Case Report

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Flagellate Dermatitis Induced by Bleomycini a Patient with Hodgkin Lymphoma

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ABSTRACT

Keywords: Bleomycin; Drug Eruptions;Dermatitis; Erythema

Introduction

Adverse skin reactions affect from 8 to 20% of patients using Bleomycin, an antiblastic medication capable of depolymerizing the DNA of the cells. One of this reactions is Flagellated Dermatitis, which manifests in erythematous-violaceous macules and plaques, linear or curvilinear, in a parallel arrangement with a typical "whipping" aspect. The incidence of flagellated dermatitis in patients using bleomycin varies from 8 to 66% and the skin injuries can appear a few hours later as well as 6 months after the drug administration [1-4]. Bleomycin represents a group of sulfur-containing polypeptide antibiotics derived from the fungus Streptomyces verticillus. It is used in the systemic treatment of various types of cancer, such as head and neck, penis, cervix and vulva carcinomas, lymphomas and testicular neoplasms. Topical or intralesional use has been shown to be efficient to treat vascular neoplasms, melanomas, recalcitrant viral warts, hypertrophic scars and keloids4. Its mechanism of action consists on direct (action of the drug itself) and indirect (formation of free oxygen radicals) DNA cleavage , followed by interruption of the cell cycle and apoptosis4. Its toxic effects occurs in tissues where there is a low concentration of the bleomycin hydrolase enzyme (which inactivates the drug), such as the skin [3,4].

Case Description

A 21-year-old man was diagnosed in August 2019 with Classic Hodgkin's Lymphoma (nodular sclerosis subtype), through left

axillary lymphadenectomy followed by immunohistochemical analysis. The positron emission tomography showed the disease spread over the supra and infradiaphragmatic lynphonodes chains, in addition to several bones. This analysis, plus the presence of all B symptoms, determined staging IV-B. Besides the disease, the patient had been in treatment for Hepatitis B for five years, using Tenofovir. The chemotherapy protocol used since the first cycle was ABVD (Doxorubicin 25mg / m2; Bleomycin 10 Ul / m2; Vinblastine 6mg / m2; Dacarbazine 375mg / m2) with the exception of Bleomycin, which was only introduced at the beginning of the second cycle and maintained until the end of the treatment. In total, 6 cycles of chemotherapy were performed. Four days after the introduction of Bleomycin, the patient presented highly pruritic and erythematous-violaceous macules. When scratched, this would become erythematous plaques. They could be seen in the hypogastric, right paraumbilical, right iliac, infra-sternal, suprasternal and left deltoid regions. The next chemotherapy session was carried out, observing the appearance of new pruritic and erythematous-violaceous macules and plaques, in addition to increased pruritus and hyperpigmentation in existing ones (Figures 1-3).

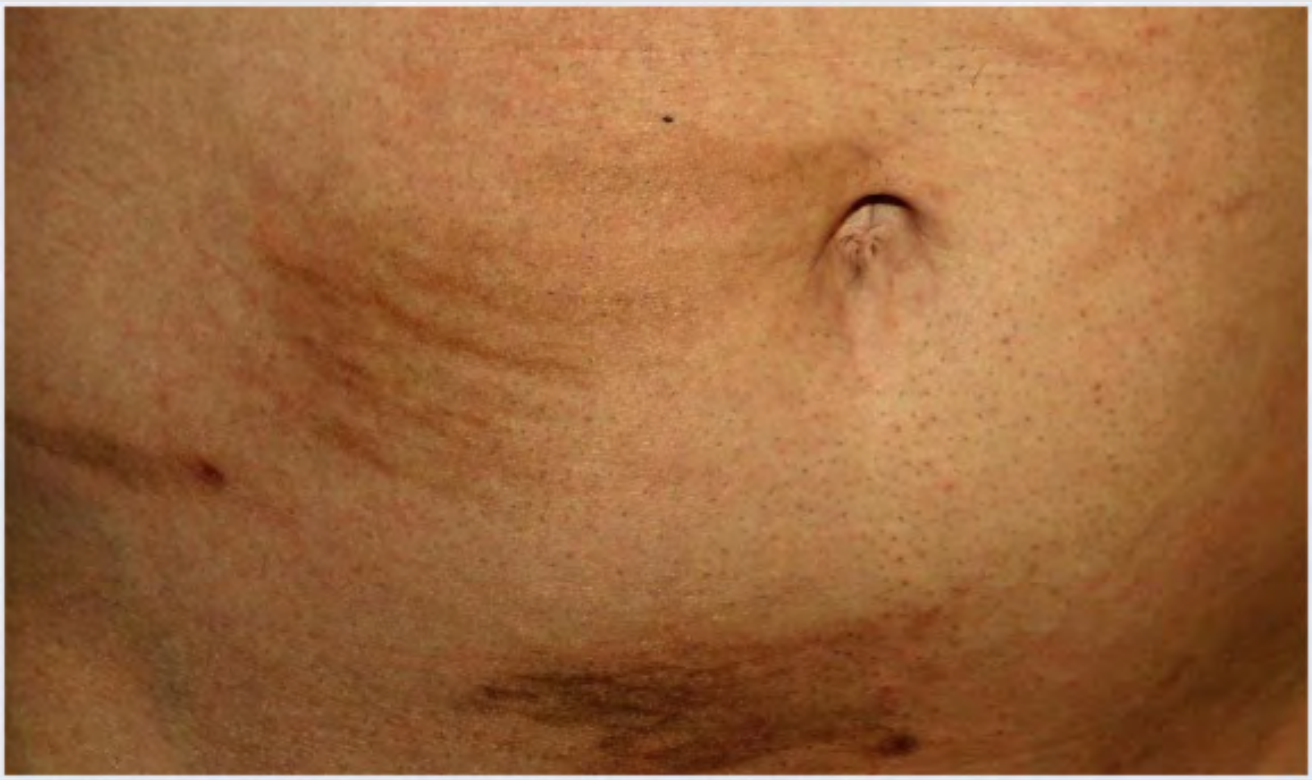

Figure 1: Hyperchromic macules in hypogastric and right paraumbilical regions, on a typical "whipping aspect".

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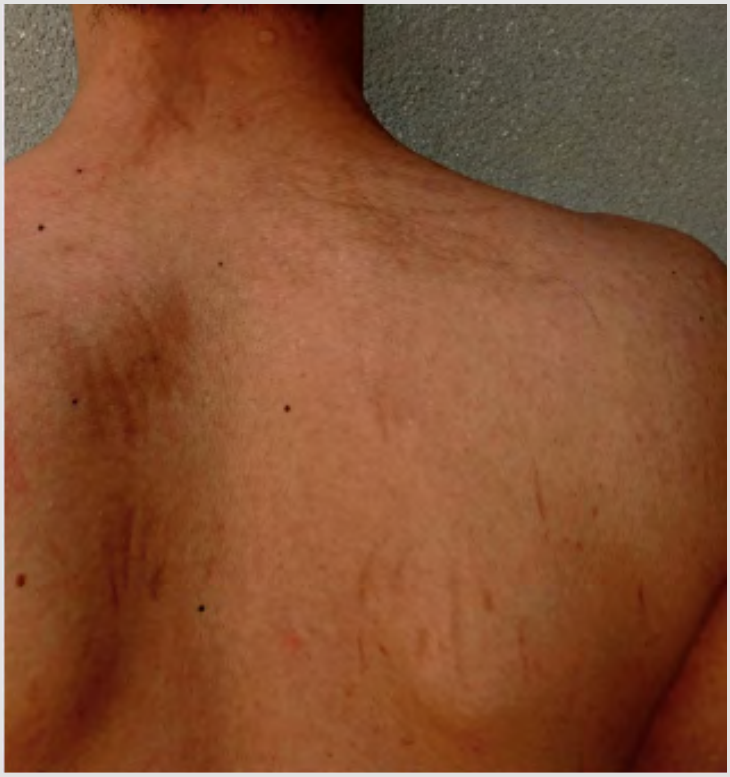

Figure 2: Linear hyperchromic macules ("whipping aspect") spreaded in the posterior chest region.

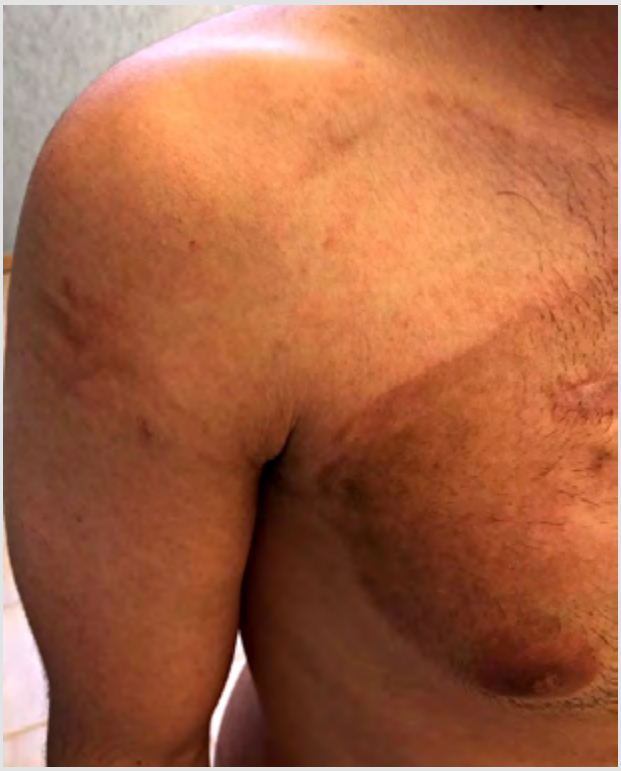

Figure 3: Hyperchromic macules in lateral deltoid and right supramammary regions.

The clinical diagnosis was supported by a suggestive histopathological exam that showed epidermal spongiosis. Interface dermatitis and dermal perivascular lymphocytic infiltrate with increased eosinophils. The treatment involved intravenous use of Diphenhydramine (50 mg) and Dexamethasone (10 mg) during subsequent chemotherapy sessions, leading to the stabilization of existing injuries and the absence of new ones. The complete treatment protocol for the Hodgkin's disease was maintained until completion, along side of corticosteroid therapy and antihistamines.

Discussion

The Flagellate Dermatitis lesions are initially erythematous, diffuse and itchy, elevated or not, usually in the upper and lower regions of the trunk, flanks and limbs. Subsequently, they give rise to hyperchromic macules that have typical "whipping" aspect [3,4]. Its pathophysiology remains speculative. One of the theories suggests that the accumulation of Bleomycin in the skin generates a Fixed Pigmented Erythema due to the direct effects of the drug on keratinocytes. Another hypothesis would be that the act of scratching or rubbing the skin causes the drug to leak from the local blood vessels, generating hyperpigmentation [1,3]. There is evidence that the dose of Bleomycin administered does not influence the onset of dermatitis, as well as the route of administration and the treated disease. In this sense, recent reports describe the occurrence of this adverse effect after administration of low parenteral doses (15Ul / m2 at 30Ul / m2) in cases of Hodgkin's Lymphoma and Lung Cancer, and after intralesional administration of 14Ul / m2 of Bleomycin in the treatment of plantar warts [2,4,5].

The differential diagnosis is based mainly on the patient's anamnesis and includes contact dermatitis (especially phytophotodermatoses), diseases that present Koebner's phenomenon, self-inflicted dermatoses, ingestion of raw or undercooked Shiitake mushrooms, Dermatomyositis and Still's disease [3]. There is no specific treatment for flagellated dermatitis, since its evolution is self-limited and dependent on the administration of Bleomycin [2]. The remission from the lesions can be spontaneous with the withdrawal of the drug or require topical and / or oral corticotherapy. In some cases, hyperpigmented macules may persist for months after drug withdraw or even the lesions reappear after new exposure to Bleomycin [2].

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Conflict of Interest

None.

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