A Case of Flagellate Hyperpigmentation Following Bleomycin Therapy

BLEOMİSİN TEDAVİSİNDEN SONRA GELİŞEN FLAGELLA BENZERİ HİPERPİGMENTASYON OLGUSU

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Abstract

Flagellate hyperpigmentation is a striking reaction to bleomycin use, and shows various clinical and histopathological features.

We present a case of bleomycin-induced flagellate hyperpigmentation. Our patient developed a pruritic, linear flagellate eruption 3 days after his first dose of bleomycin. The eruption resolved in a month leaving residual linear and flagellate hyperpigmentation.

Key Words: Bleomycin, flagellate hyperpigmentation

Case Report

A 25 year old male with seminoma of the testis was commenced on a 3-weekly course of combination chemotherapy with bleomycin, etoposide, cisplatin. Three days after his first course of bleomycin therapy (30 mg), he developed a striking eruption consist of linear erythematous papules and plaques over the neck, shoulders, upper trunk and arms with pruritus and tenderness. The eruption resolved in a month leaving residual linear and flagellate hyperpigmentation.

Discussion

Bleomycin is a sulphur-containing polypeptide, antineoplastic antibiotic which was derived from Streptomyces verticillius. It was first developed in 1965 by Umezawa. Bleomycin inhibits...
the incorporation of thymidine into DNA and causes splitting of DNA into smaller fragments. It is widely used in the treatment of malignancies including lymphomas, germ cell tumors and squamous cell carcinoma of the head and neck. Following its administration, bleomycin is inactivated by a hydrolase enzyme. This enzyme is absent in the skin and lung, and thus high concentrations of the drug in these organs cause toxic reactions. Bleomycin-induced mucocutaneous reactions are common, and include stomatitis, alopecia, nail deformities, ulcers of palms and soles, scaling erythematous bullous lesions, sclerodermoid lesions, warty hyperkeratotic plaques and inflammatory nodules, pigmentary alterations.

The overall incidence of hyperpigmentation occurring during bleomycin use is approximately 30%. The flagellate streaks of hyperpigmentation is an interesting feature that occur in 8-20% of cases. The reaction may occur from a few hours up to 9 weeks after the administration of the drug. Furthermore, it can occur after both small and large doses as 15 mg or 285 mg. The typical routes of administration are intramuscular or intravenous, and most cases of linear flagellate hyperpigmentation have followed i.v and i.m administration. However, flagellate hyperpigmentation has been reported following intraleisional bleomycin treatment of verruca plantaris and intrapleural bleomycin as a sclerosing agent.

This type of hyperpigmentation may occur de novo, but sometimes it follows a flagellate dermatosis consist of erythematous papules and plaques or urticarial -like lesions. The lesions are usually seen over the upper trunk and limbs and may be associated with pruritus. There are many theories to explain the mechanism responsible for the clinical features including post-inflammatory changes associated with intense pruritus, the local accumulation of bleomycin in the skin, an allergic drug reaction.

The local accumulation of bleomycin in the skin due to vasodilatation caused by dermographic stimulus such as scratching may lead a direct toxic effect on the keratinocytes. The mechanism of increased melanogenesis may be due to a direct effect of the bleomycin on the melanocytes, or as a result of the release of mediators from surrounding keratinocytes. However, the linear flagellate pigmentation may occur in the absence of the itching. An allergic drug reaction has been proposed, but linear and flagellate pattern of hyperpigmentation is difficult to be explained by this. Topically applied bleomycin in tape stripped skin of the patients has been found to induce marked erythema within 48 h. After 3 weeks, hyperpigmented patches occurred. This may be related with the toxic effect of topical bleomycin.

The histopathologic findings reveal an increased epidermal pigmentation with increased melanin content in basal keratinocytes, active melanocytes and some degree of pigment incontinence. Additional studies are required to explain the linear and flagellate pattern of the hyperpigmentation due to bleomycin therapy.
REFERENCES