Streaked Discoloration on the Upper Body

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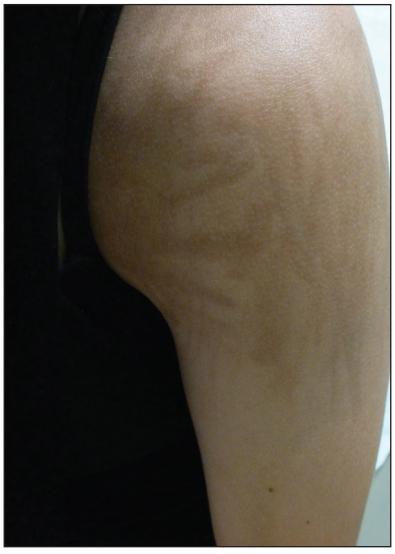

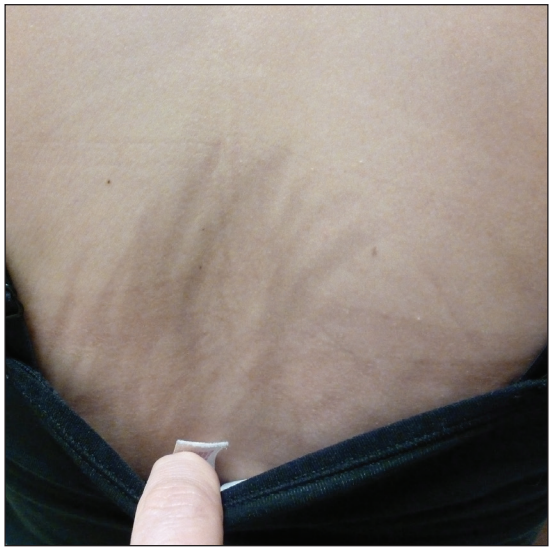

An 18-year-old woman presented to our dermatology clinic with persistent diffuse discoloration on the upper body of more than 5 years' duration. Her medical history was notable for primary mediastinal classical Hodgkin lymphoma treated with ABVE-PC (doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide) chemotherapy and 22 Gy radiation therapy to the chest 5 years prior. She reported the initial onset of diffuse pruritus with associated scratching and persistent skin discoloration while receiving a course of chemotherapy. Physical examination revealed numerous thin, flagellate, faintly hyperpigmented streaks with subtle atrophy in a parallel configuration on the bilateral shoulders (top), upper back (bottom), and abdomen. Punch biopsies (5 mm) of both affected and unaffected skin on the left side of the lateral upper back were performed.

WHAT'S THE **DIAGNOSIS?**

a. atrophoderma of Pasini and Pierini
b. bleomycin-induced flagellate hyperpigmentation
c. erythema dyschromicum perstans
d. linear atrophoderma of Moulin
e. linear morphea

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The authors report no conflict of interest.
The opinions offered are those of the authors and do not represent the official position of the US Air Force or the Department of Defense.
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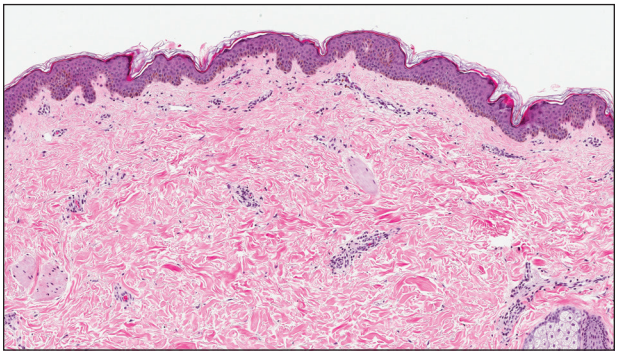
THE **DIAGNOSIS:** Bleomycin-Induced Flagellate Hyperpigmentation

Histopathology of the affected skin demonstrated a slight increase in collagen bundle thickness, a chronic dermal perivascular inflammation, and associated pigment incontinence with dermal melanophages compared to unaffected skin (Figure). CD34 was faintly decreased, and dermal mucin increased in affected skin. This postinflammatory pigmentary alteration with subtle dermal sclerosis had persisted unchanged for more than 5 years after cessation of bleomycin therapy. Topical hydroquinone, physical blocker photoprotection, and laser modalities such as the Q-switched alexandrite (755-nm)/Nd:YAG (1064-nm) and ablative CO_2 resurfacing lasers were attempted with minimal overall impact on cosmesis.

Bleomycin is a chemotherapeutic antibiotic that has been commonly used to treat Hodgkin lymphoma, germ cell tumors, and recurrent malignant pleural effusions.[1] The drug is inactivated in most tissues by the enzyme bleomycin hydrolase. This enzyme is not present in skin and lung tissue; as a result, these organs are the most common sites of bleomycin toxicity.[1] There are a variety of cutaneous effects associated with bleomycin including alopecia, hyperpigmentation, acral erythema, Raynaud phenomenon, and nail dystrophy.[2] Flagellate hyperpigmentation is a less common cutaneous toxicity. It is an unusual eruption that appears as whiplike linear streaks on the upper chest and back, limbs, and flanks.[3] This cutaneous manifestation was once thought to be specific to bleomycin use; however, it also has been described in dermatomyositis, adult-onset Still disease, and after the ingestion of uncooked or undercooked shiitake mushrooms.[4] Flagellate hyperpigmentation also was once thought to be dose dependent; however, it has been described in even very small doses.[5] The eruption has been described as independent of the route of drug administration, appearing with intravenous, subcutaneous, and intramuscular bleomycin.[2] The association of bleomycin and flagellate hyperpigmentation has been reported since 1970; however, it is less commonly seen in clinical practice with the declining use of bleomycin.[1]



Histopathology of the punch biopsy specimen of the affected skin demonstrated a slight increase in collagen bundle thickness, a chronic dermal perivascular inflammation, and associated pigment incontinence with dermal melanophages compared to unaffected skin (H&E, original magnification ×100). Image courtesy of Todd T. Kobayashi, MD (Colorado Springs, Colorado).

The exact mechanism for the hyperpigmentation is unknown. It has been proposed that the linear lesions are related to areas of pruritus and subsequent excoriations.[1] Dermatographism may be present to a limited extent, but it is unlikely to be a chief cause of flagellate hyperpigmentation, as linear streaks have been reported in the absence of trauma. It also has been proposed that bleomycin has a direct toxic effect on the melanocytes, which stimulates increased melanin secretion.[2] The hyperpigmentation also may be due to pigmentary incontinence secondary to inflammation.[5] Histopathologic findings usually are varied and nonspecific.[2] There may be a deep perivascular lymphocytic infiltrate, which is nonspecific but can be associated with drug-induced pathology.[4] Bleomycin also is used to induce localized scleroderma in mouse-model research[6] and has been reported to cause localized scleroderma at an infusion site or after an intralesional injection,[7,8] which is not typically reported in flagellate erythema, but bleomycin's sclerosing effects may have played a role in the visible and sclerosing atrophy noted in our patient. Yamamoto et al[9] reported a similar case of dermal sclerosis induced by bleomycin.

Flagellate hyperpigmentation typically lasts for up to 6 months.[3] Patients with cutaneous manifestations from bleomycin therapy usually respond to steroid therapy and discontinuation of the drug. Bleomycin reexposure should be avoided, as it may cause extension or widespread recurrence of flagellate hyperpigmentation.[3] Postinflammatory pigment alteration may persist in patients with darker skin types and in patients with dramatic inciting inflammation.

Atrophoderma of Pasini and Pierini is a form of dermal atrophy that presents with 1 or more sharply demarcated depressed patches. There is some debate whether it is a distinct entity or a primary atrophic morphea.[10] Linear atrophoderma of Moulin has a similar morphology with hyperpigmented depressions and "cliff-drop" borders, but these lesions follow the lines of Blaschko.[11] Linear morphea initially can present as a linear erythematous streak but more commonly appears as a plaque-type morphea lesion that forms a scarlike band.[12] Erythema dyschromicum perstans is an ashy dermatosis characterized by gray or blue-brown macules seen in Fitzpatrick skin types III through V and typically is chronic and progressive.[13]

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