CASE REPORT

BLEOMYCIN INDUCED FLAGELLATE DERMATITIS IN A PATIENT WITH NON-SEMINOMA GERM CELL TUMOUR WITH BILATERAL UNDESCENDED TESTES

Manzoor Khan[1], Malik Hasnat ul Hassan Khan[1], Muhammad Firdous Khan[1], Syed Aftab Ahmad[2], Sara Baloch[1], Shazia Asim[3], Eesha Akhlaque[3]

[1]Shaukat Khanum Memorial Cancer Hospital and Research Center Peshawar-Pakistan
[2]Khyber Teaching Hospital Peshawar-Pakistan
[3]Lahore Medical and Dental College, Lahore-Pakistan

Flagellate Dermatitis (FD) is a rare cutaneous manifestation of bleomycin toxicity caused by the deficiency of bleomycin hydrolase enzyme in the skin. It typically presents as erythematous patches or papules with linear, multiple flagellate structures. In this article, we report the case of FD in a 21-year-old male patient with non-seminoma germ cell tumour presenting with abdominal pain and bilateral undescended testes since birth. The patient was started on the BEP (Bleomycin, Etoposide and Cisplatin) protocol as per institutional guidelines. On the 17th day of the first cycle, the patient developed multiple whiplash skin lesions over his back, shoulders and front right frontotemporal area with intense itching. A diagnosis of FD was made clinically. Bleomycin was stopped and he was switched to etoposide and cisplatin-based chemotherapy for the remaining three cycles. The rashes were treated with topical steroids (Beclomethasone), Systemic steroids (Prednisolone) and antihistamines (Cetrzine) according to recommended protocol. The patient responded very well to the above-mentioned treatment with the rashes completely disappearing within a span of 14 days. This case highlights the need for vigilance during chemotherapy as it can cause a wide range of skin reactions. FD is a condition with multiple potential causes and mechanisms underlying cutaneous manifestations. Early recognition and prompt treatment can help prevent long-term complications and improve patients' quality of life.

Keywords: Flagellate Dermatitis; Bleomycin; Non-Seminoma Germ Cell Tumour; Undescended Testes

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INTRODUCTION

Flagellate Dermatitis is a rare cutaneous manifestation of bleomycin toxicity caused by the deficiency of bleomycin hydrolase enzyme in the skin, leading to the accumulation of bleomycin. It typically presents as erythematous patches or papules with linear, multiple flagellate structures.[1] Bleomycin, an antineoplastic agent, is derived from Streptomyces verticillus strain and is used primarily in the treatment of Hodgkin's lymphoma and germ cell tumor.[2] Although bleomycin has shown significant efficacy in the management of these cancers, its use is limited due to its reported adverse effects, including pulmonary fibrosis, Raynaud's phenomenon, alopecia, and FD. Flagellate Dermatitis is a rare cutaneous reaction to bleomycin that has been reported in 8–20% of the cases. The clinical presentation of FD is characterized by whip-like linear lesions on the skin. The term 'flagellate' is derived from the Latin word 'flagellum,' which means a whip-like appearance.[3]

In this paper we present a case of FD in a patient with germ cell tumour who was treated with bleomycin. Our aim is to summarize the clinical presentation, diagnosis and management of this unique toxic reaction to bleomycin.

CASE REPORT

We present the case of a 21-year-old married male that presented to the out patients' department (OPD) of Shaukat Khanum Memorial Cancer Hospital & Research Centre (SKMCH&RC) Peshawar. The patient presented with Inguinal swelling and diffuse periumbilical pain. Upon examination a lower abdominal mass was palpated. A Computed Tomography (CT) scan was performed followed by biopsy of the retroperitoneal lymph node identified during the CT scan. The patient had a history of bilateral undescended testes since birth. After detailed imaging and biopsy, a diagnosis of good-risk stage III-A non-seminoma germ cell tumour was made. Right sided radical orchiectomy was planned for 31st

December 2022. The surgery was uneventful and the sample was sent for histopathology. The final histopathology report further confirmed a mixed germ cell tumour consisting of 80% embryonal carcinoma, 15% mature teratoma and 5% yolk sac tumour with lymph vascular invasion. His post-surgical α-fetoprotein levels were within normal range.

Post-surgical imaging for stage evaluation showed lymphadenopathy in the bilateral inguinal region, left pelvic sidewall, and para-aortic region, along with small suspicious soft tissue lung lesions. Small, suspicious soft tissue lung lesions were seen which were compatible with lung metastases. His case was discussed in the weekly meeting of urology multi-disciplinary team and he was started on the BEP (Bleomycin, Etoposide and Cisplatin) protocol as per institutional guidelines. The recommended doses of BEP as per protocol are Bleomycin (30 units on days 1, 8, and 15), etoposide 100 mg/m2 body surface area (BSA) on days 1–5 and cisplatin 25 mg/m2 BSA on days 1–5.

The BEP protocol was started on 15/2/23. On the 17th day of the first cycle, the patient developed multiple whiplash skin lesions over his back, shoulders and front right frontotemporal area with intense itching. His symptoms gradually became worse within one-week. A diagnosis of flagellate dermatitis was made clinically. Bleomycin was stopped and he was switched to etoposide and cisplatin-based chemotherapy for the remaining three cycles. The rashes were treated with topical steroids (Beclomethasone 0.005% twice daily on the affected areas), Systemic steroids (Prednisolone 1mg/kg body weight once daily for seven days) and antihistamines (Cetrzine 10 mg once daily for seven days).[4] The patient responded very well to the above-mentioned treatment with the rashes completely disappearing within a span of 14 days.

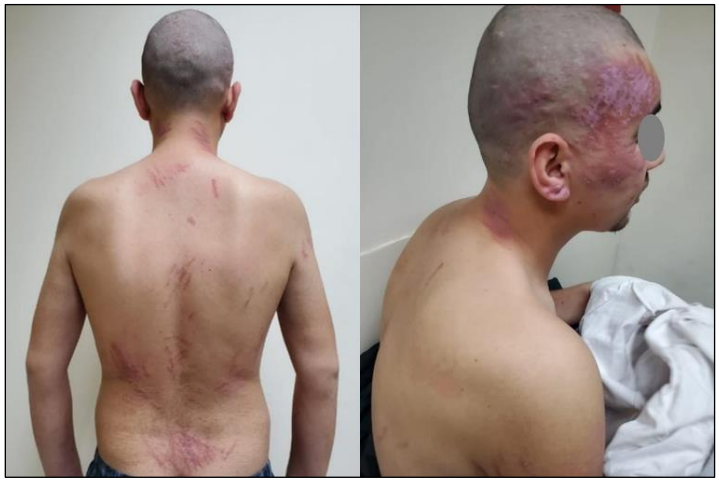

Figure-1: A and B: Showing post BEP protocol flagellate dermatitis before treatment. Images show multiple whiplash skin lesions around the back, shoulders and front right frontotemporal area

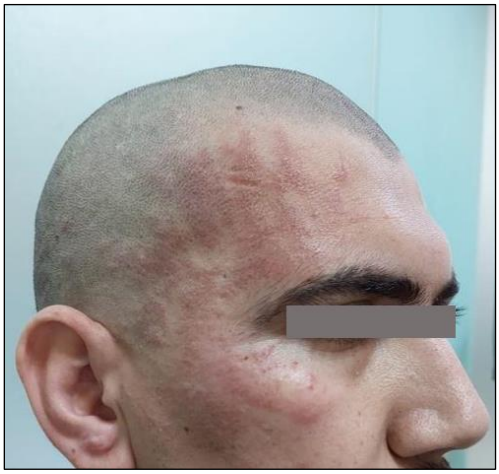

Figure-2: Showing healing of flagellate dermatitis after treatment. Image shows disappearance of the multiple whiplash skin lesions in the front right frontotemporal area

DISCUSSION

Flagellate Dermatitis is a condition with a broad differential diagnosis, i.e., Bleomycin induced FD, dermatomyositis, shiitake mushroom dermatitis and adult-onset Still's disease.[5,6] The possible mechanisms underlying cutaneous manifestations, including pruritus, inflammation, and pigmentation is still unclear, some researchers suggest that the accumulation of Bleomycin in the skin is responsible for cutaneous manifestations. This is due to the lack of Bleomycin hydrolase enzyme in the skin, which normally inactivates Bleomycin.[1] Pruritus is a common symptom of this condition and can lead to micro trauma and abrasions, causing vasodilation and further Bleomycin accumulation. This may explain the Koebner phenomenon that has been reported, but the evidence is conflicting.[7]

Another potential mechanism of cutaneous inflammation and pigmentation is that bleomycin damages endothelial cells by upregulating TGF-β, inducing keratinocyte apoptosis, and having a cytotoxic effect on melanocytes. It is likely that this is a dose-dependent reaction, with doses over 200U and higher showing cutaneous manifestations.[8]

Patients with decreased bleomycin hydrolase in conditions such as atopic dermatitis, due to a filaggrin gene mutation, may be at higher risk for developing flagellate dermatitis. Additionally, one study found a potential link between atopy and bleomycin pulmonary toxicity. The main treatment for flagellate dermatitis is to discontinue the inciting agent if possible. There is no specific treatment developed or identified, in the literature, for the treatment of FD, apart from the cessation of bleomycin. The condition is self-limiting and clears within a few weeks, however, recurrence may occur with initiation of bleomycin therapy.[9,10]

Symptomatic treatment includes bilastine, which has a high affinity for peripheral H1-receptors and inhibits inflammatory mediators. Increasing the dosage to 40 or 80mg can enhance its anti-inflammatory properties without causing sedation, as it does not cross the blood-brain barrier. Referral to a dermatologist may be necessary if the diagnosis is uncertain or if the cutaneous lesions worsen. A potential complication of flagellate dermatitis is heat-induced recall phenomenon. Patients should be advised to avoid heat in previously affected areas and to cool the skin before chemotherapy. Using the minimum effective dose of bleomycin may also help prevent heat-induced recall.[4,11] Prolonged pruritus can lead to an increased risk of infections due to chronic scratching and impairment of the skin barrier. It can also negatively affect patients' mental health and quality of life.[12] Hyperpigmentation can cause patients to become self-conscious and withdraw from daily activities.

CONCLUSION

FD is a condition with multiple potential causes and mechanisms underlying cutaneous manifestations. Early recognition and prompt treatment can help prevent long-term complications and improve patients' quality of life. This case highlights the need for vigilance during chemotherapy as it can cause a wide range of skin reactions and may lead to the discontinuation of this chemotherapeutic agent in such cases.

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Address for Correspondence:

Dr Shazia Asim, Professor of Pharmacology Lahore Medical and Dental College, Lahore-Pakistan
Cell: +92 334 991 1022
Email: shazia.asim@lmdc.edu.pk