BLEOMYCIN-INDUCED FLAGELLATE DERMATITIS: A CASE REPORT

Walfrido Bispo Junior[1], Rosane Soares Oliveira[2], Silvana Maria Barros de Oliveira[3], Monik Kelly Santos Lima[4]

[1]Pharmacist. Ph.D in Biotechnology in Healthcare. Professor Alberto Antunes Teaching Hospital. Maceió-AL-Brazil.
[2]Pharmacist. Specialist in Adult and Older Adult Health. Professor Alberto Antunes Teaching Hospital. Maceió-AL-Brazil.
[3]RN. Undertaking M.A in Nursing. Professor Alberto Antunes Teaching Hospital. Maceió-AL-Brazil.
[4]RN. Specialist in Oncology. Professor Alberto Antunes Teaching Hospital. Maceió-AL-Brazil.

ABSTRACT: Flagellate Dermatitis consists of cutaneous hyperpigmentation with a flagellate appearance, one specific cause of which is bleomycin. Bleomycin is a chemotherapy agent used in the treatment of different neoplasias. This report's objective is to describe the case of a 31-year-old patient receiving treatment for Hodgkin Lymphoma with a protocol of Antineoplastic Chemotherapy made up of four drugs, including bleomycin, which led to the development of Flagellate Dermatitis. This is a report of a case which took place in a teaching hospital in the Northeast of Brazil in 2014. The therapy used as treatment was use of corticosteroid, which led to the remission of the lesions of the flagellate type and allow the continuation of the treatment without the need for changing the chemotherapy protocol. The study's importance lies in that it raises discussion regarding the aspects involving the management of this hypersensitivity so as to ensure the continuity of the antineoplastic treatment.
DESCRIPTORS: Drug eruption; Antineoplastic combined chemotherapy protocols; Hodgkin Lymphoma.

DERMATITE FLAGELADA INDUZIDA POR BLEOMICINA: RELATO DE CASO

RESUMO: A Dermatite Flagelada consiste de uma hiperpigmentação cutânea de aspecto flagelado, tendo como causa específica a bleomicina. A bleomicina é um agente quimioterápico usado no tratamento de diferentes neoplasias. O objetivo deste relato é descrever o caso de uma paciente de 31 anos de idade, em tratamento de Linfoma de Hodgkin com protocolo de Quimioterapia Antineoplásica composto por quatro drogas, dentre elas, a bleomicina, que cursou com o desenvolvimento da Dermatite Flagelada. Trata-se de um relato de caso ocorrido num hospital universitário do nordeste do Brasil em 2014. A terapia utilizada como tratamento foi uso de corticoide, o que proporcionou a remissão das lesões do tipo flagelo e permitiu a continuidade do tratamento sem necessidade de mudança do protocolo quimioterápico. A importância do estudo se deve por levantar discussão sobre os aspectos que envolvem o manejo dessa hipersensibilidade, para garantir a continuidade do tratamento antineoplásico.
DESCRITORES: Erupção por droga; Protocolos de quimioterapia combinada antineoplásica; Doença de Hodgkin.

DERMATITIS FLAGELADA INDUCIDA POR BLEOMICINA: RELATO DE CASO

RESUMEN: La dermatitis flagelada consiste en una hiperpigmentación cutánea de aspecto flagelado y su causa específica es la bleomicina. La bleomicina es un agente quimioterápico usado en el tratamiento de diferentes neoplasias. El objetivo de este relato fue describir el caso de una paciente de 31 años de edad, en tratamiento de Linfoma de Hodgkin con protocolo de Quimioterapia Antineoplásica compuesto por cuatro drogas, entre las cuales la bleomicina, ocasionada con desarrollo de Dermatitis Flagelada. El caso ocurrió en un hospital universitario del nordeste del Brasil en 2014. La terapia utilizada como tratamiento fue uso de corticoide, lo que proporcionó la remisión de las lesiones del tipo flagelo y permitió la continuidad del tratamiento sin necesidad de cambio del protocolo quimioterápico. El papel del estudio es abrir discusión acerca de los aspectos que involucran el manejo de esa hipersensibilidad, para garantizar la continuidad del tratamiento antineoplásico.
DESCRIPTORES: Erupción por droga; Protocolos de quimioterapia combinada antineoplásica; Enfermedad de Hodgkin.

Corresponding author:
Walfrido Bispo Junior
Hospital Universitário Professor Alberto Antunes
Av. Lourival Melo Mota, s/nº - 57072-900 - Tabuleiro dos Martins-AL-Alagoas
E-mail: walfridobispojr@hotmail.com

Received: 11/01/2015
Finalized: 15/04/2015

INTRODUCTION

Bleomycin is a mixture of glycopeptide antibiotics produced by the fermentation of Streptococcus verticillus, which have antitumor activity against squamous cell carcinoma of the cervix, testicular tumors and lymphomas as is the case of Hodgkin Lymphoma[1]. Its efficacy is evidenced by its action, which culminates in cell death. This occurs through the production of free radicals which break the DNA chains of the cancer cells[2].

With the reduction in the use of bleomycin in the protocols of cytostatic drugs, Flagellate Dermatitis (FD), a rare adverse reaction, has come to be documented only rarely[3]. The literature describes FD as a specific form of hyperpigmentation with a linear appearance resembling the scars left by whipping, which can derive from an inflammation and which generally affects the trunk[4], the dorsum[5-6], and the palmar and plantar surfaces[3].

Although this is little reported, in addition to the pigmentary alterations, bleomycin can also cause digital gangrene. However, FD remains the least common of these lesions, reaching an incidence between 8 – 20% as described by the scientific community[3]. For these reasons, it is possible to infer the need to document cases of this adverse reaction, typical of the use of bleomycin, in order to increase the production of knowledge regarding this issue, promoting the exchanging of experiences regarding the management of this toxicity. In accordance with this, the aim is to report a case of FD which occurred in a teaching hospital in the Brazilian Northeast.

REPORT

M. I. A. S., female, 31 years old, of mixed black and white descent, a teacher, with Hodgkin Lymphoma, receiving treatment with doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD), treated in the first semester of 2014, presented erythematous and itchy plaques on her face, trunk and limbs, days after the undertaking of the first cycle of chemotherapy in a teaching hospital in the Brazilian state of Alagoas. The lesions, characterized by hyperpigmentation, began on the upper limbs. From the very beginning, the suspicion of local chemotherapeutic extravasation was excluded, given that both the limbs were compromised and that chemotherapy had been administered intravenously in only one of them.

Bactrim®, Hixizine® and topical Diprisone® were prescribed, and referred for evaluation by the dermatology service. The patient reported slight improvement of the erythematous plaques with the use of antihistamines, with the lesions on the upper limbs disappearing almost totally, although there was progression into the trunk, dorsum and cervical region with the course of cycles of chemotherapy.

The dermatological examination presented erythematous-violaceous plaques, some of which were desquamating, others with vesicles and blisters on the surface, in a linear configuration, spread on the auricle, limbs and trunk. Prednisone and Hixizine were prescribed, following which biopsy and immunohistochemistry were undertaken. The results of the biopsy showed skin with focal erosion, which was parenchymatous with scale-crust and spongiosis of the epithelium, dermis with moderate mixed perivascular inflammatory infiltrate, made up of numerous histiocytes, eosinophils, and lymphocytes, without exocytosis.

These findings correspond to the drug eruption type of hypersensitivity reaction, which can be caused by bleomycin. After this diagnosis, the hypothesis of FD was raised. The patient was liberated to undertake further cycles of chemotherapy maintaining in association the use of a corticosteroid (Prednisone).

The immunohistochemistry confirmed the initial hypothesis raised with the result of the biopsy. The treatment with antihistamines and corticosteroids resulted in the partial remission of the FD while the use of bleomycin was maintained, and total remission occurred four weeks after the end of the cytostatic treatment.

DISCUSSION

FD receives this name as it takes a linear form, which resembles lesions of the flagellate type caused by blows with a whip. This cutaneous lesion is induced by bleomycin and begins approximately 12 to 24 hours following the exposure to this cytostatic drug[2]. The relationship

between the cause and the dose or the means of administration is not yet firmly established. There are, however, those who argue that a cumulative dose of bleomycin of 16-286 mg intravenously or intraperitoneally can trigger the hypersensitivity reaction which leads to FD[7]. In the case described, the lesions began subsequent to the first cycle of infusion of bleomycin.

The metabolism of bleomycin occurs through the hydrolase enzyme, which is present in low levels in the pulmonary tissues and in the skin, leading to the inference that this is the reason why these tissues are affected by the adverse reactions, as in the case of FD[8]. Another possible cause for this toxicity affecting the skin could be small traumas such as abrasions or pressure on areas of bony prominences, or even pruritus, which can provoke an increase in the blood flow, resulting in a high concentration of bleomycin in these areas, this process triggering the lesions[9].

Remaining on this issue, although bleomycin is administered as a polychemotherapy protocol (ABVD) for Hodgkin Lymphoma, FD is not related to the other drugs in this protocol[9].

The results of the biopsy and of the immunohistochemistry were compatible with the reaction of the hyperpigmentation inflammatory type such as FD, in conformity with what the literature describes in the aspects of spongiosis, degeneration of the basal layer, inflammatory lympho-histiocytic infiltrate in the dermis, melanophages in the papillary dermis and lymphocytic vasculitis without epidermal change[4].

There are few reports on the management of FD, although the use of antihistamines and topical and oral corticosteroids have been described as capable of bringing benefits for the reduction of the pruritus[9]. Regarding the disappearance of the lesions, there are authors who establish a period of five weeks following the end of treatment with bleomycin[3] or following interruption of the exposure to the drug[7].

Use was not made of corticosteroids and antihistamines in the case described, there being a progressive reduction of the lesions, allowing the continuity of the treatment without the need for change of protocol.

CONCLUSION

Bleomycin is already recognized as a cytostatic drug capable of triggering FD, which is configured by lesions which are disseminated on the skin with hyperpigmentation, post-inflammatory, linear, of the flagellate type resembling marks left by blows from a whip, which generally affects the trunk, the dorsum, the limbs, and the palmar and plantar surfaces, and which requires further information regarding management favoring the continuity of the treatment, reducing the harm to the antitumor therapy.

REFERENCES

1. Brunton L, Parker K, Blumenthal D, Buxton, I. Goodman & Gilman: Manual de Farmacologia e Terapêutica. 11a ed. Porto Alegre: AMGH; 2010. Agentes Antineoplásicos. p. 853-908.

2. Gangas CS, Tuma MC, Osses MS. Eritema flagelado por bleomicina, A propósito de un caso. In Reunião Anual de Dermatologistas Latino-Americanos; 2014, Maio, Santiago de Chile, Chile; 2014.

3. Biswas A, Chaudhari PB, Sharma P, Singh L, Julka PK, Sethuraman G. Bleomycin induced flagellate erythema: revisiting a unique complication. Journal of Cancer Research and Therapeutics. 2013;3(9):500-3.

4. Kondo RN, Pontello-Júnior R, Pontello R. Dermatite flagelada: relato de caso. Revista Brasileira de Medicina. 2012;69(2):31-3.

5. Manoj J, Kaliyadan F, Dharmaratnam AD. Palmar and flagellate hyperpigmentation following low dose intralesional injection of bleomycin for cystic hygroma. Dermatol Online J. 2008;14(8):19.

6. Maciá ES, Guillén PC, Rodriguez LA, Laita UM, Carrato MA. Varón con enfermedad de Hodgkin con exantema vesiculoso de distribución simétrica en manos tras tratamiento quimioterápico. An. Med. Interna. 2006;23(5):252-3.

7. Peçanha, C.; Constanza, G.; Dacier, B.; Sodré, C. T. Flagellate dermatitIs by bleomycin [apresentação ao Curso de Especialização em Dermatologia da Universidade Federal do Rio de Janeiro; 2007; Rio de Janeiro, Brasil].

8. Diao DY, Goodall J. Bleomycin-induced flagellate dermatitis. Canadian Medical Association Journal. 2012;184(11):1280.

9. Mota GD, Penna AMD, Soares RC, Baiocchi OCG. Bleomycin-induced flagellate dermatites. Rev. Bras. Hematol. Hemoter. 2014;36(4):297-9.