

SHORT COMMUNICATION

FLAGELLATE PIGMENTATION AND SCLERODERMOID CHANGES: CUTANEOUS MARKERS OF BLEOMYCIN TOXICITY

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Bleomycin therapy causes multiple side effects. Linear or flagellate pigmentation of the skin is a pattern of pigmentation unique to bleomycin therapy. We report 3 cases of testicular tumors on bleomycin therapy, all of whom manifested with flagellate pigmentation on the neck, trunk and upper limbs and one of whom developed sclerodermoid changes on the arm. Bleomycin, though used in different drug combinations, has consistently resulted in the manifestation of flagellate streaks of pigmentation.

Key words: Bleomycin, flagellate pigmentation, sclerodermoid changes

Introduction

Bleomycin is a mixture of low-molecular weight (1500 daltons) peptides isolated from the fungus *Streptomyces verticillus*.¹ It possesses both antitumour and antimicrobial activity. It has been extensively used in the treatment of lymphomas and selectively kills tumour cells without affecting intestinal mucosa or bone marrow.¹ The administration of bleomycin has been associated with alopecia, Raynaud's phenomenon, sclerodermoid changes, various pigmentary changes, mucocutaneous ulcerations, stomatitis and radiation recall.²⁻⁷ The pigmentary changes which have been reported are peculiar linear or flagellate streaks of hyperpigmentation of the skin, hyperpigmentation in striae distensae, pigmentary nail banding, pigmentation of nail bed, localized pigmentation and pigmentation over venous channels used for injection of bleomycin.⁸⁻¹² The specific cases of testicular tumours on

bleomycin in various drug combinations presenting with the unique cutaneous manifestation of flagellate streaks of pigmentation and sclerodermoid changes are reported.

Case 1



Fig. 1. Sclerodermoid changes observed near the right axilla of the patient in Case Report 1

A 25-year-old male patient was admitted with complaints of scrotal swelling of one year duration (left side), left supraclavicular swelling and retroperitoneal mass of 6 months duration. Diagnosis of teratoma testis stage III was established, following a biopsy. On admission, his alpha-feto protein value was 208.9 mg/ml and Bhcg value was 36.9 IU/ml, USG abdomen

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revealed multiple para-aortic lymphnodes. The left kidney was enlarged with parenchyma showing multiple hyperechoic lesions. Left renal vein thrombosis was seen. Hepatomegaly and splenomegaly with multiple secondaries were also seen. Blood urea nitrogen, serum electrolytes and uric acid levels were normal. An orchidectomy was performed and the left testis removed. Three weeks following surgery the patient was started on chemotherapy. He was administered.

- [1] Injection bleomycin 30 mg, i.v.day 1
- [2] Injection etoposide 700mg, as i.v. infusion (day 1-5)
- [3] Injection cisplatin 170mg, as i.v. infusion (day 1-5)

The schedule was repeated every 3 weeks. The patient was observed till the fourth schedule was administered. Following the administration of the third cycle, the alpha- feto protein value fell to 30.6 mg/ml and Bhcg value fell to 16.6 mIU/ml. Linear flagellate streaks of black pigmentation over the side of the neck, right arm, upper back, left flank and forehead developed after 10 days of administration of the first cycle. Sclerodermoid changes developed near the right axilla. Histopathology revealed increased pigmentation of the basal layer with a few pigmented dermal macrophages. Masson Fontana staining showed increased pigmentation. The dermal collagen showed homogenization, especially around the vessels and adnexae. The finger nails also developed diffuse dark grey pigmentation. He reported diffuse hair loss after 2 weeks of administration of the first cycle of chemotherapy. After the third cycle he presented with near total alopecia, including loss of scalp, eyebrows and moustache hair. These changes persisted even after the administration of the fourth cycle of treatment.

Case 2

A 35 - year old male, was admitted with scrotal swelling, progressive weight loss, generalized weakness and hemoptysis. Diagnosis of seminoma testis was established, based on histopathological studies, following

a biopsy. The patient was administered a combination chemotherapy protocol comprising of

- [1] Cisplatin 170 mg, intravenous infusion
- [2] Vinblastin 10 mg, intravenously and
- [3] Bleomycin 30 mg, intravenously

The treatment was repeated every 3 weeks, till fifth cycle, totalling a period of 4 months. Linear flagellate streaks of black pigmentation over the trunk and limbs

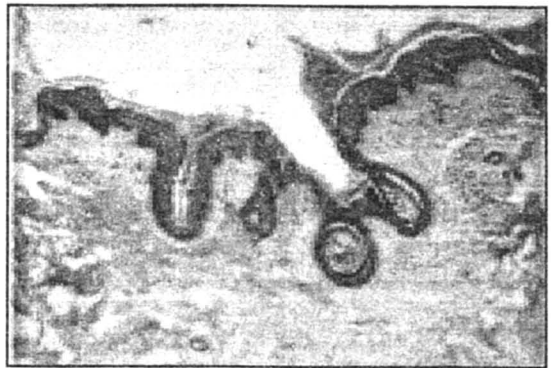


Fig 2. Biopsy section of flagellate pigmentation [case Report1] showing increased pigmentation of the basal layer with a few pigmented dermal macrophages. H&E stain x 200.

developed after the third cycle of chemotherapy after a cumulative dose of 90 mg bleomycin had been administered. The nails developed diffuse dark -grey pigmentation. Buccal mucosa and lateral aspects of tongue showed blue-black mottled pigmentation. Palmar creases and areola also showed hyperpigmentation. Severe alopecia appeared 20 days after the first cycle of chemotherapy, progressively involving wider areas of the body. It persisted. The patient expired after the fifth cycle of chemotherapy.

Case 3

A 38-year old male patient was admitted with scrotal swelling and pedal oedema of one year duration, left neck mass of four months duration. Diagnosis of seminoma testis was made, based on histopathological report of a biopsy specimen from the right testis. The

patient was administered a combination chemotherapy protocol comprising of.

[1] Etoposide 100 mg as intravenous infusion, daily for 5 days and repeated every three weeks,

[2] Cisplatin 30 mg, intravenous infusion daily for 5 days and repeated every 3 weeks and, [3] Bleomycin 30 mg, intravenously administered on the second, ninth and sixteenth day of a 3-week treatment cycle. Severe alopecia was observed 2 weeks after the first course of chemotherapy. A week later linear flagellate streaks of black pigmentation over the trunk, shoulders and back of neck and diffuse blackish pigmentation of the face were observed. Oral candidiasis and peeling of skin of upper lips and soles were also observed after the first course of chemotherapy. The black pigmentation of the trunk, face, back of neck and shoulders persisted. Oral candidiasis responded to treatment with fluconazole and the lesions disappeared. Peeling of the skin of soles and alopecia persisted. The patient expired before completing the second cycle of chemotherapy.

Discussion

Hyperpigmentation of the skin has been observed mainly with bleomycin, doxorubicin, busulfan, nitrosoureas, methotrexate, dactinomycin and daunorubicin.^{5,7,13-16,18}

Peculiar linear or flagellate streaks of hyperpigmentation have been reported as a unique manifestation of bleomycin therapy. In the 3 cases presented in the paper, flagellate streaks of hyperpigmentation has been an outstanding feature amongst other patterns of hyperpigmentation of the skin, nails and mucosa. Diffuse black pigmentation of the back of the neck, face, shoulders and trunk could be attributed to the toxicity of bleomycin therapy. The same can explain the occurrence of hyperpigmentation of palmar creases, areola, buccal mucosa, blue-black mottled pigmentation of the tongue and diffuse dark pigmentation of the finger

nails observed in the cases reported. Sclerodermoid changes in the skin have been reported with bleomycin therapy. Clinical improvement of the bleomycin associated scleroderma has been observed coincident with the cessation of the drug and the brief use of high-dose steroids.⁶

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