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Abstract

The development of flagellate erythema secondary to bleomycin treatment is a rare adverse effect. The prevalence varies between 8 to 22% of patients and it is becoming rarer. Flagellate erythema presents as a scaly erythematous papule. A lower amount of bleomycin hydrolase in regions with reduced production, such as skin and lungs, decreases bleomycin degradation, which allows its accumulation in tissues, triggering an inflammatory process, especially in patients with lower basal enzyme function. We report a clinical case of a severe presentation of flagellate erythema secondary to a patient ongoing bleomycin, etoposide and platinum (BEP) based chemotherapy of non-seminomatous testis cancer.

Keywords: Bleomycin; Flagellate Erythema; Adverse Effect; Chemotherapy; Testis cancer.

Introduction

Bleomycin (BLM) is an antineoplastic antibiotic that can fragment DNA [1]. This process leads to greater cell cycle interruption and accumulation at the G2 cell division phase. BLM mechanism of action is most likely related to compromising the

interaction of oxygen and iron (Fe^{+2}). Exposed to reducing agents and oxygen, activates the metalbleomycin complex, which works as a ferrous oxidase inside the cells. BLM associates with amines located in terminal DNA regions, leading to the activation of reactive oxygen species, degrading DNA chains [2]. BLM metabolization occurs through

its inactivation mediated by a cytosolic cysteine hydrolase, called bleomycin hydrolase. The availability of this enzyme varies through the body tissues and is usually lower in the skin and lungs. However, patients with lower than usual tissue levels of the enzyme may accumulate the drug substance, in its undegraded form, in susceptible body tissues, especially the skin [3]. Thus, its accumulation in the dermis may trigger the development of typical skin lesions, called flagellate erythema. In some older studies, the prevalence ranged from 8% to 22% and its turning rarer because of its limited clinical use [4]. This article reports this unusual adverse effect in the context of treating a non-seminomatous testis cancer.

Case report

A-20 years old male patient presents painless testicular nodule. His past medical history is relevant for depression, orchitis and hypertension. He had ultrasonography showing hypoechoic areas. Tumor markers were evaluated at the time of the presentation: LDH 291, AFP 1, 21 and HCG 63. Also magnetic resonance (MRI) of scrotum presented left intratesticular infiltration. Left Orchiectomy was performed and non-seminomatous neoplasia was found (pT2pN1M0, S1). The immunohistochemistry panel for testicular cancer was done and the results were compatible with embryonal carcinoma.

Adjuvant treatment was started with 30 UI of bleomycin, 201 mg of etoposide and 40,2 mg of cisplatin (BEP), for 3 cycles. After the first dose of BLM he started with progressive, diffuse, severe and pruritic erythematous papules (Figures 1-5), associated with an itchy aspect at the beginning of treatment, and worsening.

Diagnosis of flagellate erythema was done, followed by treatment with prednisone and antihistamines, with consequent improvement of the lesions. The patient completed two cycles without bleomycin (EP). On follow up, the patient had presented a significant improvement of the pruritus. Nowadays he is under a complete remission of the disease.

Discussion and Conclusion

Flagellate erythema is a rare adverse effect [4]. Characteristic lesions with erythematous papule formation, associated with linearly shaped plaques were found diffusely in the patient's body, affecting the trunk, head, upper and lower limbs [5] This condition may develop in any of the drug administration forms [6]. Flagellate erythema usually manifests in both men and women within the first 72 ours of drug use. In contrast, this case report presents a clinical manifestation on the eighth day of the medication [4]. The mechanism of this adverse effect is probably on the increase of melanogenesis, pigmentary incontinence due to the inflammatory

process and toxic effects of the drug itself, such as neutrophilic eccrine hidradenitis [7].

In the majority of cases of flagellate erythema, the resolution is spontaneous, however, as in this case, the high intensity of the skin manifestation inflammatory response required the use of oral corticosteroids, antihistamines and permanent

discontinuity of the drug [3]. Heat in the compromised regions may recurrently lead to worsening of cases. Cooling the chemotherapy before its administration may be a way to alleviate the severity of cases [8]. The patient presented in this clinical case had clinical improvement of the erythematous condition and after a few weeks the bleomycin was interrupted.



Figure 1: 1. Low back flagellate erythema. 2. Forearm flagellate erythema. 3. Head and neck flagellate erythema. 4. Right hand flagellate erythema. 5. Right leg flagellate erythema.

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