Flagellate hyperpigmentation from bleomycin

Sir,

Mucocutaneous side effects associated with bleomycin are stomatitis, ulcers, scaly erythematous and bullous lesions, sclerosis, nail changes, digital gangrene and pigmentary alterations.[1] Hyperpigmentation occurring mainly on the pressure areas of the skin as well as in areas of scratch marks is seen in approximately 30% of patients. Flagellate hyperpigmentation is very characteristic of bleomycin.

A 42-year-old woman was diagnosed to have granulosa cell tumor of the ovary stage IV (multiple lung metastasis). After debulking surgery she was given combination chemotherapy with bleomycin, etoposide, and cisplatin. After 2 cycles (180 mg of bleomycin), she noted hyperpigmentation of the hands and linear pigmented lesions over the anterior abdominal wall, shoulder region and back (Figure 1). She denied permission for biopsy of the lesions. She was continued on chemotherapy and she attained complete remission after 3 cycles. Chemotherapy was discontinued after one more cycle due to poor tolerance. The hyperpigmented lesions resolved completely over a period of 3 months after the discontinuation of chemotherapy.

Bleomycin is an antineoplastic antibiotic derived from *Streptomyces verticillius*. After intravenous administration it is widely distributed throughout the body. It is rapidly inactivated in all organs by bleomycin hydrolase except in the lungs and skin where it is deficient. This results in primarily cutaneous and pulmonary toxicities.

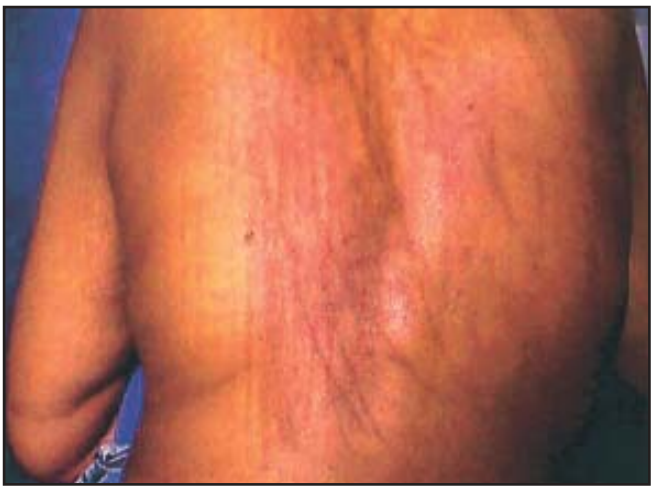

Figure 1: Flagellate hyperpigmentation over back

Flagellate linear hyperpigmentation is the characteristic lesion associated with bleomycin and is seen in about 20-30% of cases, primarily on the upper trunk and limbs.[2] It is dose dependent, occurring after a cumulative dose of 90 and 285 mg, but some cases have been reported with doses as low as 15 mg given parenterally. It follows the administration of bleomycin by a duration ranging from 1 day to 9 weeks[2] and may persist for up to 6 months.[3]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.[1] It is also speculated that scratching induces subclinical local vasodilatation by a dermographic mechanism resulting in an excessive in situ accumulation of bleomycin.[4] The reason for the increased pigmentation is thought to be due to increased melanocyte stimulation by melanocyte stimulating hormone, inflammatory oncotaxis and stimulation of melanocytes by adrenocorticotrophic hormone.[5] Further studies are needed to determine the cause of the pruritus and to explain the linear pattern of the skin lesions following bleomycin therapy.

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Hiccups following steroid oral mini-pulse (OMP) therapy

Sir,

Oral mini-pulse therapy (OMP) with corticosteroids has been successfully used for the treatment of alopecia areata with minimal side effects.[1] Persistent hiccups is a rare complication of oral and intravenous corticosteroid therapy.[2] We report a case who developed hiccups following betamethasone OMP, a side effect that has not been reported earlier.

A 22-year-old man presented with alopecia areata on the scalp of six months' duration. It was progressive both in terms of size and number of lesions. He gave no history of atopy, hypertension or diabetes. He had been intermittently applying various topical corticosteroids and salicylic acid and had been injected intralesional triamcinolone twice, but without any improvement. His routine hematological and biochemical tests and urine analysis were normal.

He was started on 5 mg betamethasone, as a single oral dose after breakfast, on two consecutive days per week. On the second day after consuming the tablets, he reported with persistent hiccups. He was treated with antacids, domperidone 10 mg orally and injection chlorpromazine. The hiccups stopped after two days.

A hiccup is a distinctive sound caused by the contraction of inspiratory muscles terminated abruptly by closure of the glottis. Brief episodes may occur due to gastric distension, a sudden change in temperature, ingestion of alcohol, excess smoking or excitement. Persistent hiccups may be due to a structural lesion or infection of the central nervous system, diaphragmatic irritation, metabolic derangement, vascular lesion, or intra-abdominal infection. Drugs, including barbiturates and sedatives, and general anesthesia may cause hiccups.[3] Hiccups have been reported as a side effect of intravenous dexamethasone cyclophosphamide pulse therapy.[4]

Our patient was started on betamethasone OMP for progressive alopecia areata and subsequently developed hiccups. The sudden intake of a high dose of corticosteroids may have caused gastric irritation and hiccups. It has also been proposed that corticosteroids lower the threshold for synaptic transmission in the mid-brain and directly stimulate the hiccup reflex arc.[2]

Various remedies like swallowing dry granulated sugar or vinegar; sudden pain or fright; pharyngeal irritation; breathing into a closed paper (not plastic) bag; holding the breath and increasing pressure on the diaphragm; sips of iced water; stomach washes; tongue traction; lifting the uvula with a cold spoon; and drugs like antacids, chlorpromazine, haloperidol, metoclopramide, domperidone, quinidine, phenytoin, valproic acid, nifedipine, amitriptyline and baclofen have been advocated in the management of hiccups.[5]

Although a rare adverse effect of corticosteroids, hiccups can be distressing. One should be aware of this complication and its management.

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