

Case Report

Flagellate erythema presenting as linear erythema over both ankles

雙足踝呈線狀形紅斑的鞭狀紅斑：華人案例一宗

WY Leung 梁偉耀 and WY Lam 林永賢

Flagellate erythema may be unusually caused by bleomycin therapy. We present a 22-year-old male, who received bleomycin for treatment of a germ cell tumour, developing such characteristic flagellate pigmentation.

鞭狀紅斑可以不尋常地由藥物博來霉素引發。我們呈交一名二十二歲的生殖細胞瘤男性患者個案，因接受博來霉素治療而出現此典型鞭狀色斑。

Keywords: Bleomycin, Flagellate erythema

關鍵詞：博來霉素，鞭狀紅斑

Introduction

Flagellate erythema is a well-documented cutaneous complication following bleomycin therapy. It is not a manifestation specific to bleomycin, as it is also rarely associated with various skin disorders. The mechanism for such

hyperpigmentation following bleomycin is at present unknown.

Case report

A 22-year-old male was admitted to the Accident and Emergency Department with sudden onset of severe dyspnoea and a 3 month history of subjective weight loss. He had no fever, chills, muscle tenderness or joint pains. His past medical history and family history were unremarkable and he had no recent ingestion or occupational exposure to raw shiitake mushrooms. On examination, his chest was clear and he had neither splenomegaly, adenopathy, hepatomegaly, or skin lesions. A complete blood count revealed leukocytosis. X-ray of the chest suggested a huge mediastinal lung mass. He was then admitted to the medical ward for investigation of the lung mass. Additional blood studies showed

Social Hygiene Service, Department of Health, Hong Kong

WY Leung, FHKCP, FHKAM(Med)

Department of Clinical Pathology, Tuen Mun Hospital, Hong Kong

WY Lam, FHKCPath, FHKAM (Pathology)

Correspondence to: Dr. WY Leung

Social Hygiene Service, Department of Health, 12/F Yau Ma Tei Dermatology Clinic, 143 Battery Street, Yau Ma Tei, Kowloon

a sky high alpha-fetoprotein (AFP:36475 IU/mL), but normal beta-human chorionic gonadotropin (HCG<1 IU/L), creatinine kinase levels. Anti-ENA antibodies and antinuclear antibodies were negative. Computerized tomography scan of the chest confirmed a huge right mediastinal mass. Fine needle aspiration (FNAC) of the mediastinal mass for morphology analysis revealed a mediastinal germ cell tumour. The patient was treated with intravenous bleomycin, cisplatin and etocid (BEP regimen). Two weeks later, he developed neutropenic fever that subsided with antibiotics. One day after admission, he

developed intensive pruritus and multiple linear erythematous papular lesions initially affecting the trunk and progressively spreading to the hands and lower limbs.

On examination, he had linear streaks formed by rows of adjoining papules on his back, hands and ankles, some of which contained punctuate haemorrhages and pustules (Figures 1-3).

A skin biopsy of a lesion on his back was taken for histopathological examination (Figures 4-6). Given his clinical history and the typical



Figure 1. Linear streaks of erythematous to violaceous papules.



Figure 2. Similar linear streaks of papules on left ankle.



Figure 3. Some of the papules contained punctuate haemorrhages and pustules.

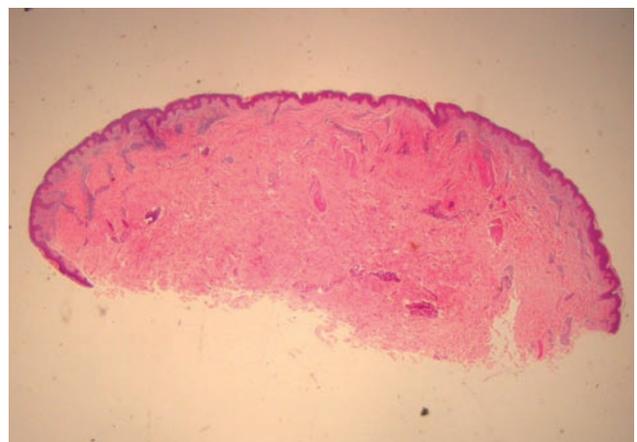


Figure 4. The skin biopsy shows a superficial perivascular lymphocytic infiltrate with relative mild epidermal changes, consistent with exanthematous drug eruption. (H&E, Original magnification x 20)

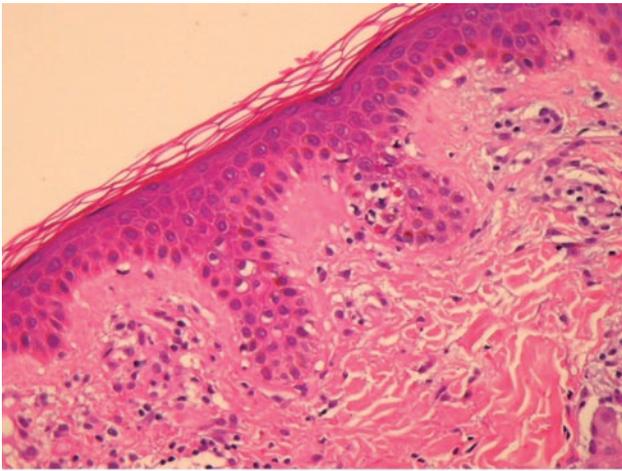


Figure 5. Focally in the epidermis are tiny aggregates of necrotic keratinocytes, providing a clue to this exanthematous lesion as an eruption related to use of drug. (H&E, Original magnification x 200)

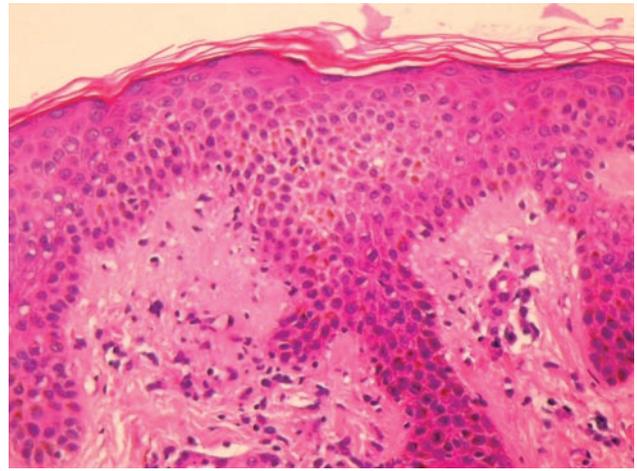


Figure 6. There are foci of spongiosis in the epidermis. (H&E, Original magnification x 200)

skin lesions, his diagnosis was compatible with a bleomycin-induced flagellate erythema.

Discussion

Bleomycin is commonly used as a chemotherapeutic agent to treat various kinds of malignancy. Owing to the lack of the bleomycin-detoxifying enzyme, bleomycin hydrolase, in the skin and lungs¹, it appeared that bleomycin toxicities are most significant in these two organs. Flagellate erythema was once described to be the cutaneous side effect of bleomycin and was commonly found during systemic bleomycin therapy. It is characterized by linear erythematous to violaceous streaks with hyperpigmentation. The lesions are usually seen over the upper trunk and limbs and may be associated with pruritus.

Bleomycin related flagellate pigmentation was first described by Moulin in 1970² and was originally described as a characteristic side effect of bleomycin. However, more findings

have suggested that flagellate erythema is not a specific manifestation of bleomycin. It is also associated with dermatomyositis, shiitake dermatitis and Adult-Onset Still's disease.³

A number of theories have been postulated in the pathogenesis of flagellate erythema but the exact mechanism remains to be determined. The mechanism may be due to a direct effect of bleomycin on the melanocytes, such as slowing down the turnover of the keratinocytes and arresting the melanocytes in the pigment synthesis phase, or simply a fixed drug eruption or post-inflammatory effect secondary to leaking out of bleomycin from blood vessel after scratching.⁴⁻⁶

Bleomycin induced flagellate erythema is believed to be a dose related toxicity. Studies have shown that around one third of patient developed hyperpigmentation during bleomycin usage and the incidence rate of flagellate erythema after administration of bleomycin is around 8-20%.⁷⁻⁹ The interval between the administration of drug and the onset of flagellate erythema ranges

variably from days to several months. Fortunately, it is usually reversible within months after stoppage of bleomycin. However, permanent hyperpigmentation in affected skin is not unusual.

There is no specific treatment for flagellate erythema and the treatment consists of exclusion of bleomycin as well as symptomatic relief. Itchiness is the most common symptom and addressing the itchiness is usually the only treatment required. Other than symptomatic treatment, the use of systemic steroids may delay the onset of the rash or hasten its resolution. Some patients may experience the so-called heat-induced recall phenomenon, which means the recurrence of flagellate erythema in an area previously affected by bleomycin.¹⁰ Thus, cooling of the previously affected site before chemotherapy administration may be able to prevent its recurrence.

In the present case, the patient received topical steroid and antihistamines for his flagellate erythema and his skin condition improved. He finally completed 6 cycles of bleomycin with a culminative dose of 300 mg for his germ cell tumour.

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