JAMA Dermatology Clinicopathological Challenge

An Elderly Woman With Painful Buttock and Vulvar Ulcers

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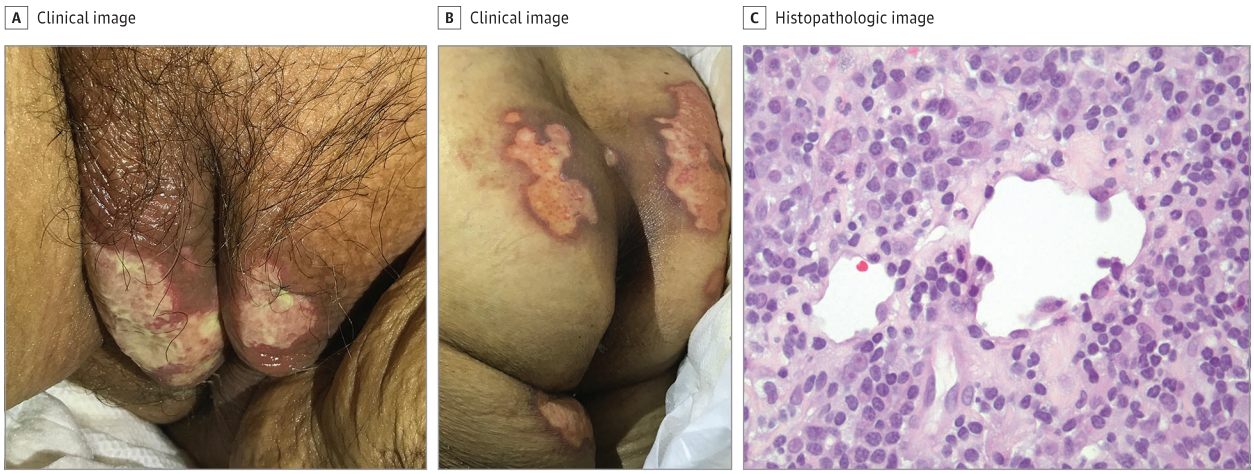

Figure 1. A and B, Clinical photographs showing vulvar and buttock ulcers at the time of presentation. C, Hematoxylin-eosin stain (original magnification ×40).

A woman in her 80s presented to hospital with somnolence and fatigue of 2 days' duration. Medical history included lower urinary tract symptoms of 1-week duration for which she was prescribed cotrimoxazole with no improvement. She also reported progressively worsening vulvar and buttock pain of 5 days' duration. The patient was admitted to the intensive care unit 3 weeks prior to presentation for pneumonia and remained hospitalized for 10 days. She was not sexually active and had no medical history of sexually transmitted infections. Anogenital examination revealed vulvar (**Figure 1**A) and buttock ulcers (Figure 1B) tender to palpation. Initial blood workup showed leukopenia with a white blood cell count of 2400 cells/μL (to convert to cells/L, multiply by 10^6), a differential of 72% neutrophils, and a hemoglobin level of 8.5 g/dL with a hematocrit differential of 27% (to convert hemoglobin to g/L, multiply by 10.0). Cotrimoxazole was discontinued on admission. A biopsy specimen was obtained from the left vulvar ulcer (Figure 1C).

WHAT IS YOUR DIAGNOSIS?

- **A.** Fixed drug eruption
- **B.** Cutaneous candidiasis
- **C.** Cytomegalovirus ulcers
- **D.** Genital herpes simplex virus infection

Diagnosis

C. Cytomegalovirus ulcers

Discussion

Histopathologic examination revealed dense mixed inflammatory cell infiltrates with enlarged endothelial cells (Figure 1C). Immunohistochemical staining for cytomegalovirus (CMV) confirmed the diagnosis of CMV cutaneous ulcers (**Figure 2**). Results of quantitative plasma CMV polymerase chain reaction (PCR) were positive with 2240 copies/mL. The CMV immunoglobulin G level was 57 Au/mL (positive >6; the manufacturers did not provide conversion tables from arbitrary units [AU/mL] to SI units) and CMV IgM results were negative. She had no previous baseline CMV immunoglobulin levels. These findings are consistent with CMV viremia presenting as severe anogenital ulcers in an otherwise immunocompetent patient most likely secondary to CMV reactivation. She was prescribed intravenous ganciclovir (5 mg/Kg every 24 hours). Somnolence and fatigue improved after 3 days of treatment, and her white blood cell count increased gradually to reach 9100 cells/μL after 5 days. The patient was eventually discharged home with a prescription for oral valganciclovir (450 mg orally twice daily). On follow-up 2 weeks later, the ulcers were healing and quantitative CMV PCR results were negative. She completed a 21-day course of antiviral therapy.

Cytomegalovirus infection is common in immunocompromised patients and causes a variety of diseases including but not limited to pneumonitis, colitis, esophagitis, hepatitis, and bone marrow suppression. Cutaneous manifestations are rare but have been reported in the literature in immunocompromised patients (eg, HIV, hematologic malignant abnormalities, transplant patients) and less frequently in immunocompetent patients.[1-4] No skin appearance is pathognomonic for CMV because clinical presentations can range

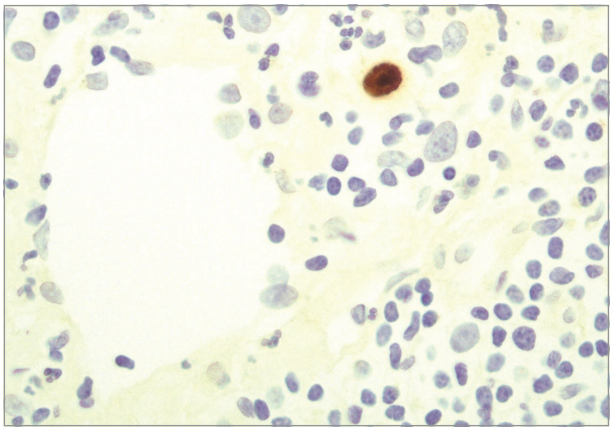

Figure 2. Immunohistochemical stain for cytomegalovirus confirming the diagnosis (original magnification ×40).

from maculopapular eruptions, petechiae, vesiculobullous lesions, hyperpigmented nodules,[1] pruritic papules and plaques with levido pattern,[2] and anogenital ulcerations mainly involving the buttock;[3] the latter is the most common presentation, as in this patient.

Histopathologic findings on hematoxylin-eosin stain are variable and may show dermal vessel dilation and prominent neutrophilic infiltration.[3] Enlarged, endothelial cells with basophilic intracytoplasmic or intranuclear inclusions (owl-eye inclusions) are classic, but cytomegalic changes particularly affecting vascular endothelial cells and macrophages without the characteristic inclusion have also been reported.[2,3]

Primary CMV infection typically occurs in childhood, is usually asymptomatic, and around two-thirds of adults become immune.[5] Lifelong latency follows the primary infection and reactivation typically occurs in immunocompromised patients, such as those with HIV, hematologic malignant diseases, and transplantation because of the suppression of cell-mediated immunity.[6] However, CMV has been shown to reactivate in critically ill, nonimmunosuppressed patients admitted to the ICU,[6,7] which we believe is the only identifiable risk factor for CMV reactivation in this patient.

The differential diagnosis of genital ulcers is extensive and can be broadly categorized into infectious vs noninfectious causes.[8] Sexually transmitted infections (eg, syphilis, herpes, chancroid) and non–sexually transmitted infections such as *Candida* can present with genital ulcers. Among noninfectious causes, lichen planus, Behçet disease, pyoderma gangrenosum, fixed drug eruptions, pressure ulcers, contact dermatitis, and some neoplasms such as squamous cell carcinoma and melanoma can also present with ulcerations.[8] In this patient, documentation of viremia by PCR coupled with histopathologic findings confirmed the diagnosis of CMV ulcers and ruled out other diagnoses.

Cytomegalovirus cutaneous disease can be challenging to diagnose given the lack of a pathognomonic dermatologic presentation. Clinicians should be aware of this entity even in immunocompetent patients given the appropriate clinical picture, risk factors, and laboratory profile. A thorough evaluation and early biopsy of the lesion with identification of CMV by immunohistochemical stain will help in establishing a diagnosis and initiating appropriate treatment.

ARTICLE INFORMATION

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Published Online: June 13, 2018. doi:10.1001/jamadermatol.2018.0632

Conflict of Interest Disclosures: None reported.

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REFERENCES

1. Kaisar MO, Kirwan RM, Strutton GM, et al. Cutaneous manifestations of cytomegalovirus disease in renal transplant recipients: a case series. *Transpl Infect Dis*. 2008;10(3):209-213.

2. Drago F, Aragone MG, Lugani C, Rebora A. Cytomegalovirus infection in normal and immunocompromised humans. a review. *Dermatology*. 2000;200(3):189-195.

3. Choi YL, Kim JA, Jang KT, et al. Characteristics of cutaneous cytomegalovirus infection in non-acquired immune deficiency syndrome, immunocompromised patients. *Br J Dermatol*. 2006;155(5):977-982.

4. Durkin J, Martinez-Diaz GJ, Gehris RPA. A 7-week-old Nepali girl with a perianal ulcer: brief report. *Pediatr Dermatol*. 2014;31(2):e65-e66.

5. Sweet C. The pathogenicity of cytomegalovirus. *FEMS Microbiol Rev*. 1999;23(4):457-482.

6. Frantzeskaki FG, Karampi ES, Kottaridi C, et al. Cytomegalovirus reactivation in a general, nonimmunosuppressed intensive care unit population: incidence, risk factors, associations with organ dysfunction, and inflammatory biomarkers. *J Crit Care*. 2015;30(2):276-281.

7. Papazian L, Hraiech S, Lehingue S, et al. Cytomegalovirus reactivation in ICU patients. *Intensive Care Med*. 2016;42(1):28-37.

8. Rosen T. Update on genital lesions. *JAMA*. 2003;290(8):1001-1005.