Cytomegalovirus infection presenting as an isolated petechial eruption in an immunocompromised patient

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INTRODUCTION

Cytomegalovirus (CMV), a prevalent human herpesvirus, infects 59% of people 6 years of age and older in the United States.[1,2] Early detection of this opportunistic infection is imperative, particularly in immunocompromised patients, to prevent morbidity and mortality. The diagnosis can be difficult due to the varied clinical presentations of CMV infection, manifesting from asymptomatic to severe visceral disease.[3] Rarely, cutaneous CMV infection can occur as well, sometimes as the first sign of infection. However, because of the diverse clinical and histologic manifestations, cutaneous CMV infection can be easily missed without a high degree of clinical suspicion.[3] The typical cutaneous manifestations of CMV include mucosal and cutaneous ulcers.[4] Less common manifestations include morbilliform eruptions, plaques, nodules, vesicles, purpura, and petechiae.[4] We present an immunocompromised patient with the presentation of cutaneous CMV in the form of an isolated petechial eruption on the upper extremities.

Abbreviations used:

CMV: cytomegalovirus
IV: intravenous

CASE REPORT

A 40-year-old woman with a past medical history of ambiguous lineage acute leukemia with a low level of BCR/ABL expression who was undergoing treatment with dasatinib was admitted for recurrent gastrointestinal bleeding and rash that had been present for 2 weeks. Physical examination revealed scattered petechiae and purpura on the bilateral hands and forearms (Fig 1). Review of systems revealed new-onset severe bilateral arthralgia of the hands and diarrhea. Laboratory review revealed a positive CMV quantitative polymerase chain reaction value of 57,400 copies/mL (a negative result is <390 copies/mL). Complete blood count showed a

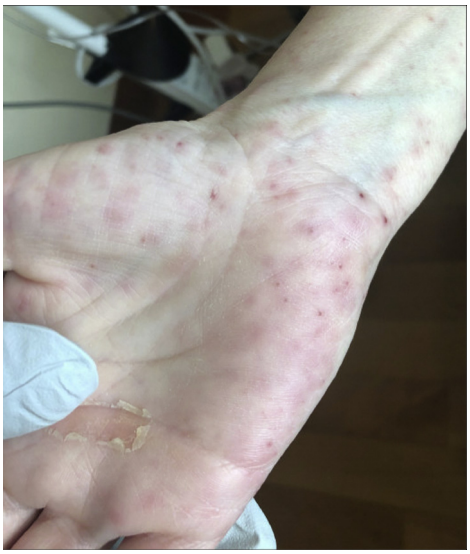

Fig 1. Petechiae and purpura scattered on the volar surface of the hand.

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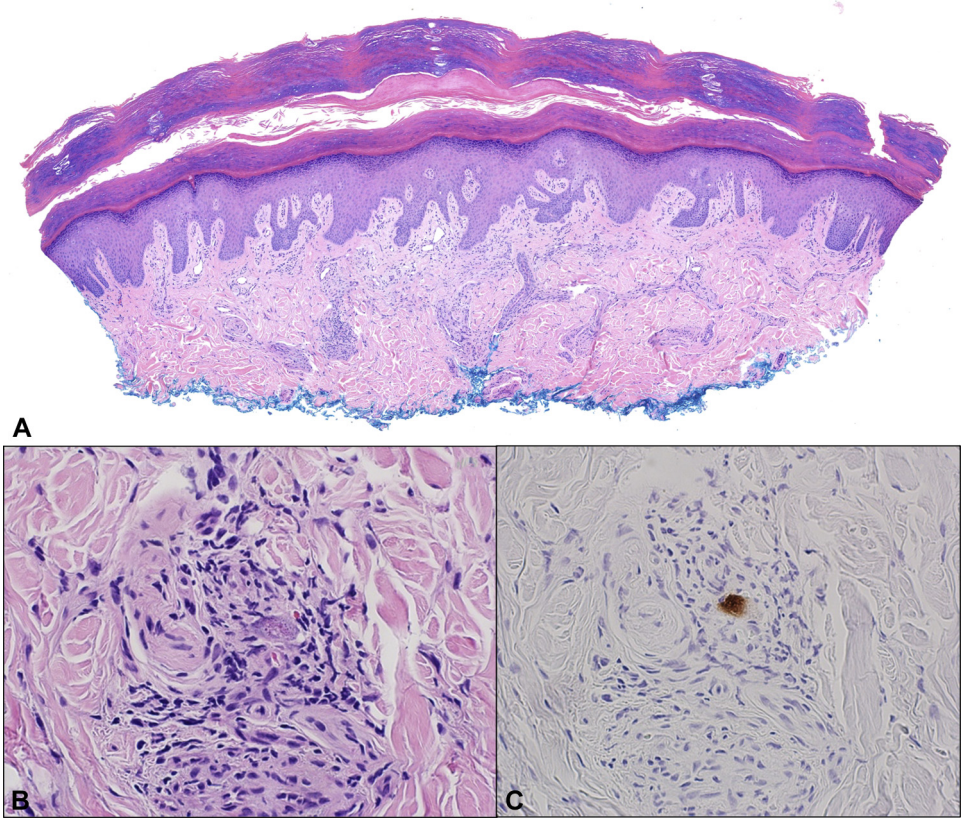

Fig 2. A, Perivascular lymphocytic infiltrate and increased small-caliber vessels on volar skin. **B,** Cytomegalic endothelial cell with enlarged nucleus containing eosinophilic intranuclear inclusion bodies. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A,** ×50; **B,** ×400.) **C,** Immunopositivity with cytomegalovirus antibody stain. (Cytomegalovirus antibody stain, CCH2 and DDG9 clones; original magnification: ×400.)

white blood cell count of 6500/mm^3, hemoglobin of 5.7 g/dL, a hematocrit of 17.6%, and a platelet count of 65,000/mm^3. The patient's anemia was attributed to hemorrhoids. After transfusion of packed red blood cells, the hemoglobin level was stabilized, and endoscopy to exclude gastrointestinal bleeding was deferred. The results of coagulation studies were unremarkable: the international normalized ratio was 1.0, the prothrombin time was 11.4 seconds, and the partial thromboplastin time was 33 seconds. The differential diagnosis included dasatinib hypersensitivity reaction versus cutaneous CMV. A punch biopsy from the fifth digit on the right hand was performed. Hematoxylin and eosin stain revealed a markedly enlarged endothelial cell with eosinophilic intranuclear inclusions (Fig 2, *A* and *B*). Subsequent immunohistochemical analysis showed that the intranuclear inclusion was positive for CMV antigen (Fig 2, *C*). The patient was started on intravenous (IV) ganciclovir due to clinical suspicion of CMV viremia, given her gastrointestinal symptoms, arthralgia, cutaneous involvement, and positive CMV polymerase chain reaction. After administration of IV ganciclovir, the patient showed rapid improvement in her cutaneous and systemic manifestations. She continued to improve, and after 13 days of ganciclovir treatment, she was discharged home in stable condition.

DISCUSSION

Manifestations of CMV infection range from asymptomatic to severe with systemic disease. Asymptomatic infections are more common in immunocompetent patients, whereas immunocompromised patients are at risk for severe disease.[1] Systemic manifestations of CMV are most commonly visceral, notably pneumonitis, gastroenteritis, meningoencephalitis, and retinitis or blindness.[3]

Cutaneous manifestations of CMV infection are found in 10% to 20% of patients with systemic CMV infection (Table I).[5-8] The cutaneous manifestations are variable and can mimic those of other infections.[3] The most common cutaneous finding is genital ulcers; less common findings are ulcers of the oral mucosa or the lower extremities[4]; the least common findings include morbilliform rash, plaques, nodules, vesicles,

Table I. Cutaneous manifestations of cytomegalovirus infection

Reference	Skin manifestations	Location	Concurrent disease	Treatment
Tan et al 2006[4]	Ulcers, morbilliform rashes, petechiae and purpura, necrotic papules, vesiculobullous eruptions	Not listed	HIV/AIDS, organ transplant recipients	IV or oral ganciclovir, oral valganciclovir, foscarnet, or cidofovir
Drozd et al 2019[5]	Ulcers, morbilliform rash, plaques, nodules, vesicles, purpura, and petechiae	Ulcers: 18 genital, 9 oral, 6 lower extremity, 9 dispersed	HIV/AIDS, HSV, drug-induced hypersensitivity syndrome, immune thrombocytopenic purpura, antiphospholipid-associated microangiopathy, EBV, SJS, TEN, Gianotti-Crosti syndrome, leukocyte adhesion deficiency type 1 and natural killer cell deficiency, common variable immune deficiency, erythema multiforme	Most common: IV or oral ganciclovir or valganciclovir. Less common: combination therapy with prednisolone, IVIg, or foscarnet
Rao et al 2020[6]	Pyoderma-like ulcerations	Abdominal around surgical incision	Renal transplant recipient	Oral valganciclovir and IV ganciclovir
Choi et al 2006[7]	Maculopapular rash, ulcers, nodules	Whole body, buttock, back, genitals	Aplastic anemia, lymphoma, leukemia, chronic renal failure, cirrhosis	IV ganciclovir
Tanaka et al 2020[8]	Subcutaneous nodules that develop into ulcers	Genitals	Multiple myeloma	Ganciclovir

CMV, Cytomegalovirus; *EBV*, Epstein-Barr virus; *IV*, intravenous; *IVIg*, intravenous immunoglobulin; *SJS*, Stevens-Johnson syndrome; *TEN*, toxic epidermal necrolysis.

purpura, and petechiae, usually in conjunction with ulcers.[4] In a systematic review from 2007 to 2017, only 3 patients were described with purpura or a petechia as an isolated dermatologic finding.[4]

Treatment is necessary because cutaneous CMV infection can signal systemic disease, which is associated with a 6-month mortality rate of 85%.[6] First-line treatment for most patients is IV ganciclovir or oral valganciclovir, whereas foscarnet is reserved for severely neutropenic patients or hematopoietic stem cell transplant recipients.[6] Antiviral therapy is continued for weeks to months, until clinical recovery or until serum viral DNA levels decrease.[7] In the case presented here, administration of IV ganciclovir resulted in rapid improvement of the petechial rash within 48 hours.

Cutaneous CMV infection is most commonly diagnosed by biopsy. Characteristic histopathologic findings include dense inclusion bodies within the nucleus or cytoplasm of endothelial cells, with or without surrounding halos.[4] Additionally, immunohistochemical analysis can be performed with antibodies to either CMV or the CMV viral antigen pp65.[4] In a case series of 9 patients, the most common histopathologic findings were vessel dilation and cytoplasmic changes, such as cytomegaly, irregular cellular contours, and bubbly cytoplasm. The characteristic "owl's eye" intranuclear inclusions were uncommon and typically were limited to established infections.[7] For this reason, immunohistochemical analysis can be useful to identify early infections lacking this pathognomonic feature.[7] Polymerase chain reaction for CMV DNA can also be used for diagnosis in patients at increased risk of systemic disease, particularly immunocompromised hosts.

Conflicts of interest

None disclosed.

REFERENCES

1. Gupta M, Shorman M. Cytomegalovirus. In: StatPearls [Internet]. StatPearls Publishing; 2020.
2. About cytomegalovirus and congenital CMV infection. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2020.. Accessed October 9, 2021. https://www.cdc.gov/cmv/overview.html
3. AbdullGaffar B, Raman LG, Al Muala A. Cutaneous cytomegalovirus infection in a patient with acquired immunodeficiency syndrome. *Int J Dermatol*. 2008;47(9):944-946. https://doi.org/10.1111/j.1365-4632.2008.03742.x
4. Drozd B, Andriescu E, Suárez A, De la Garza Bravo MM. Cutaneous cytomegalovirus manifestations, diagnosis, and treatment: a review. *Dermatol Online J*. 2019;25(1):13030/qt84f936cp.
5. Tan HH, Goh CL. Viral infections affecting the skin in organ transplant recipients: epidemiology and current management strategies. *Am J Clin Dermatol*. 2006;7(1):13-29. https://doi.org/10.2165/00128071-200607010-00003
6. Rao S, Cheeley J. Postsurgical skin ulcers caused by cytomegalovirus vasculopathy in a renal transplant recipient. *JAAD Case Rep*. 2020;6(7):643-645. https://doi.org/10.1016/j.jdcr.2020.04.037
7. 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. https://doi.org/10.1111/j.1365-2133.2006.07456.x
8. Tanaka A, Yamashita C, Hinogami H, Shirai H, Matsuura A. Cytomegalovirus-induced vasculopathy and anogenital skin ulcers in a patient with multiple myeloma. *JAAD Case Rep*. 2020;6(1):57-59. https://doi.org/10.1016/j.jdcr.2019.04.017