Pruritic rash in a man with seminoma

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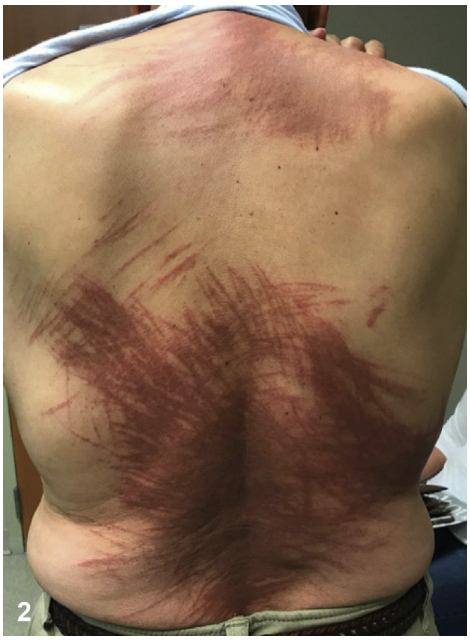
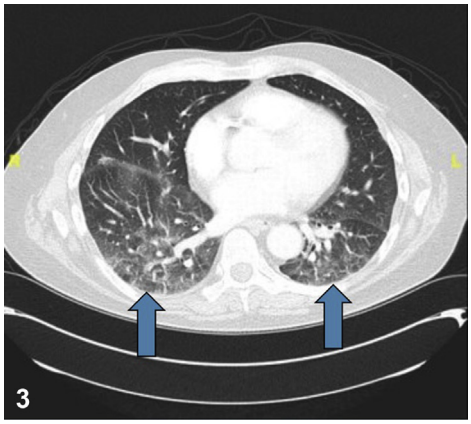
Key words: bleomycin; erythema; flagellate; lung toxicity; melanonychyia.





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Funding sources: None
Conflicts of interest: None disclosed.

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JAAD Case Reports 2021;7:8-10.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.05.036

A 64-year-old man with stage III seminoma presented with a skin rash that began after starting bleomycin, etoposide, and cisplatin (BEP) chemotherapy 4 weeks earlier. He reported darkened fingernails (Fig 1) and intense itchiness of his back, which evolved into dermatographia (Fig 2). He denied allergies to medications or exposure to possible irritants. He was prescribed oral antihistamines and 0.1 % triamcinolone cream, which improved symptoms in 3 weeks. Three BEP cycles were completed, and the erythema resolved, but hyperpigmentation persisted. Over the next month, he had persistent dry cough. Computed tomography (CT) scan of the chest was obtained (Fig 3).

Question 1: What is the most likely diagnosis?

A. Metastatic seminoma

B. Adult-onset Still disease

C. Bleomycin toxicity

D. Erythema ab igne

E. Shiitake flagellate dermatitis

Answers:

A. Metastatic seminoma — Incorrect. Although seminoma commonly spreads to the lungs, CT imaging would likely find multiple variably sized confluent soft tissue nodules and masses.

B. Adult-onset Still disease — Incorrect. Adult-onset Still disease is a rare systemic autoinflammatory disease characterized by the classic triad of fever, joint pain, and a distinctive bumpy salmon-colored rash. This disease is often considered a diagnosis of exclusion.

C. Bleomycin toxicity — Correct. This is a case of bleomycin-induced flagellate erythema (BIFE), bleomycin-induced melanonychia, and bleomycin-induced lung toxicity (BILT). BIFE and persistent hyperpigmentation occur in approximately 10% to 20% of patients on bleomycin.[1] It can present from hours to months after bleomycin exposure and is characterized by pruritic, erythematous-to-hyperpigmented, linear streaks in a whip-like pattern primarily affecting the trunk.[1,2] Bleomycin-induced melanonychia is a rare brown-to-black pigmentation of the nail caused by the presence of melanin in the nail plate associated with bleomycin use.[2] The key to diagnosis in this patient is the clinical symptomatic respiratory impairment, recent bleomycin therapy and skin toxicity, and the exclusion of infection or pulmonary involvement of the primary malignancy.[1-4]

D. Erythema ab igne — Incorrect. Erythema ab igne is a disorder characterized by a localized macular rash in a reticulated pattern that may lead to red or brown hyperpigmentation following chronic exposure to infrared radiation in the form of heat. It is commonly seen with the use of laptop computers or heating packs and can be associated with pruritis. Erythema ab igne is a localized reaction and would not explain the systemic findings of melanonychia or lung toxicity in our patient.

E. Shiitake flagellate dermatitis — Incorrect. Shiitake flagellate dermatitis is a toxic reaction to lentinan, a polysaccharide found in shiitake mushrooms. It is characterized by pruritic erythematous, linear streaks that resemble whiplash marks. However, this condition is not associated with melanonychia or lung toxicity.[1]

Question 2: What is the best initial treatment of BIFE in a patient without evidence of lung toxicity?

A. Permanent discontinuation of bleomycin

B. Antihistamines and topical steroids

C. Oral corticosteroids

D. Topical ketoconazole

E. Avoid sun exposure

Answers:

A. Permanent discontinuation of bleomycin — Incorrect. It is important for dermatologists to recognize that bleomycin-induced cutaneous toxicities can frequently be treated symptomatically without interrupting chemotherapy.[4] An attempt to treat the patient symptomatically is warranted before interrupting chemotherapy. If the skin symptoms severely worsen or do not improve with antihistamines and topical steroids, discontinuation of bleomycin may be considered.

B. Antihistamines and topical steroids — Correct. BIFE is typically self-limited and resolves upon cessation of bleomycin. Oral antihistamines and topical steroids are found improve the itching associated with BIFE.[4] Hyperpigmentation may persist after therapy and occurs in 10% to 20% of patients on bleomycin.[1] If the skin symptoms severely worsen or do not improve with antihistamines and topical steroids, discontinuation of bleomycin may be considered.

C. Oral corticosteroids — Incorrect. Local corticosteroids should be considered before systemic corticosteroids.

D. Topical ketoconazole — Incorrect. Given the patient's history, fungal skin infection is unlikely. There is no indication for ketoconazole, an antifungal.

E. Avoid sun exposure — Incorrect. Limiting sun exposure can be beneficial to all patients. However, avoidance of sun exposure alone is not the best treatment option.

Question 3: What should be done next regarding the findings on imaging in Fig 3?

A. Obtain pulmonary function test (PFT)

B. Initiate inhaled glucocorticoids

C. Initiate systemic glucocorticoids

D. Initiate azithromycin

E. Positron emission tomography (PET) scan

Answers:

A. Obtain PFT — Incorrect. PFT would not confirm the diagnosis of BILT nor change future management. Baseline PFTs are sometimes obtained prior to the initiation of bleomycin therapy especially in patients with a history of pulmonary disease.[5] In asymptomatic patients, PFTs may be performed for screening of BILT, but there is no consensus on the utility of this practice.[5] This patient finished BEP therapy and is symptomatic (cough). Given his history of bleomycin-induced skin toxicity, there is high suspicion for BILT.

B. Initiate inhaled glucocorticoids — Incorrect. Inhaled glucocorticoids are used for the treatment of asthma and chronic obstructive pulmonary disease but do not play a role in the treatment of BILT.

C. Initiate systemic glucocorticoids — Correct. Early identification and discontinuation of bleomycin is the mainstay of BILT treatment, but corticosteroids may be beneficial in patients who have symptoms after treatment, although consensus is unclear.[1,3] Symptomatic patients (new cough or respiratory symptoms) should be evaluated with a high index of suspicion, as BILT can be irreversible and fatal. CT findings (Fig 3) and clinical presentation are consistent with moderate BILT.

D. Initiate azithromycin — Incorrect. CT scan and clinical presentation favor BILT over respiratory infection. Azithromycin is often used for the treatment of pneumonia and chronic obstructive pulmonary disease exacerbation, but it does not play a role in the treatment of BILT.

E. PET scan — Incorrect. PET scans are helpful in distinguishing primary or metastatic malignant lesions. However, the CT findings are more consistent with lung toxicity versus metastatic seminoma lesions.

The authors acknowledge Dr Kelsey Reeley for his selfless devotion to the transference of knowledge and commitment to the exchange of ideas in medicine.

Abbreviations used:

BEP: bleomycin, etoposide, and cisplatin
BIFE: bleomycin-induced flagellate erythema
BILT: Bleomycin-induced lung toxicity
CT: computed tomography
PFT: Pulmonary function tests
PET: Positron emission tomography

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