Bleomycin-induced Flagellated dermatitis: a case report

Dermatitis flagelada inducida por Bleomicina; a propósito de un caso

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Abstract

Introduction: Flagellated dermatitis is an infrequent pathology, with characteristic skin lesions, which is developed due to the use of bleomycin. Clinically it occurs as erythematous or hyperpigmented maculae of linear disposition with flagellar pattern, in trunk and/or upper extremities. It presents self-limited evolution, therefore, its treatment varies from expectant management to the use of topical or oral corticosteroids. Objective: Presentation of a clinical case of flagellated dermatitis secondary to bleomycin in a pediatric patient with history of central nervous system neoplasia.

Clinical case: 8 years, schoolchild, female, with a history of primary intracranial mixed germ cell tumor (sellar and suprasellar) and secondary panhypopituitarism. She receives chemotherapeutic treatment according to the PEB protocol, with use of IV bleomycin during three days. After two days, intermittent pruritus begins, associated with erythematous and pigmented maculae of linear distribution, followed by a flagellated pattern, with isolated signs of excoriation, in the abdominal region and upper back. topical treatment with mild potency corticosteroids is indicated for ten days, with a satisfactory clinical response. Conclusions: There should be a high diagnostic suspicion in pediatric patients with a history of prior administration of the drug and the appearance of characteristic skin lesions, which will allow adequate behavior regarding its management and the continuity of chemotherapy.

Keywords: Flagellated Dermatitis; Bleomycin; Children; Chemotherapy; Self-limited
Introduction

Bleomycin is an antitumor antibiotic derived from Streptomyces verticillus. Its cytotoxic effects are produced by the generation of oxygen free radicals, causing the rupture of DNA strands and cell death. Bleomycin is usually used as part of the BEP protocol, associated with etoposide and cisplatin for the treatment of different types of tumors, mainly germ cells, including testicular cancer, ovarian cancer and central nervous system tumors and also in Hodgkin lymphoma. In dermatology, it is used for the treatment of recalcitrant warts and in the management of keloid and hypertrophic scars.

The adverse effects of bleomycin are most frequently seen in lungs and skin, due to the low concentration of bleomycin hydrolase, which metabolizes the molecule, causing a higher accumulation of the drug. From the adverse reactions described in lungs, it has been observed pneumonitis in the 46% of the cases and pulmonary fibrosis in a frequency of 2-40%. In the skin, its toxicity can cause multiple manifestations, including Raynaud’s phenomenon, hyperkeratosis, palmoplantar desquamation, stomatitis, fibrosis, alopecia, hyper or hypopigmentation of the hair, edema, digital gangrene, Beau’s lines, onycholysis, neutrophilic eccrine hidradenitis and pigimentary alterations. The objective of this publication is to describe a case of flagellate dermatitis in a pediatric patient, due to the use of bleomycin, an extremely rare adverse reaction, and to conduct a bibliographical review focused on the diagnosis and treatment.

Clinical case

Female patient, eight years old with a history of intracranial mixed germ cell tumor (sellar and suprasellar) and secondary panhypopituitarism, hospitalized for left preseptal cellulitis secondary to left ethmoiditis; she completed 14 days of antibiotic treatment (ceftriaxone iv), with a good therapeutic response. During the hospitalization, a brain tomography was performed and it was observed the growth of the sellar tumor, therefore chemotherapy was restarted with BEP protocol (bleomycin, etoposide, and cisplatin). The patient received intravenous treatment from day one to three, bolus 12 mg/day of bleomycin (15 mg/m²/day) and etoposide (80 mg/m²/day) and then cisplatin (20 mg/m²/day) on day four to eight. On the fifth day of treatment, the patient reported intermittent pruritus and the physical examination showed erythematous and brown maculae of linear and irregular disposition, with flagellar pattern looking like “lashes”, in abdomen and back, with isolated signs of excoriation. (Figure 1 and 2). The clinical picture is compatible with bleomycin-induced flagellate dermatitis, therefore, mild potency topical corticosteroids were indicated (fluticasone cream 0.05%), twice a day for ten days in the affected region, having a good therapeutic response, which attenuates injuries and reduced itching.
Discussion

Flagellate dermatitis is an uncommon adverse reaction to bleomycin, reported in 8-20% of patients in treatment\(^8\). It is a rare pathology in adults and very rare in children. Less than ten cases have been reported in the literature in pediatrics, mainly among adolescents\(^10,11,12,13,14,15,16\). The development of lesions depends on the dose and occurs with doses higher than 100 U (1 U = 1 mg/dL)\(^17\), although it has been described that their occurrence takes place at doses used for scintigraphic purposes, that can be as low as 15 mg\(^18\). The time of appearance can vary from one day to nine weeks\(^19,20\). Clinically, it is characterized by the presence of erythematous or hyperpigmented maculae of linear disposition, pruriginous or not, distributed in a flagellar pattern mainly in trunk, back and upper limbs\(^21\). Its differential diagnosis includes dermatomyositis, Still’s disease and the intake of Shiitake mushroom\(^22\).

Histologically, in the acute phase, their findings are similar to those observed in the fixed drug eruption, with vacuolization of the basal layers of the epidermis, melanin incontinence and dispersed dyskeratosis keratinocytes\(^37\). In later stages, post inflammatory changes are observed\(^17\).

There are multiple hypotheses about its pathogenesis, including a local increase in melanogenesis and/or localized eruption secondary to trauma, which would occur due to increased pressure or scratching, with subsequent leakage of bleomycin through the blood vessels and consequent higher concentration of the chemotherapeutic agent in skin, producing a local inflammatory response\(^6,7\).

The treatment is controversial because the eruption is self-limited, resolving itself within six to eight months after the suspension of the drug, which can reappear, even with more intensity, during a new treatment\(^17\). It is important to note that, in general, chemotherapy cycles do not require suspension\(^23\). The treatment is symptomatic, with a good response to management with antihistamines, topical or systemic corticosteroids\(^2,24,25\). A severe rash, with no response to symptomatic treatment, may require stopping chemotherapy\(^2,25\).

Conclusions

The use of intravenous bleomycin presents the appearance of flagellate dermatitis as an adverse skin effect. In children, it is a very rare pathology; in fact, our case is the first pediatric case published in Chilean literature. There should be a high suspicion of diagnosis in pediatric patients with a history of previous administration of the drug and the appearance of characteristic skin lesions, especially pediatricians and pediatric oncologists, which will allow appropriate management and the continuity of chemotherapy. The management of the dermatitis is symptomatic and usually does not require stopping chemotherapy.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.
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