A Young Girl with Bleomycin-Induced Flagellate Erythema

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ABSTRACT

Bleomycin, an antineoplastic medicine, is used to treat malignancies such as Hodgkin's lymphoma, germ cell tumours (GCT) and squamous cell carcinomas. As bleomycin degradation by enzyme hydrolase is less in the skin and lungs, a considerable risk of cutaneous and pulmonary toxicity exists. Flagellate dermatitis is a rare but characteristic adverse reaction seen with bleomycin. It presents as erythematous dermatitis with residual post-inflammatory hyperpigmented scarring. We report here a case of a 10-year girl with a germ cell tumour who developed this rash after bleomycin injection. It started as an erythematous rash on the upper back associated with itching and was managed conservatively with antihistamines and oral steroids. There was no recurrence of rash with further doses of bleomycin and it started fading away at 3-year follow-up. This case report describes the clinical course of bleomycin-induced rash and a review of the literature.

Key Words: *Bleomycin, Germ cell tumour, Flagellate erythema.*

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INTRODUCTION

Bleomycin is a chemotherapeutic agent which belongs to the family of glycopeptide antibiotics that have antineoplastic activity. It works by blocking the DNA uptake of thymidine in the S-phase of the cell cycle. Bleomycin hydrolase inactivates the medicine in the majority of body tissues except skin and lung tissue, which may explain the adverse effects (AEs) commonly seen in these sites.[1]

Various dermatological AEs of bleomycin have been documented in the literature. Flagellate erythema is a rare but distinct sign of bleomycin toxicity. Its reported incidence is 8-20%.[2] Herein, we report a case of a 10-year girl who developed flagellate erythema after treatment of a germ cell tumour (GCT) with bleomycin.

CASE REPORT

A 10-year girl presented to OPD with abdominal pain and distension. Examination showed a distended abdomen and a firm mass palpable in the pelvic area extending to the umbilicus. The contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis showed a large mass measuring 9.2 × 9.0 × 8.0 cm (TR × AP × CC) adjacent to the left ovary with internal septations and calcifications.

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Her baseline investigations including complete blood counts (CBC), renal function and liver function tests were normal. Serum alpha-fetoprotein (AFP) was raised at 12700 ng/ml and beta-human chorionic gonadotropin (β-HCG) was normal. The karyotyping showed normal female karyotype, which was 46 XX.

Elective laparotomy was performed, the mass was removed and left salpingo-oophorectomy with omentectomy was done as the mass was adherent to the omentum. Histopathology of the mass and omentum both showed mixed GCT with a yolk sac component of 80% and dysgerminoma of 20%.

The patient was staged as Stage III disease and chemotherapy was started with JEB (carboplatin, etoposide, and bleomycin; carboplatin 600 mg/m^2 on day 2, etoposide 120 mg/m^2 on day 1, 2, 3, and bleomycin 15 mg/m^2 on day 3). Each course of chemotherapy was given every three weeks for three days.

The patient tolerated the first course of chemotherapy very well but during the second course, 48 hours after completing chemotherapy, she developed an itchy rash on her back starting from the nape of the neck down to the upper back. Initially, there was just erythema at scratch sites which later on turned to erythematous streaks with the characteristic appearance of bleomycin-induced whip-like rash. A clinical diagnosis of bleomycin-induced flagellate rash was made. The patient was given antihistamines with oral steroids and her itching improved. The patient was discharged and after three weeks, when she presented for her next chemotherapy course, hyper-pigmented streaks were seen at the site of the rash with no clinical symptoms (Figure 1). Since the rash was not severe, it was decided to continue further courses of chemotherapy with bleomycin. There were no recurrent lesions with subsequent doses of bleomycin; however, the patient complained of itching in previously affected areas during each course of chemotherapy, which

was managed with intravenous antihistamines. She completed all four courses of chemotherapy with bleomycin. Later on, this flagellate rash turned into post-inflammatory dark scarring (Figure 2). Post-chemotherapy CT scan showed no residual mass in the abdominopelvic area. Serial serum AFP levels returned to normal after the second course of JEB chemotherapy and remained normal thereafter.

The patient was kept on regular follow-up and the rash was asymptomatic and it started fading away one-year post-treatment. At three-year follow-up, the rash had faded considerably (Figure 3).

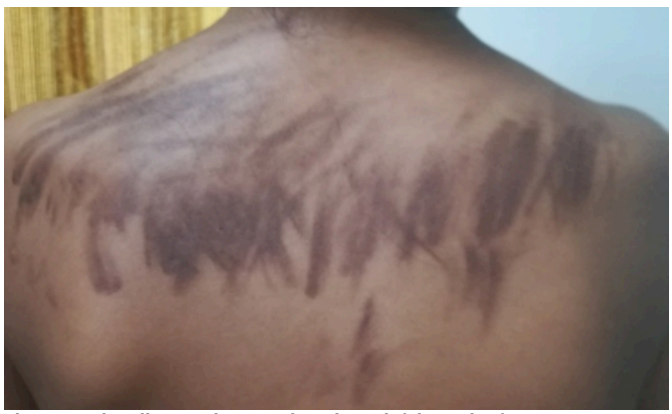

Figure 1: Flagellate rash on neck and trunk (close view).

Figure 2: Hyperpgimented Flagellate rash (close view).

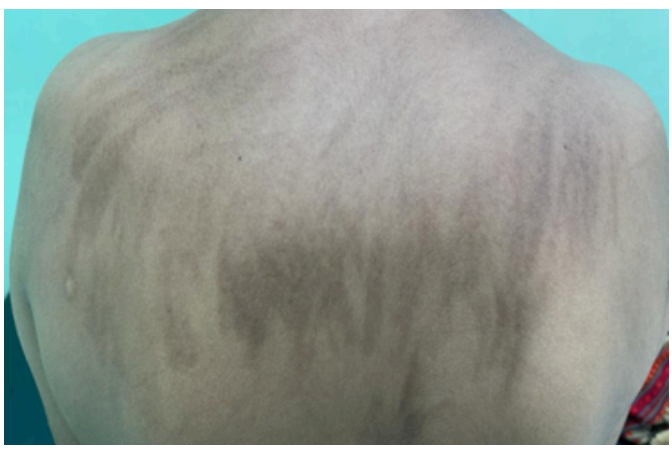

Figure 3: Improvement in rash observed at three-year follow-up.

DISCUSSION

Bleomycin-induced flagellate dermatitis is reported to have an incidence of 8-20% appearing equally in males and females. In the present patient, the rash did not appear with the first dose of bleomycin. It appeared on repeat exposure to bleomycin during the second course, 48 hours after bleomycin was given. No specific time limit is mentioned in the literature for the appearance of the rash after bleomycin and it can occur from day 1 to several weeks after receiving the medicine, irrespective of route of administration or type of disease.[3] It has been documented in the literature that although males and females are equally affected but patients developing rash within 72 hours of bleomycin administration are mostly females.[4]

Flagellate erythema is a striking characteristic sign of cutaneous toxicity associated with bleomycin. It is believed to be caused due to the lack of a detoxifying enzyme in the skin. This enzyme is called bleomycin hydrolase. The rash is a characteristic whip-like dermatitis which can also be described as multiple linear hyper-pigmented streaks intermingled with each other.[5] It is sometimes associated with a prodrome of erythema and itching which settles later on. These lesions can be found anywhere on the face, trunk, or extremities. These characteristic findings mentioned in the literature are consistent with the clinical presentation of our patient. In our patient, the rash appeared at the neck and back only. It initially started as an erythematous itchy rash and then turned into hyper-pigmented lesions. However, during each course, our patient had aggravation of itching but no recurrence of active new lesions was seen. Linear pattern development due to scratching is questionable, as in many cases there is no evidence of direct trauma.[6]

Histologically, inflammatory and post-inflammatory changes have been described in the epidermis and dermis. Electron microscopy reveals increased melanosomes with no increase in melanocytes.[7] We did not perform a skin biopsy on this patient and made the clinical diagnosis due to the characteristic appearance of the rash and its association with bleomycin.

No specific treatment is usually required for flagellate erythema. It resolves spontaneously over months to years. Occasionally, antihistamines or corticosteroids may be used orally or topically for this rash. If severe, discontinuation of bleomycin is necessary. Reappearance of rash is reported with re-exposure to the medicine.[1] In the present patient, the rash was settled with conservative treatment and there was no recurrence with repeated exposure to the medicine and subsequently rash started fading away.

Bleomycin-induced flagellate dermatitis is a distinct and rare sign of cutaneous toxicity associated with this drug. It may appear days to weeks after bleomycin administration. This case is reported to increase awareness among clinicians prescribing bleomycin for prompt diagnosis and appropriate management of this unique skin rash.

PATIENT'S CONSENT:
The patient's father has given written consent for publication of the case report.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
SK: Conceptualised, drafted, and revised the manuscript.
SIF: Collected the clinical data and drafted the manuscript.
HSK, KMT, AT: Proofread and revised the manuscript for intellectual content.
All authors approved the final version of the manuscript to be published.

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