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Case Letter

A 63-year-old woman presenting with sacral, labial, and leg ulcers,,

Samantha M. Guhan, BA [a], Janelle S. Nassim, MD [b], Melissa Krystel-Whittemore, MD [c], Rosalynn M. Nazarian, MD [c], Bonnie T. Mackool, MD [d,*]

[a] Harvard Medical School, Boston, MA, United States
[b] Harvard Combined Dermatology Residency, Harvard Medical School, Boston, MA, United States
[c] Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
[d] Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States

Dear Editor,

A 63-year-old woman with a history of chronic lymphocytic leukemia presented with ulcers on the sacrum, labia majora, and the left anterior lower leg. She had first noted a small ulcer in the gluteal cleft 2 months prior to presentation. The ulcer grew rapidly within days and was managed conservatively without improvement. One month later, the patient was admitted to the local hospital and was found to have *Klebsiella pneumoniae* and *Citrobacter bacteremia* infection, for which she received antibiotics. The patient was then transferred for further management.

Upon transfer, she was afebrile with a leukocytosis of 17,000/μL. Her CD4+ cell count was low at 143/μL (normal: 348–1456/μL). Physical examination revealed a full thickness sacral ulcer with areas of green-to-brown necrotic tissue and surrounding plaques of light intensity erythema (Fig. 1a). Adjacent smaller discrete ulcers with green-to-brown crust were present on the labia majora. Ulcers on the lower leg were well demarcated, irregularly shaped, and covered with black eschar (Fig. 1b). Punch biopsies were performed on the left buttock and left lower leg (3 and 4 mm, respectively).

Viral antigen detection and culture of the wound was positive for herpes simplex virus (HSV) 2. HSV 2 viral load on day 11 of hospitalization was 75,800 copies/mL. Histopathologic examination demonstrated ulceration and enlarged cells with multinucleation, nuclear molding, and chromatin margination, consistent with herpes viral cytopathic changes (Fig. 1c). Immunohistochemistry was positive for HSV. The biopsy included subcutaneous adipose tissue and showed no evidence for a primary vasculitis/vasculopathy. Immunofluorescence studies were not submitted. Tissue cultures were negative other than for rare *Candida tropicalis*. Upon further questioning, the patient endorsed a history of recurrent genital herpes.

Treatment with intravenous acyclovir was initiated on the third day of hospitalization. The patient successfully underwent a diverting colostomy to avoid fecal contamination of the sacral ulcer. The viral titer decreased to 37,600 copies/mL by day 19 of treatment with acyclovir. On day 25, the patient requested to be transitioned to comfort care only. She died 3 days later.

HSV lesions typically present as clusters of fluid-filled vesicles on an erythematous base. They form a characteristic scalloped border and can progress into erosions and ulcerations (Vassantachart and Menter, 2016). Infections are usually more severe in immunocompromised patients, including neonates, pregnant women, and those with hematologic malignancies or receiving immunosuppressants. These patients typically fail to clear the infection quickly, and lesions can last for months. Lesions in immunocompromised patients typically appear larger and deeper than those in immunocompetent individuals. Moreover, ulcers can occur in atypical areas and may have verrucous or hyperkeratotic surfaces (Bacon et al., 2003). This case demonstrates the potentially aggressive nature of HSV infection in immunocompromised patients, especially when initially unrecognized. Our patient was immunocompromised secondary to her hematologic malignancy, chronic lymphocytic leukemia, and a reduced CD4+ T cell count.

Viral dissemination is also seen in immunocompromised patients (Berrington et al., 2009). HSV can spread through a hematogenous or neuronal route (Johnson, 1964). The most common symptoms seen in patients with HSV viremia include fever, sepsis, central nervous system alterations, skin lesions, hepatitis, and abdominal pain. Viremia due to HSV also occurs in immunocompetent patients and is more common in women than men (Johnston et al., 2008).

Differential diagnosis includes pressure ulcers complicated by bacterial superinfection, a paraneoplastic ulcer, and pyoderma gangrenosum. The most common tests to confirm HSV infection include real-time HSV polymerase chain reaction and viral culture. Skin biopsy may be indicated in some cases. Diagnostic workup in these patients should include tissue cultures to rule out bacterial, fungal, or mycobacterial infections. Patients should be treated with intravenous acyclovir, but there is a higher rate of acyclovir resistance in immunocompromised patients (Chilukuri and Rosen, 2003). If resistance is found, treatment should be switched to intravenous foscarnet.

* Corresponding author.
E-mail address: bmackool@mgh.harvard.edu (B.T. Mackool).

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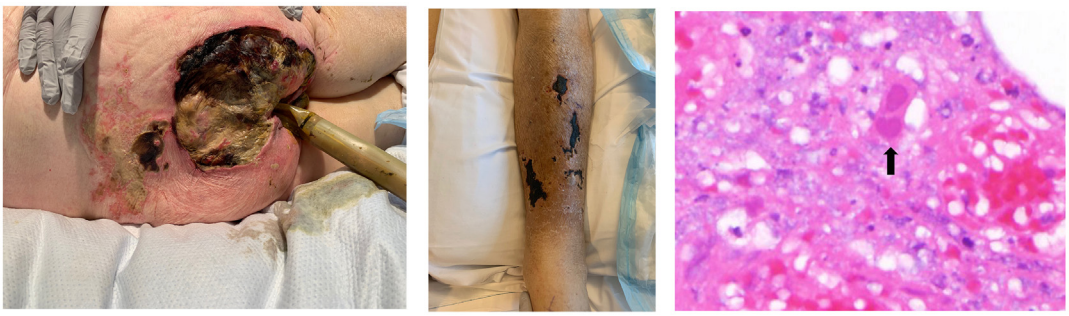

Fig. 1. Clinical and histopathologic manifestation of sacral and left lower extremity ulcers. (A) Sacral ulcer; (B) left lower extremity ulcer; (C) Skin biopsy revealed presence of large, multinucleated cells with viral inclusions (arrow; hematoxylin and eosin, 60×).

Conflict of Interest

None.

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Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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