


A Case of Disseminated Cutaneous Herpes Simplex Virus-1 as the First Manifestation of Human Immunodeficiency Virus Infection

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Abstract

Reported clinical manifestations of active herpes simplex virus type 1 (HSV-1) infection include typically painful vesicular cutaneous rash in a dermatomal distribution, temporal lobe encephalitis, and rarely, fulminant septic shock with multiorgan failure. In immunocompromised patients, the cutaneous rash can become disseminated. We report a case of a 33-year-old male patient with undiagnosed human immunodeficiency virus (HIV) infection who presented to our emergency department (ED) with a disseminated cutaneous rash. The rash was extensive, involved 90% of his total body surface area. It began 5 days prior as small ulcerations localized to the left arm, sought care at an outside ED, diagnosed as severe dermatitis with bacterial superinfection and discharged with a cephalexin prescription. Laboratory results were positive for HIV test with a CD4 count of 254, white blood cell count (WBC) of 7.4 k/microL with 54% neutrophils, 9% lymphocytes, 0% eosinophils, 0% basophils, and serum creatinine and sodium of 3.05 mg/dL and 119 mEq/L, respectively. The burn team and dermatology ruled out Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis due to the absence of mucosal involvement, negative nikolsky sign, and absence of skin sloughing. Polymerase chain reaction of samples obtained from the skin lesions was positive for HSV-1. The rash resolved with intravenous acyclovir and was started on highly active antiretroviral therapy (HAART) on outpatient follow-up. To the best of our knowledge, comparable cases of significantly disseminated cutaneous HSV-1 infection as the initial presentation of HIV infection have been rarely reported.

Keywords

herpes simplex virus, human immunodeficiency virus, disseminated, cutaneous, acyclovir, dermatology

Introduction

Herpes simplex virus type 1 (HSV-1) infection is common among the general population with an estimated prevalence of 47.8% in persons aged 14 to 49 in the United States.¹ The clinical manifestations of an active HSV infection are numerous and depend on several factors, one of the most important being the immune status of the host.² Reported presentations include painful cutaneous rash in a dermatomal distribution, temporal lobe encephalitis, and fulminant septic shock with multiorgan failure.^{2,3} The typical cutaneous rash presents as grouped lesions, each with a diameter of 2 to 4 mm with an underlying erythema.² These evolve into painful vesicles which eventually erode and crust over within an average of 19 days. They commonly involve the face and oral mucosa.^{2,3} However, like those of herpes simplex virus type 2, genital and anal involvement of HSV-1 lesions are becoming more common.² In addition, some patients experience associated systemic symptoms such as headaches, fever, malaise, and myalgias.²

HSV-1 infection may disseminate, resulting in a range of signs and symptoms involving multiple organ systems, culminating in fatal multiorgan failure in the worst-case scenario.⁴⁻⁶ We present a case of a male patient with undiagnosed human immunodeficiency virus (HIV) infection who presented to our institution with a disseminated cutaneous rash involving approximately 90% of his total body surface area.

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Figure 1. Extensive ulcerated cutaneous rash involving the face, torso, and extremities.

Case Presentation

A 33-year-old man with a reported history of sickle cell anemia and a penicillin allergy presented to the emergency department (ED) with an extensive ulcerative rash involving his face, extremities, trunk, genitals, and back with sparing of the mucous membranes, eyes, palms, and feet (Figure 1). The rash initially began 5 days prior to presenting at our hospital as painful, small ulcerations localized to the left arm. The patient originally sought care at an outside ED where he was diagnosed with severe dermatitis with suspected bacterial superinfection, but the patient declined admission and was subsequently discharged with a prescription of cephalexin. The rash progressively worsened and disseminated despite antibiotic treatment, prompting the patient to present to our ED. He denied a history of eczema, asthma, allergic rhinitis, recent exposure to a new environmental allergen, shortness of breath, headaches, and visual disturbances. Cardiovascular, pulmonary, and neurologic examinations were normal.

The patient's social history is remarkable for a monogamous relationship with 1 male partner. He endorsed consistent use of barrier contraception during intercourse. He denied a history of sexually transmitted infections, prior blood transfusions, and intravenous (IV) drug use.

Given the severity of the rash, recent antibiotic exposure, and history of serious penicillin allergy, initial differential diagnoses were drug allergy and a disease on the Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) spectrum. However, the latter was ruled out by the burn team and dermatology (virtually) due to the absence of mucosal

involvement, negative nikolsky sign, and absence of skin sloughing.

Laboratory studies in the ED revealed a reactive HIV antigen/antibody screen with a subsequently positive HIV-1 antibody and negative HIV-2 antibody. In addition, his labs were significant for CD4 count of 259, white blood cell count (WBC) of 7.4 k/microL with 54% neutrophils, 9% lymphocytes, 0% eosinophils, 0% basophils, and creatinine and sodium of 3.05 mg/dL and 119 mEq/L, respectively. These findings suggested an immune deficiency cause rather than an allergic reaction, and dermatology subsequently recommended starting IV acyclovir for possible disseminated HSV-1 infection. Infectious disease (ID) was consulted, and he was admitted for further workup of the skin lesions.

Screening for hepatitis, syphilis, gonorrhea and chlamydia was negative. Further tests for opportunistic infections, including coccidiomycosis antigen/antibody, cryptococcal antigen, tuberculosis, varicella zoster virus (VZV), and cytomegalovirus (CMV) were also negative. In addition, autoimmune disease screening with antinuclear antibodies (ANAs), antineutrophil cytoplasmic antibodies (ANCA), and serum complements were unremarkable. However, HSV polymerase chain reaction (PCR) from the skin lesions was positive for HSV-1 and negative for HSV-2. A positive repeat test further suggested a diagnosis of disseminated HSV-1, and subsequent HSV antibody testing showed elevated IgM. A skin punch biopsy of the left upper extremity revealed irregular psoriasiform hyperplasia with epidermal hypergranulosis, hyperkeratosis, and superficial pigmentary incontinence. There was superficial perivascular inflammation consisting of lymphocytes and histiocytes. No spongiosis and



Figure 2. Significant improvement in the rash with post-inflammatory hypopigmentation after intravenous acyclovir.

intraepidermal vesicles were present. There was no evidence of viral morphologic changes.

The patient was continued on IV acyclovir and emollients with gradual improvement in the lesion throughout the admission (Figure 2). He was discharged with 2 weeks of oral valganciclovir followed by lifelong daily acyclovir prophylaxis. He was scheduled to follow up with ID outpatient for initiation of highly active antiretroviral therapy (HAART).

Discussion

In the context of a positive HSV PCR, elevated HSV IgM, and positive HIV test and the negative tests described above, this patient's generalized rash was more likely secondary to a disseminated cutaneous HSV-1 infection. However, the presence of disseminated HSV infection is quite rare and is largely observed in immunocompromised individuals.⁴ The reasoning behind this may be attributed to the role that the adaptive immune response plays in the course of the infection.³ Although the innate response may help suppress an initial infection, it is the activity of CD8+ and CD4+ T cells that is responsible for the sustained latency of the virus.³ In patients with HIV, reactivation of HSV-1 would not be subdued by these T cells, resulting in extensive sequelae and longer periods of viral shedding due to their inability to control the virus.²

Interestingly, the biopsy findings described above are not typical for those commonly seen with HSV infection.⁷ These include but are not limited to multinucleated cells, Cowdry type A bodies, and margination of chromatin.⁷ However, these findings are not sensitive enough to warrant ruling out the above diagnosis.⁷ In fact, the biopsy findings from our

patient are not specific for any disease process and can be found in a wide variety of skin diseases.⁸ Biopsies showing hyperkeratosis can be seen in diseases such as psoriasis, verrucous keratosis, verrucous lupus erythematosus, and much more.⁸ On the contrary, hypergranulosis can be seen in several other diseases, including psoriasiform keratosis, prurigo nodularis, and acanthoma fissuratum, to name a few.⁸ However, to support the diagnosis of disseminated HSV infection, HSV PCR is favored over other tests including viral culture and is often combined with type-specific serologic testing to differentiate HSV-1 and HSV-2.⁹

In addition to disseminated cutaneous HSV infection, other differential diagnoses for this patient's rash include atopic and contact dermatitis, drug reaction with eosinophilia and systemic symptoms (DRESS), and acute HIV exanthem.¹⁰ The patient could have contacted an unknown sensitized allergen which caused atopic dermatitis with eczema herpeticum as a complication. However, the absence of peripheral eosinophilia, mast cells, and spongiosis on biopsy is atypical of atopic dermatitis.¹⁰ In addition, the generalized nature of the rash makes contact dermatitis less likely. Furthermore, while this patient also presented with acute kidney injury, the absence of fever and peripheral eosinophilia makes DRESS less likely.¹⁰ The acute kidney injury and hyponatremia were outcomes of dehydration due to fluid loss from the extensive cutaneous ulceration. These were resolved with adequate IV fluids and emollients. Finally, the presentation of ulcerated generalized rash is atypical for acute HIV exanthem, as this mostly presents as a maculopapular rash.¹⁰ On the contrary, the absence of these important discriminants could also be attributed to the patient's immunocompromised state.

This patient's presentation is unique in certain regards. Although few cases of disseminated cutaneous HSV in the setting of HIV have been described in the literature,¹¹⁻¹⁴ comparable cases of cutaneous HSV-1 infection involving such an extensive body surface area (as in our patient) have not been reported. In addition, the patient had no visceral involvement. Furthermore, severe disseminated cutaneous HSV-1 as an initial presentation of HIV is uncommon. It also highlights the importance of considering a broad differential when approaching a patient with a disseminated cutaneous rash. Finally, considering the ongoing pandemic and use of virtual learning, this case signifies how virtual learning through rash image recognition could greatly improve patient care and be used in the ED and Internal medicine training curriculum.

Conclusions

Our HIV-positive patient presented with a severely disseminated rash that involved approximately 90% of his total body surface area. Although a broad list of differential diagnoses including SJS/TEN were considered, the positive HSV-1 PCR from samples obtained from the lesions and the

resolution of the rash with IV acyclovir makes HSV-1 the most likely cause. Similar cases of significantly disseminated HSV-1 infection involving such an extensive body surface area have been rarely reported. In addition, due to the rarity of such presentation in immunocompetent patients, it further highlights the importance of assessing for associated immunocompromising diseases and initiation of treatment.

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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References

1. McQuillan G, Kruszon-Moran D, Flagg EW, Paulose-Ram R. Prevalence of herpes simplex virus type 1 and type 2 in persons aged 14-49: United States, 2015-2016. *NCHS Data Brief*. 2018;304:1-8.
2. Fatahzadeh M, Schwartz RA. Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management. *J Am Acad Dermatol*. 2007;57:737-763.
3. Zhang J, Liu H, Wei B. Immune response of T cells during herpes simplex virus type 1 (HSV-1) infection. *J Zhejiang Univ Sci B*. 2017;18:277-288.
4. Fernandez-Nieto D, Jimenez-Cauhe J, Ortega-Quijano D, Burgos-Blasco P, Pindado-Ortega C, Bea-Ardebol S. A case of atypical disseminated herpes simplex virus 1 with hepatitis in a liver transplant recipient: the need for dermatologic evaluation. *Dermatol Online J*. 2020;26:11.
5. Fancher W, Marsch A, Landers J, Scribner J, Landers J, Scribner J. Disseminated Herpes Simplex Virus presenting as crusted papules on the palms and soles of an immunosuppressed patient. *Dermatol Online J*. 2014;20:6.
6. Glas M, Smola S, Pfuhl T, et al. Fatal multiorgan failure associated with disseminated herpes simplex virus-1 infection: a case report. *Case Rep Crit Care*. 2012;2012:359360.
7. Laggis C, Wada D, Shah A, Zussman J. Eosinophils are surprisingly common in biopsy specimens of cutaneous herpes simplex virus and varicella zoster virus infections: results of a comprehensive histopathologic and clinical appraisal. *J Cutan Pathol*. 2020;47:6-11.
8. Fernandez-Flores A. Lesions with an epidermal hyperplastic pattern. *Am J Dermatopathol*. 2016;38:1-19.
9. Strick LB, Wald A. Diagnostics for herpes simplex virus: is PCR the new gold standard. *Mol Diagn Ther*. 2006;10:17-28.
10. DynaMed. Dermatologic diagnosis: approach to the patient. www.dynamed.com/approach-to/dermatologic-diagnosis-approach-to-the-patient. Published 2020, Accessed April 7, 2021.
11. Umar SH, Kanth A. Disseminated cutaneous herpes simplex virus type-1 with interstitial pneumonia as a first presentation of AIDS. *J Natl Med Assoc*. 1999;91:471-474.
12. Maalouf E, Moutran R, Maatouk I. Disseminated primary HSV-2 infection of the face. *Dermatol Online J*. 2012;18:15.
13. Langtry JA, Ostlere LS, Hawkins DA, Staughton RC. The difficulty in diagnosis of cutaneous herpes simplex virus infection in patients with AIDS. *Clin Exp Dermatol*. 1994;19:224-226.
14. Dinotta F, De Pasquale R, Nascia MR, Tedeschi A, Micali G. Disseminated herpes simplex infection in a HIV+ patient. *G Ital Dermatol Venereol*. 2009;144:205-209.