Photo Quiz

Hyperpigmentation of the Hands, Feet, and Tongue

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FIGURE 1

FIGURE 2

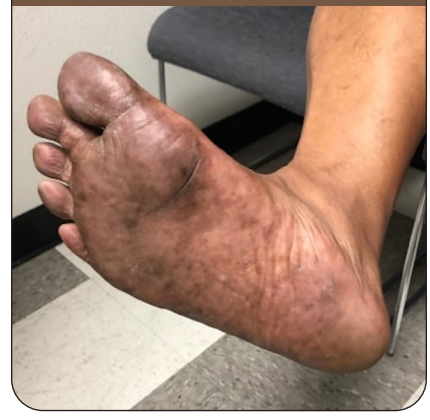
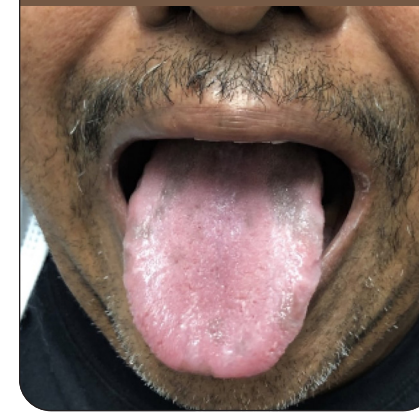


FIGURE 3



A 55-year-old patient presented with a one-month history of a painless, nonpruritic rash involving the palms, soles, and tongue. Apart from intermittent tingling of the hands and dry skin, the rash was not bothersome and was improving with the application of petroleum jelly. There was no swelling, blisters, erythema, or desquamation. The patient did not have fever, adenopathy, recent travel, or new sex partners.

The medical history included poorly controlled type 2 diabetes mellitus, hypertension, obesity, and metastatic appendiceal carcinoma. In the months leading up to development of the rash, the patient had been treated with several chemotherapeutic agents, including fluorouracil, capecitabine (Xeloda), and bevacizumab (Avastin).

Physical examination revealed reticular, nonblanching, hyperpigmented lesions on the palms and soles bilaterally *(Figures 1 and 2)*. Linear hyperpigmentation was present on the dorsal surface of the tongue *(Figure 3)*. Physical examination was otherwise unremarkable.

Question

Based on the patient's history and physical examination findings, which one of the following is the most likely diagnosis?

- ☐ A. Chemotherapy-induced hyperpigmentation.
- ☐ B. Fixed drug eruption.
- ☐ C. Palmar-plantar erythrodysesthesia (hand-foot syndrome).
- ☐ D. Rocky Mountain spotted fever.
- ☐ E. Secondary syphilis.

See the following page for discussion.

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This series is coordinated by John E. Delzell Jr., MD, MSPH, associate medical editor.

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Discussion

The answer is A: chemotherapy-induced hyperpigmentation, which appears as a painless rash that can occur over various regions of the body, including the hands, feet, and mucous membranes. It often presents as hyperpigmented macules, patches, or reticular lesions and usually appears two to three weeks after initiating chemotherapy. It can be caused by a number of chemotherapy agents, including fluorouracil, doxorubicin (Adriamycin), and cytarabine.[1] Lesions usually resolve spontaneously within a few weeks of stopping the causative agent.

A fixed drug eruption is an allergic reaction that presents as single or multiple well-defined, erythematous macules or plaques that reappear in the same location with reexposure to the causative drug. The lesions can occur anywhere on the body and typically appear within hours after drug administration.[2] As the lesions resolve, hyperpigmentation may occur at the site.[3] Treatment includes antihistamines, topical corticosteroids, and discontinuation of the causative agent.[3]

Palmar-plantar erythrodysesthesia, or hand-foot syndrome, is also a reaction to chemotherapy agents but presents as erythema and swelling of the hands and feet, often followed by blistering, moist desquamation, ulceration, and severe pain.[4] Many of the same agents that cause chemotherapy-induced hyperpigmentation can also cause hand-foot syndrome. Capecitabine causes hand-foot syndrome in approximately 50% of patients receiving the drug.[4] Treatment options are discontinuing the causative drug or modifying the regimen by reducing the dose or lengthening the interval between doses.[5]

The rash associated with *Rickettsia rickettsii* infection, which causes Rocky Mountain spotted fever, is characterized by small, blanching, erythematous macules on the wrists and ankles that advance centrifugally to the palms and soles and then spread centripetally to the limbs and trunk. The rash may become papular with central petechiae.[6] Systemic symptoms include fever, headache, myalgia, malaise, nausea, and vomiting.

The rash associated with secondary syphilis is characterized by diffuse, painless, occasionally pruritic, reddish-brownish macules and papules on the palms, soles, and trunk.[7] Lesions affecting the oral mucosa appear as shallow erosions or whitish plaques and are usually painful. Adenopathy and systemic symptoms are common.

SUMMARY TABLE

Condition	Characteristics
Chemotherapy-induced hyperpigmentation	Painless hyperpigmented macules, patches, or reticular lesions; can occur over various regions of the body and may involve mucous membranes; typically appears two to three weeks after initiating chemotherapy and resolves spontaneously within a few weeks of stopping the causative drug
Fixed drug eruption	Well-defined, erythematous macules or plaques following a drug exposure; lesions reappear in the same location with subsequent exposures
Palmar-plantar erythrodysesthesia (hand-foot syndrome)	Erythema and swelling of the hands and feet after chemotherapy; often causes blistering, moist desquamation, ulceration, and severe pain
Rocky Mountain spotted fever	Small, blanching, erythematous macules on the wrists and ankles with proximal spread; rash may become papular with central petechiae
Secondary syphilis	Diffuse, painless, occasionally pruritic, reddish-brownish macules and papules on the palms, soles, and trunk; patches are often present on the mucous membranes; adenopathy and systemic symptoms are common

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