



Diffuse skin rash, altered mental status

This patient's rash followed recent treatment for back pain. Was this a drug reaction or something else?

A 74-YEAR-OLD CAUCASIAN MAN presented to the hospital with intractable back and chest pain, a diffuse skin rash, and altered mental status. He said that 2 days ago, he'd gone to a different local hospital for treatment of back pain and a headache that had begun 3 days earlier. He was treated with intravenous hydromorphone and sent home with a prescription for meperidine. He said that several hours after being treated with the hydromorphone, the rash developed on his head and then spread to his trunk and upper extremities.

On physical examination, the patient was afebrile. He had numerous erythematous papules and vesicles in various stages of development on his scalp, face, neck, chest (FIGURE), abdomen, back, upper extremities, and groin. The lesions continued to spread and eventually involved his posterior oropharynx. The patient also developed conjunctivitis.

Laboratory findings included a white blood cell count of 4000/mcL (normal: 4500-11,000/mcL) with 65.9% segmented neutrophils (normal: 40%-60%), and 16.7% lymphocytes (normal: 20%-40%). Lab tests also revealed an aspartate aminotransferase level of 263 U/L (normal: 10-40 U/L), alanine aminotransferase of 236 U/L (normal: 7-56 U/L), and lactate dehydrogenase of 628 U/L (normal: 140-280 U/L).

The patient's medical history was significant for hypertension, osteoarthritis, and IgG-kappa multiple myeloma, which had been treated with multiple chemotherapy regimens that included lenalidomide. Five years earlier, he'd undergone an autologous bone marrow transplant (BMT). At the time of presentation,

the patient was being treated with daratumumab; he received his most recent treatment approximately one month earlier. Other medications included amlodipine, esomeprazole, and escitalopram.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE

Lesions on chest



PHOTO COURTESY OF LAUREN CRAIG, MD

The patient had erythematous papules and vesicles in various stages of development on his chest.

Caitlyn T. Reed, MD; Allison R. Cruse, MD; Jeremy D. Jackson, MD

University of Mississippi Medical Center, Department of Dermatology, Jackson

caitreed11@gmail.com

DEPARTMENT EDITOR

Richard P. Usatine, MD
University of Texas Health at San Antonio

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➤ About half of all patients who receive bone marrow transplants develop varicella-zoster virus infection within 5 years.

Diagnosis: Disseminated varicella-zoster virus infection

Because of the patient’s immunocompromised state, his presentation with altered mental status and diffuse rash was concerning. On hospital Day 2, a sample was taken from one of his skin lesions. Polymerase chain reaction (PCR) detected varicella-zoster virus (VZV), and we diagnosed disseminated VZV infection. On hospital Day 3, we performed a lumbar puncture because of worsening confusion and discovered that the cerebrospinal fluid was also positive for VZV.

Disseminated VZV is the most common cause of late infection in patients who have received an allogenic BMT; it is usually due to reactivation of the virus.¹ In one study of 1186 patients who underwent BMT, 52% developed VZV infection within 5 years.² Disseminated VZV may also involve visceral organs, causing pneumonitis, pancreatitis, hepatitis, or encephalitis. Mortality rates for disseminated VZV are as high as 50%.³ Because of this, physicians should be vigilant when patients who have received a BMT present with a rash and signs of systemic involvement.

■ **Two reliable tests.** Even when lesions are classic for VZV, the diagnosis must be confirmed by laboratory testing. Real-time PCR assay is a rapid and highly sensitive test for diagnosing VZV.⁴ Another rapid test that can be used to confirm the clinical diagnosis of VZV is a direct fluorescent antibody assay, which is becoming more widely available.

In contrast, the sensitivity of viral culture for VZV has been reported to be as low as 20%.⁵ Viral culture also takes much longer and has a significantly lower yield compared with newer methods.⁶ A biopsy of skin lesions will reveal multinucleated giant cells, but cannot differentiate between herpes simplex virus (HSV) and VZV.⁷

These lesions can be mimicked

When a rash develops following the use of intravenous hydromorphone, as occurred with our patient, a drug reaction must be ruled out. A drug reaction can cause almost any skin manifestation and may present as vesicles, a macular rash, a papular rash, or diffuse erythema. In this case, drug rash was ruled out by the positive VZV PCR.

■ **Viral exanthems** can also present in a variety of ways. They may cause a macular, papular, or vesicular rash.

Prompt management is crucial

Prompt treatment of VZV with acyclovir improves outcomes, but death may still occur, even with early diagnosis.³ Immunocompromised patients with VZV should be closely monitored for secondary infections, which may rapidly progress and become fatal.⁸ The Centers for Disease Control and Prevention recommends both airborne and contact precautions for patients with disseminated VZV until all lesions are dry and crusted.⁹

While the live zoster vaccine is approved for prevention of shingles in patients <60 years of age, it is contraindicated in patients with a history of primary or acquired immunodeficiency states including leukemia, lymphoma, or other malignant neoplasms affecting bone marrow.

■ **Our patient.** On admission, he was treated with intravenous (IV) acyclovir 10 mg/kg TID; IV vancomycin 15 mg/kg every 12 hours; and IV ceftriaxone 2 g/d. Slowly, his mental status returned to baseline, and his rash and conjunctivitis resolved. We discharged him on hospital Day 12. He was transitioned to oral valacyclovir 1000 mg TID. Including both inpatient and outpatient treatment, the patient received 3 weeks (total) of acyclovir/valacyclovir therapy. **JFP**

CORRESPONDENCE

Caitlyn T. Reed, MD, School of Medicine, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216; caitreed11@gmail.com.

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