Mucocutaneous ulcers in an immunocompromised patient

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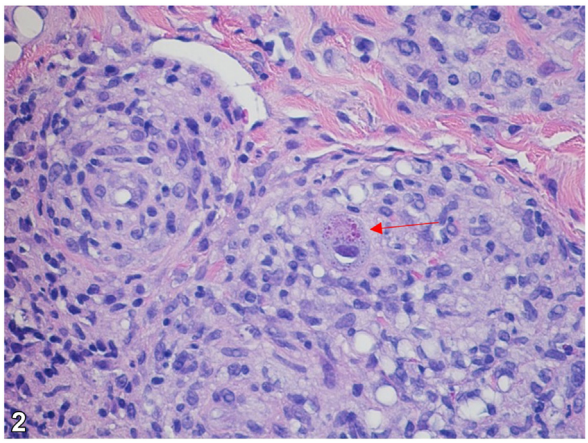

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HISTORY

A 49-year-old female with systemic lupus erythematosus (SLE) on hydroxychloroquine, prednisone, and mycophenolate mofetil presented with 6 months of nonhealing labial and perianal ulcers. On prior inpatient admission, she received acyclovir for polymerase chain reaction-positive herpes simplex virus (HSV) isolated from a vulvar lesion, without resolution. In the dermatology clinic, punched-out ulcers were on the perianal and perilabial skin (Fig 1, *A*) with crusted plaques on the lip (Fig 1, *B*). She had anemia (hemoglobin of 7.7), elevated dsDNA (624), and elevated C3 (78). Platelets (152,000), white blood cells (5040), and C4 were normal. Biopsies were performed of the perilabial ulcerations (Fig 2).

Question 1: What is the most likely diagnosis?

A. Cutaneous manifestation of systemic lupus erythematosus (SLE)

B. Cutaneous cytomegalovirus (CMV)

C. Pyoderma gangrenosum (PG)

D. Herpes simplex virus (HSV)

E. Behçet's disease (BD)

Answers:

A. SLE — Incorrect. Oral ulceration is common in SLE, especially during flaring. Cutaneous ulcerations are more likely associated with SLE vasculitis on the lower extremities. The pathology would show leukocytoclastic vasculitis, not the cytoplasmic inclusions seen in Fig 2.

B. CMV — Correct. Ulcers are the most common cutaneous manifestation of cutaneous CMV infection.[1] Histopathology for cutaneous CMV shows neutrophilic vasculitis and enlarged endothelial cells with large basophilic nuclear and cytoplasmic inclusions surrounded by a clear halo[2] (Fig 2). This patient was susceptible to CMV infection due to chronic immunosuppression.

C. PG — Incorrect. Even though PG can develop in the setting of immunosuppression, the ulcers most commonly occur on the arms and legs, and the ulcers are usually ill-defined with gray overhanging borders, unlike this patient. PG is associated with inflammatory bowel disease and acute myelogenous leukemia.

D. HSV — Incorrect. Morphologically, HSV can present very similarly to CMV. CMV may have a deeper, more ragged border. However, the patient was polymerase chain reaction-positive for genital HSV on a prior inpatient admission and received acyclovir, but the ulcers remained. On pathology, cellular margination, molding, and multinucleation are more characteristic of HSV infections.

E. BD — Incorrect. Behçet's disease is an autoimmune inflammatory condition causing orogenital ulcers in addition to systemic involvement affecting the gastrointestinal, pulmonary, musculoskeletal, and nervous systems. Cutaneous inflammation, uveitis, and a positive pathergy test are common. This patient had no systemic involvement at the time of presentation.[3]

Question 2: What is the best treatment?

A. Increase oral prednisone and hydroxychloroquine doses

B. Intravenous (IV) ganciclovir

C. Oral prednisone and subcutaneous infliximab

D. Oral valacyclovir

E. Oral prednisone and azathioprine

Answers:

A. Increase oral prednisone and hydroxychloroquine doses. Incorrect — Increase oral prednisone and hydroxychloroquine are appropriate for cutaneous lupus erythematosus. The patient had increased susceptibility to CMV due to chronic systemic steroid use.

B. IV ganciclovir. Correct — IV ganciclovir is the most effective treatment choice for CMV, and the patient was switched to oral valganciclovir on discharge. Acyclovir was previously ineffective in the patient. Acyclovir is a prodrug that is phosphorylated by thymidine kinase to its active form in HSV. CMV lacks thymidine kinase but has an alternative UL97 protein kinase, which phosphorylates acyclovir less efficiently. High-dose acyclovir can be used for CMV prophylaxis, but not for treatment. However, UL97 can effectively phosphorylate ganciclovir to its active form.[4]

C. Oral prednisone and subcutaneous infliximab. Incorrect — tumor necrosis factor inhibitors are indicated for PG.

D. Oral valacyclovir. Incorrect — Valacyclovir has limited activity as CMV treatment but may be used for HSV infections. Valacyclovir is phosphorylated by thymidine kinase, similar to acyclovir.

E. Oral prednisone and azathioprine. Incorrect — Azathioprine is appropriate for recalcitrant BD ulceration.

Question 3: What is the most common site for ulcers in a patient with cutaneous CMV?

A. Perianal

B. Lower extremity

C. Buccal mucosa

D. Stomach

E. Distal toes

Answers:

A. Perianal — Correct. It has been postulated that the perianal region is a common location for CMV ulcers due to the latency of the CMV virus frequently occurring in the GI tract, resulting in fecal shedding when the virus is reactivated.[5]

B. Lower extremity — Incorrect. This is the location for ulcers secondary to venous insufficiency, arterial ulcers, or PG.

C. Buccal mucosa — Incorrect. This can be a site affected by CMV, but it is not the most common site.

D. Stomach — Incorrect. Gastric ulcers are not commonly caused by CMV.

E. Distal toes — Incorrect. This is the location for arterial ulcers or diabetic foot ulcers.

Abbreviations used:

BD: Behçet's disease
CMV: cytomegalovirus
EBV: Epstein-Barr virus
HSV: herpes simplex virus
IV: intravenous
PG: pyoderma gangrenosum
SLE: systemic lupus erythematosus

Key words

cutaneous; cytomegalovirus; immunosuppression; mucocutaneous; systemic lupus erythematosus; ulcer

Conflicts of interest

None disclosed.

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