

BLEOMYCIN - INDUCED FLAGELLATE HYPERPIGMENTATION

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Abstract : This male patient, a diagnosed case of Hodgkins Lymphoma (nodular sclerosis) developed linear hyperpigmentation on the chest, abdomen, trunk, when on combination chemotherapy which included bleomycin. Bleomycin is metabolised in all parts of the body by bleomycin hydrolase except in skin and lung, resulting in cutaneous and pulmonary toxicities. the cutaneous lesions usually appear on normal skin without proceeding inflammatory lesions. Although many hypothesis regarding the pathogenesis have been postulated but the exact cause is not known.

CASE REPORT

A 52 years old male patient was diagnosed as Hodgkin's Lymphoma, (nodular sclerosis,) stage IIIA at our Institute. He was planned for ABVD combination chemotherapy (adriamycin, bleomycin, vinblastine, and dacarbazine). Four days after the first course of the chemotherapy, he noted linear hyperpigmentation on his chest, abdomen, trunk (Fig.). On close examination the rash was linear, erythematous, excissated plaque on the chest and abdomen with a flagellate appearance. He denied permission for biopsy of the lesions. During this time the patient developed similar, linear eruptions at new areas by scratching the skin. The patient was continued with COPP chemotherapy instead (cyclophosphamide, vincristine, procarbazine, predinisolone), following which, hyperpigmented lesions resolved completely over a period of three months of discontinuation of ABVD regimen.

DISCUSSION



Bleomycin induced hyperpigmentation

Bleomycin is an antineoplastic antibiotic derived from streptomyces verticillius. After intravenous administration it is widely distributed through out the body. Bleomycin has cell cycle specific cytotoxic effects. The most pronounced inhibition of cell growth is during the S phase. The during also damages prophase chromosomes and induces a G₂ phase maturation arrest. It is rapidly inactivated in all organs by bleomycin hydrolase except the lungs and skin where it is deficient. This results in

primarily cutaneous and pulmonary toxicities. In addition to pneumonia and pulmonary fibrosis, muco cutaneous reactions associated with the use of bleomycin are common and include stomatitis, alopecia, ulcers on palms and soles, warty keratotic plaques and inflammatory nodules¹. Almost every patient may experience fever within first 4 to 12 hours after

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Bleomycin injection which is usually brief and not clinically troublesome. Chills, myalgias, nausea, vomiting and anorexia may accompany fever but less frequently. Anaphylactoid reactions and rarely anapylaxis² were noted exclusively in lymphoma patients receiving first dose of Bleomycin and it was recommended to give test dose of Bleomycin prior to the actual dose. However, flagellate linear hyper pigmentation is seen in a majority of cutaneous reactions, which occur in 8-20% of cases³. These generally occur after a cumulative dose of 90 and 285mg. However, some cases have been reported with doses as low as 15mg given parenterally; as was in our case. The time lapse between the administration of drug and onset of clinical signs and symptoms ranges from 1 day to 9 weeks³ and may persist for upto 6 months⁴. The flagellate dermatitis occurs primarily on the upper trunk and limbs^{1,5}. They usually appear on normal skin without preceding inflammatory lesions. The exact pathogenesis of these lesions is not known. Some authors consider that the linear lesions result from increased leakage of the drug from dilated vessels after rubbing or scratching the skin, but others have been unable to reproduce linear hyperpigmentation by these means. It is also speculated that scratching induces subclinical local vasodilatation by a demographic mechanism resulting in an excessive in situ accumulation of bleomycin². The reason for the increased pigmentation is thought to be due to increased melanocyte stimulation by melanocyte stimulation hormone, inflammatory oncotaxis and stimulation of melanocytes by adrenocorticotrophic hormone¹.

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