Diagnostic Snapshot

Can you identify this skin rash?

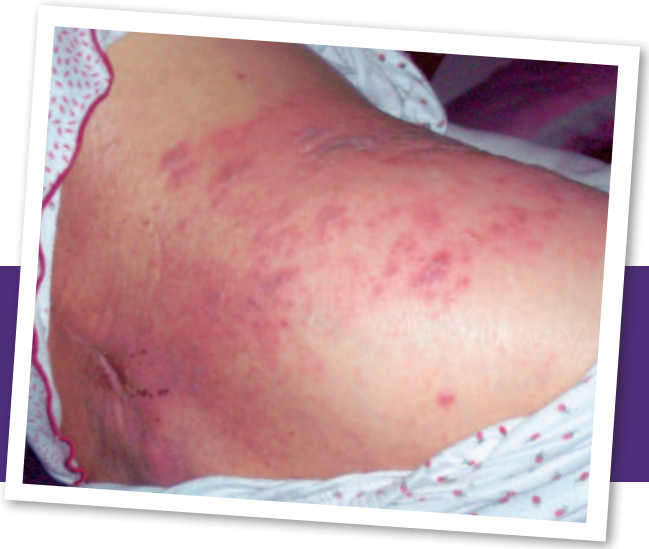

Figure 1

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History

Mrs. L., a 72-year-old non–English-speaking woman, was diagnosed with papillary thyroid cancer in 1995, at which time she underwent a total thyroidectomy. Unfortunately, her disease trajectory was riddled with multiple recurrences from April 2007 through January 2011. She developed metastasis to her lung, which was treated with palliative radiation, and she received radioactive iodine treatments six times throughout this time course.

In the winter of 2010, Mrs. L. relocated from Taiwan to the United States to live with her daughter. She was started on off-label sorafenib (Nexavar) 400 mg twice daily in January 2011. On day 14, she presented with thick callus formation on the ball of her right foot, with accompanying blisters there and between the toes. She rated the pain as a 10 on a 0–10 scale when walking. This cutaneous toxicity from sorafenib, known as palmar-plantar erythrodysesthesia (PPE), was assessed as grade 2 using the Common Terminology Criteria for Adverse Events (CTCAE) grading system (National Cancer Institute [NCI], 2009). Palmar-plantar erythrodysesthesia is characterized by redness, marked discomfort, swelling, and tingling in the palms of the hands or soles of the feet. A grade 2 PPE is described as skin change such as peeling, blisters, bleeding, edema, or hyperkeratosis interfering with instrumental activities of daily living (NCI, 2009). Her sorafenib was held for 7 days, at which point her PPE decreased to grade 1 with residual hyperkeratosis on the soles of the feet without pain; she was restarted on sorafenib at 75% dosing.

Chief Complaint

Four days after restarting sorafenib, Mrs. L.'s daughter called to report that her mother had developed a rash 3 days prior. Based on her description, I envisioned the rash appearing on the right lateral aspect of her trunk at the waistline extending to the upper right hip, crossing to the lower posterior flank and middle of her back but not beyond the spine. She identified the rash as flat, red, and inflamed; however, she noted that fluid-filled blisters were developing in the affected area. She conveyed that her mother stated it was "itchy and uncomfortable." This patient was assessed further through telephone communication with her daughter and an electronic photograph (see Figure 1 above).

Review of Systems

The patient was afebrile without chills. She had no evidence of rash outside of the described area. The photo revealed an erythematous rash with fluid-filled vesicles extending from the right lateral aspect of the waistline to the upper hip wrapping around to the posterior lower flank but not intersecting the spine. She described "pruritus and a pain sensation" at the site of the rash but was unable to rate it on a 0–10 scale. She acknowledged that oxycodone 5 to 10 mg adequately relieved this pain. She continued to experience grade 1 PPE on the soles of her feet, yet this was significantly decreased.

DIFFERENTIAL DIAGNOSIS

CHOOSE THE CORRECT DIAGNOSIS

A ☐ *Dermatologic side effect of sorafenib*

B ☐ *Herpes zoster (shingles)*

C ☐ *Impetigo*

SEE BACK FOR ANSWER ▶

Correct Answer B

Herpes zoster (shingles) is a painful rash caused by the *Varicella zoster* virus, the same virus that causes chickenpox. This virus can remain inactive after recovery from chickenpox and reactivate years later for reasons unknown; however, patients in an immunocompromised state are at greater risk. More than half of all cases occur in adults over 60 years old (Oxman et al., 2005).

Shingles presents as a painful rash that is unilateral and does not cross the midline. The pain typically follows a dermatome of skin that covers a nerve that starts in the spinal cord and tracks in a band-like fashion along one side of the body. However, it may occur in up to three dermatomes (Cartwright, 2011). Other less common symptoms include fever, headache, chills, and nausea. The hallmark rash forms fluid-filled blisters on one side of the trunk, buttocks, head, or face (Courey, 2006). This presentation, specifically following a dermatome of skin, is classic; it is differentiated from the macropapular rash experienced on sorafenib, which is more commonly isolated to the face, neck, upper chest, and back, but can present as generalized including the upper and lower extremities. It is also differentiated from impetigo symptoms, which often present as a small dot that is red and itchy and quickly expands into an entire affected area not specific to a dermatome.

Once this hallmark rash emerges, *Herpes zoster* can be diagnosed clinically; further laboratory testing should be considered if the diagnosis is uncertain (Cartwright, 2011). These blisters will break and crust over in approximately 7 to 10 days. Once the rash crusts, the patient is no longer contagious (CDC, 2011).

Explanation of Incorrect Answers

Dermatologic side effects of sorafenib include hand-foot skin reaction (HFSR), facial erythema, alopecia, pruritus, and xerosis (Ratain et al., 2006). Patients receiving this therapy may also experience a maculopapular rash, pustules, exfoliative dermatitis, and pain (Esper, Gale, & Muehlbauer, 2007). These lesions can be located on the face or on the body and usually present within several weeks or months of treatment (Robert, Mateus, Spatz, Wechsler, & Escudier, 2008). Sorafenib-induced HFSR can have features such as erythema, fissures, or paresthesia, but more frequently is associated with palmar and/or plantar hyperkeratosis, particularly located on pressure points.

Impetigo is a skin condition caused by *Staphylococcus aureus*, which is most common, and *Streptococcus pyogenes*. Impetigo can manifest as red sores that rupture, ooze, and crust; as fluid-filled blisters; or as painful fluid- or pus-filled sores. There are three types of impetigo: impetigo contagiosa, bullous impetigo, and ecthyma. Older adults and those with compromised immune systems are at greater risk of developing ecthyma. Ecthyma is characterized by painful fluid- or pus-filled sores that can convert to ulcers, usually on the legs and feet (Mayo Clinic, 2010).

Management

There are three antiviral agents approved by the US Food and Drug Administration for treatment of *Herpes zoster*: acyclovir, famciclovir, and valacyclovir. Mrs. L. was prescribed famciclovir 500 mg three times a day for 7 days. She did receive relief of pain with oxycodone 5 to 10 mg, thus her daughter was instructed to continue this every 4 to 6 hours as needed. Dworkin and colleagues (2009) identified that oxycodone had statistically significant efficacy in treating acute *Herpes zoster* pain compared with gabapentin or placebo. Additionally, colloidal oatmeal baths were recommended to help relieve itching, as well as oral diphenhydramine (Benadryl) 25 mg every 6 hours as needed (CDC, 2011).

Follow-Up

Mrs. L.'s vesicles broke and crusted over 6 days following initiation of famciclovir. Her pain decreased at that time. She stopped taking oxycodone by day 10, with no residual pain reported. Data suggest that the acute pain and hypersensitivity at the site of the rash can resolve in several days to weeks or more (Cartwright, 2011).

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