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Disseminated herpes zoster with increased CD4 counts in 3 HIV-infected patients

Pooja Lidhoo, MBBS, Patrick Unemori, MD, Kieron S. Leslie, MBBS, MRCP, and Toby Maurer, MD

Department of Dermatology, University of California San Francisco

Abstract

It has been reported that the diagnosis of multidermatomal herpes zoster in HIV-infected patients occurs at a lower CD4 level than zoster involving a single dermatome. Herein, we describe 3 cases of HIV-infected patients presenting with disseminated zoster at high CD4 counts and low HIV viral loads.

Herpes zoster, the reactivation of latent varicellazoster virus (VZV) infection, occurs commonly in HIV-infected patients and sometimes is the initial clue to the underlying immunodeficiency.^{1,2} An increasing number of atypical presentations have been reported, demonstrating the wide spectrum of VZV-induced skin manifestations. These manifestations include acute herpes zoster, zoster sine herpette, chronic zoster, and disseminated zoster. The clinical polymorphism of herpes zoster reactivation may be dependent on the patient's age, fluctuations in immune status, prior treatment, and VZV gene expression. Increased incidence of zoster has been reported in patients with low CD4 cell counts.^{3,4} Because of their decreased cell-mediated immunity, immunocompromised patients are at an approximately 20-fold increased risk for zoster than age-matched control patients.⁵ Immunocompromised patients may develop several episodes, atypical manifestations, or increased severity of herpes zoster.⁶ Disseminated visceral disease, diffuse cutaneous dissemination, chronic hyperkeratotic skin lesions, acyclovir resistance, bullous ecthymatous zoster, lichenoid reactions, and follicular herpes zoster have been reported in immunocompromised persons.^{7–11} A review of literature suggests that the diagnosis of multidermatomal zoster in HIV-infected patients occurs at a lower CD4 level than zoster involving a single dermatome.^{6,12,13}

We report 3 cases of HIV-infected patients presenting at our institution with disseminated zoster and high CD4 counts.

Correspondence to: Toby Maurer, MD, Department of Dermatology, University of California San Francisco, 1001 Potrero, Bldg 90, Ward 92, Room 215, San Francisco, CA 94110. maurert@derm.ucsf.edu.

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CASE REPORTS

Case 1

A 40-year-old HIV-infected man with a CD4 count of 762 cells/mm³ (500–1500 cells/mm³) and viral load of 10,000 copies/mL presented with a vesicular scalp dermatitis that was concerning for zoster. He was initially treated with acyclovir (800 mg three times a day by mouth) and trimethoprim-sulfamethoxazole for possible superinfection for 4 days. At follow-up, the patient's rash had disseminated to his torso, back, and lower extremities. The patient had intense pain, headache, fever, chills, and nausea, but denied vomiting. History was significant for Giardia, syphilis, depression, hepatitis C, and substance abuse. The patient was antiretroviral therapy (ART) naïve.

A review of systems revealed generalized malaise and headache. Findings from physical examination revealed papulovesicular lesions, denser on scalp and less dense on the trunk and extremities. These were small, 1- to 2-mm papulovesicles on an erythematous base. In addition, several small crusts and erosions were noted on the back of the scalp.

Laboratory findings showed that complete blood cell count, electrolytes, and liver function tests were within normal limits. Sodium was 132 mEq/L (135–145 mEq/L). Direct fluorescent antibody was positive for varicella zoster, with a sample taken from his torso.

Valacyclovir (1000 mg three times a day by mouth) was started and the patient was empirically treated with trimethoprim-sulfamethoxazole for possible methicillin-resistant *Staphylococcus aureus* for 7 days. The hyponatremia was normalized with fluid restriction. Within a week, the patient's initial lesions completely resolved, with some residual crusted lesions on his chest. The patient is currently not on ART.

Case 2

A 56-year-old HIV-infected man on ART (CD4 = 420 cells/mm³, viral load 40 copies/mL) noticed an itchy eruption on his scalp 3 days before admission. At presentation in the emergency department the rash had spread to his face, torso, and limbs. He had fever 1 day before admission and denied any previous experience with this condition.

The patient was given a diagnosis of HIV infection 7 years before presentation and had been on ART for 4 years. His current ART regimen was atazanavir/ritonavir/emtricitabine-tenofovir. He had been given a diagnosis of plasmablastic lymphoma of oral cavity 15 months before admission. He underwent a course of chemotherapy (cyclophosphamide, Adriamycin, vincristine, and prednisone; and methotrexate) and was in complete clinical remission. Treatment was completed 9 months before admission and lymphoma was in remission. History was significant for gastroesophageal reflux disease, depression, and gonorrhea.

A review of systems produced negative results. Findings from physical examination revealed blistering and crusting on right upper lip and vesicles on red bases on face, mouth, torso, and arms. Laboratory findings showed that complete blood cell count, electrolytes,

and liver function tests were within normal limits. Direct fluorescent antibody was positive for varicella zoster, with a sample taken from the vesicles of the upper aspect of the back.

Intravenous acyclovir was initially started, but was switched to oral administration to complete a 7-day course. On follow-up, after a week, the patient showed no recurrence of the rash.

Case 3

A 26-year-old HIV-infected man on ART (CD4 = 540 cells/mm³, viral load 40 copies/mL) was admitted for disseminated VZV with possible periorbital-cellulitis/bacterial superinfection. The patient first noticed a papule on his right eyebrow 4 days before admission that expressed clear fluid in the following days. He also noticed increased redness over the eyebrow spreading to the temporal area. During the morning of admission, the patient noticed papules developing over the body, specifically over his right third digit, back, left thigh, and right arm.

The patient was known to be HIV infected for 3 years and was on ART at presentation, which had been commenced 6 months prior. The ART regimen consisted of fixed-dose emtricitabine/tenofovir/efavirenz (Atripla). History was significant for a previous episode of unidermatomal VZV reactivation affecting the right forearm. At admission, the patient had evidence of abscess of anal and rectal region.

A review of systems showed no eye pain and no visual changes. Findings from physical examination revealed a small vesicle on the right fourth finger; crusted, tender, red induration on right eyebrow with scant clear discharge; tender red swelling over right cheek bone and positive preauricular nodes; scattered papules on erythematous base, vesicular on back, left thigh, and right arm; eyelid edema; and ptosis. Laboratory findings showed that complete blood cell count, electrolytes, and liver function tests were within normal limits. Direct fluorescent antibody was positive for varicella zoster, with a sample taken from the vesicles on right third digit.

Intravenous acyclovir was started and then transitioned to valacyclovir (1000 mg three times a day by mouth). He was also empirically treated with clindamycin to cover periorbital cellulitis. The patient showed marked improvement in 3 days and was discharged on valacyclovir and clindamycin by mouth.

DISCUSSION

We have described the presentation of 3 HIV-infected patients with disseminated herpes zoster. Cutaneous lesions of zoster in HIV-positive adults can be unidermatomal, multidermatomal, disseminated, or chronic and ulcerative.¹⁴ Disseminated lesions are defined as those extending over 3 contiguous dermatomes or with lesions going outside the initial dermatome.¹⁴ These patients are unusual in that their zoster disseminated from a zosteriform patch of lesions in the setting of high CD4 counts (762, 420, and 520 cells/mm³) and low or undetectable viral loads. Furthermore, two of the 3 patients described were on effective ART at the time of their disseminated zoster. It is conceivable that the zoster

outbreak in patient 3 was related to an immune reconstitution phenomenon as noted in other reports,¹⁵ however, this rarely occurs 6 months after initiation of ART¹⁶ as was described in our patient. Disseminated zoster in the setting of high CD4 counts and suppressed viral load raises questions with regard to exhausted immune resources and T-cell dysfunction despite good virologic control. This phenomenon is of interest in our HIV-infected patients, many of whom are aging while on appropriate antiretroviral medication. These 3 patients responded to antiviral medication without systemic sequelae of herpes zoster. The benefit of intravenous acyclovir in this group of HIV-infected patients with good HIV control and disseminated zoster is yet to be studied. Furthermore, the role of zoster vaccine in HIV-infected patients has not been determined but may be of importance in this type of patient. We encourage clinicians to recognize this phenomenon in an effort to further clarify the risk factors for these types of patients.

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