



# Bleomycin-Induced Flagellate Dermatitis in Indian Patients with Germ Cell Tumors

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Bleomycin is an antibiotic antineoplastic agent commonly used in systemic therapy for Hodgkin lymphoma, germ cell tumor, squamous cell carcinoma, and gestational trophoblastic disease. Bleomycin-induced pulmonary toxicity is well-known and dose-limiting, though skin reactions have also been occasionally reported. Both pulmonary and cutaneous adverse events are attributed to low concentration of bleomycin hydrolase, a metabolizing enzyme.<sup>1</sup> Several dermatologic appearances including palmar–plantar peeling, nail-bed discoloration, hyperkeratosis, Raynaud's phenomenon, and gangrene of digits are described. Flagellate erythema is a less often described but characteristic toxicity; the reported incidence is 8 to 20% but declining use of bleomycin has reduced incidence of this toxicity as well.<sup>2</sup> Indian or tropical skin may mask the erythematous component in many patients, and the lesions are picked up only if involving large areas of skin. The name is derived from the Latin word “flagellare,” meaning whipping or flogging, often for religious or sexual gratification purposes, and the rash mimics that appearance. We encountered two consecutive patients with nonseminomatous germ cell tumors (NSGCT), post-high inguinal orchiectomy, who developed flagellate pattern hyperpigmentation without erythema or itching within 4 weeks of starting first cycle of BEP regimen (plan: bleomycin 30IU intravenously D1, 8, 15, etoposide 165 mg/m<sup>2</sup> D1–3, cisplatin 35 mg/m<sup>2</sup> D1–3 q 3 weeks for 4 cycles). The first patient was an 18-year boy with left testicular NSGCT (intermediate risk) and the second patient was a 27-year-old man with right testicular NSGCT (poor risk). Both were post-orchiectomy and had Karnofsky's performance status of  $\geq 70$ . The first patient developed the characteristic interlacing streaks, most marked over upper back, right inguinal, and right thigh region (–Fig. 1A, B).

The second patient had limited hyperpigmentation limited to upper back only, though he had palmar–plantar hyperpigmentation and nail changes as well (–Fig. 1C, D). Since the patients had good performance status, normal biochemical parameters, and less than 10% of body surface area involved with the rash, chemotherapy was continued on original schedule with weekly monitoring of rash. Both patients completed the planned chemotherapy without further progression of the flagellate rash. The incidence of this rash appears unrelated to cumulative bleomycin dose, or duration of drug administration. It is mostly self-limiting but requires monitoring and possibly bleomycin discontinuation if progressive or extensive. Skin examination should be a routine part of monitoring bleomycin toxicity in addition to pulmonary function testing so that the rash is not missed especially in dark-skinned individuals.

Flagellate erythema, though a characteristic toxicity, may be associated less often with other systemic agents such as doxorubicin, docetaxel, trastuzumab, and bendamustine, as well as following intake of shiitake mushrooms.<sup>3–5</sup> Rheumatologic conditions such dermatomyositis and Still's disease (adult onset) may also have centripetal flagellate erythema as a cutaneous manifestation.<sup>6</sup> Histopathologic examination may be undertaken in doubtful cases when the association with implicated drugs or dietary items is less clear on history and there are no other predisposing rheumatologic conditions, when the appearance of rash is not characteristic, when infective/parasitic etiology has to be ruled out, or when the rash progresses despite discontinuation of the implicated agent and supportive management. Typically, lymphocytic infiltrates in dermis with high number of eosinophils and occasionally lymphocytic vasculopathy may be observed in flagellate dermatitis.<sup>7</sup>

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**Fig. 1** (A) Photograph of patient 1 (18-year boy with intermediate risk nonseminomatous germ cell tumor, NSGCT) with flagellate hyperpigmentation over upper back and (B) right thigh and inguinal region. (C) Photograph of patient 2 (27-year-old gentleman with poor risk NSGCT) with limited flagellate rash over upper back and (D) palmar hyperpigmentation.

#### Authors' Contributions

S and SG were involved in data collection, literature review, manuscript preparation, and final approval, while KP and RM were involved in manuscript review, revision, and final approval.

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#### Conflict of Interest

None declared.

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