Title

Non-dermatomal varicella-zoster skin infection: disseminated cutaneous herpes zoster without dermatome in an immunosuppressed woman

Authors

Osborn, Lindsay P
Cohen, Philip R

Peer reviewed

Non-dermatomal varicella-zoster skin infection: disseminated cutaneous herpes zoster without dermatome in an immunosuppressed woman

Lindsay P Osborn[1] BA,, Philip R Cohen[2] MD

Affiliations: [1]Medical College of Georgia, Augusta, Georgia, [2]University of California, San Diego, California

Corresponding Author: Lindsay P. Osborn, 1 Seventh Street, Suite 1403, Augusta, GA 30901, Email: osbornlindsay@gmail.com

Abstract

Disseminated herpes zoster is defined as the presence of more than 20 lesions outside the dermatome. This unusual presentation is more common in immunosuppressed patients. Complications such as hepatitis, encephalitis, and pneumonitis are more likely in individuals with disseminated varicella zoster virus infection.

A 63-year-old woman being treated for breast cancer developed multiple pustules and vesicles days after starting doxorubicin and cyclophosphamide chemotherapy. Ten individual lesions appeared on her chest, abdomen, back, and leg. Non-dermatomal disseminated herpes zoster was suspected. She was treated with oral antiviral therapy, as well as with oral and topical antibiotics. Varicella zoster virus infection was confirmed by direct fluorescent antibody staining. After one month, her skin lesions had resolved and she resumed chemotherapy.

In a setting of immunosuppression, the rare presentation of disseminated herpes zoster without dermatome should be considered. Appropriate antiviral therapy should be administered while waiting for confirmation of the diagnosis, so as to reduce the risk of visceral dissemination of the varicella zoster virus infection.

Keywords: cancer, cutaneous, dermatome, disseminated, herpes zoster, immunosuppression, varicella

Introduction

Herpes viral infection in humans includes both herpes simplex (HSV) and herpes zoster. The varicella zoster virus (VZV) is the etiology of both primary varicella and herpes zoster (commonly known as chicken pox and shingles, respectively), with herpes zoster being the re-activated form of the virus. The classical presentation of herpes zoster is a unilateral distribution of vesicles along a single or adjacent dermatome [1]. Disseminated herpes zoster is defined as having more than 20 lesions outside the primary or adjacent dermatome [2].

Although uncommon among all herpes zoster infections, the prevalence of disseminated VZV in a setting of immunosuppression is thought to be anywhere from 10 to 40% [3, 4]. VZV is the most frequent infection seen in allogeneic bone marrow transplant recipients [5]. Immunosuppressed individuals are at risk for complications such as encephalitis, hepatitis, and pneumonitis owing to the possibility of visceral dissemination. Clinical suspicion for disseminated zoster should extend beyond the presence of cutaneous lesions. Abdominal zoster can present with severe abdominal pain up to two weeks prior to the development of skin vesicles [5]. Delayed diagnosis leads to high mortality rates despite antiviral therapy. A woman who recently initiated chemotherapy for breast cancer and subsequently developed disseminated cutaneous herpes zoster without dermatomal skin lesions is described.

Case Synopsis: A 63-year-old woman was diagnosed with left T2N0 breast cancer. Within one month of diagnosis, she began cycle 1 of doxorubicin and cyclophosphamide chemotherapy. Ten days after starting chemotherapy, she developed painful and

Figure 1. *A view of the back of a 63-year-old woman who developed widespread pustules within ten days after starting chemotherapy for treatment of breast cancer. Lesions are seen bilaterally and across multiple dermatomes. Closer inspection revealed individual pustules on an erythematous base. The lesions were painful and pruritic.*

Figure 2. *The chest and abdomen also show widespread skin lesions without any dermatomal pattern.*

pruritic lesions on her chest, abdomen, back, and right leg; neither central nervous system, hepatic, nor pulmonary symptoms were present. When she presented to her oncologist, her chemotherapy was discontinued and she was referred to a dermatologist for evaluation and treatment.

Cutaneous examination revealed lesions that were distributed across the patient's body without any dermatomal pattern. The widespread individual pustules with surrounding erythema were located on her chest, abdomen, and back (**Figures 1, 2**). She also

had large erosions on her right knee and posterior right leg (**Figures 3, 4**).

Because the patient had a history of chicken pox as a child, the possibility of primary varicella was ruled out. The differential diagnosis included disseminated herpes simplex and disseminated herpes zoster. A direct fluorescent antibody (DFA) staining was performed on the material obtained after removing the roof of a blister and scraping its base with a #15 blade. Results from DFA were positive for herpes zoster virus and negative for herpes simplex virus, thus confirming a diagnosis of disseminated cutaneous herpes zoster virus infection.

Figure 3. *A view of several large pustules noted on the patient's right posterior thigh.*

Figure 4. *View of additional pustules on the patient's right knee of disseminated cutaneous herpes zoster without dermatomal skin lesions.*

Table 1. *Antiviral therapy dosages for primary episode of herpes zoster versus herpes simplex [9, 10].*

Therapy	Dosing for herpes zoster [10]	Dosing for herpes simplex [9]
Oral acyclovir	800 mg PO 5x/day for 7-10 days	200 mg PO 5x/day for 10 days
Valacyclovir	1 g PO q8h for 7 days	500 mg PO q12h for 10 days
Acyclovir IV	10 mg/kg q8h IV	5 mg/kg q8h IV for 10 days

Abbreviations: h: hour; kg: kilogram; mg: milligram; PO: by mouth; q: every

Therapeutic intervention was initiated: a ten-day course of oral valacyclovir (one gram three times daily) and cefdinir (300 mg orally twice daily) to treat possible bacterial impetiginization of the lesions. Topical treatment of her lesions included dilute vinegar soaks (one part white vinegar and four parts water) twice a day followed by application of mupirocin 2% ointment. At follow-up examination by the dermatologist one week later, the patient was clinically improved. There were no new vesicles or pustules and her existing lesions were crusted and no longer painful.

The patient completed the ten-day courses of valacyclovir and cefdinir; she continued the vinegar soaks until her oncology appointment two weeks later. Her oncologist noted that all of her lesions were nearly resolved and none of them were painful. Given the successful management of the varicella zoster virus infection, she was able to begin her second cycle of chemotherapy.

Case Discussion

Herpes zoster, commonly known as shingles, is the re-activated form of the varicella zoster virus. It is most prevalent in people over the age of 50 with the lifetime risk of herpes zoster shown to be 20% [6]. The classic clinical presentation of herpes zoster is several days of severe pain within the affected dermatome, followed by an eruption of unilateral dermatomal skin lesions. This characteristic presentation of the infection often allows for a diagnosis to be made solely on a clinical basis.

However, in patients who develop cutaneous disseminated herpes zoster infection without dermatomal skin lesions, the diagnosis is not as readily apparent. Dissemination of VZV infection occurs primarily in immunocompromised individuals and is defined as having greater than 20 lesions outside the primary or adjacent dermatomes. Rarely, as in our patient, disseminated cutaneous herpes zoster can occur with an absence of skin lesions in a dermatome.

A Tzanck smear is a quick, inexpensive way to confirm a herpes infection, but it cannot distinguish between herpes simplex and herpes zoster. However, it can easily be performed in the office or at the bedside to allow for rapid initiation of antiviral therapy. A scraping to obtain epidermal cells from the base or underside of the roof of one of the blisters will show the multinucleated giant cells characteristic of herpes viral infection. The Tzanck smear is positive in 75% of VZV cases [7, 8].

When the possibility of herpes simplex and herpes zoster are both in the clinical differential diagnosis, direct fluorescent antibody (DFA) or polymerase chain reaction (PCR) can be conducted for confirmation. DFA is performed by scraping the base of the lesion with a #15 blade without causing bleeding. The obtained material on the tip of the blade is applied to the glass microscope slides to be submitted for testing. A negative DFA cannot rule out herpes zoster owing to its low sensitivity and additional testing is necessary. PCR has significantly higher sensitivity than DFA, but a positive result for either test is diagnostically definitive [9].

Prompt treatment is required if disseminated herpes zoster infection is suspected, particularly in the setting of immunosuppression. Progression from cutaneous dissemination to visceral involvement of the brain, lungs, or liver can be seen in up to 10% of immunocompromised individuals [5]. Because the antiviral dosage for treating herpes zoster is at least twice that of herpes simplex, conservative treatment

with a higher antiviral dose is recommended prior to diagnostic confirmation of herpes zoster or herpes simplex (**Table 1**), [10, 11]. In a hospital setting, intravenous acyclovir is shown to shorten the course of cutaneous VZV, as well as to reduce the risk of visceral dissemination [1, 12].

Historically, acyclovir has been the drug of choice for herpes zoster therapy, but valacylovir has become more commonly used owing to its increased bioavailiability, and thus its greater effectiveness in preventing new lesions and reducing time to healing for existing lesions [10, 13]. Additionally, valacyclovir has been shown to be effective in reducing the duration of postherpetic neuralgia [14]. Antiviral therapy is most effective if initiated within 72 hours of viral onset, underlining the need for rapid diagnosis and treatment of suspected disseminated herpes zoster [15].

The progression of the herpes zoster virus skin lesions from erythematous macules and papules to vesicles to crusts occurs in about two weeks. Postherpetic neuralgia (PHN) is the most common residual symptom following infection of herpes zoster and immunocompromised individuals are thought to be at greater risk for developing PHN [16]. Rates of herpes zoster recurrence in immunocompromised patients eight years after the initial episode are as high as 12% [17]. In our patient, disseminated herpes virus infection was suspected after examination of her cutaneous lesions; antiviral therapy (empirically treated with valacyclovir at a dose appropriate for herpes zoster virus infection) was promptly initiated, allowing for rapid resolution of her lesions without development of PHN.

Conclusion

Our patient exhibited painful pustular lesions without any dermatomal pattern. Her chemotherapy-induced immunosuppression made disseminated herpes virus infection a likely possibility. The differential diagnosis included cutaneous lesions of either disseminated herpes simplex or disseminated herpes zoster (without dermatome skin lesions). She was promptly started on oral valacyclovir as antiviral therapy and the diagnosis of herpes zoster was confirmed by a positive DFA. Her lesions resolved within a few weeks and she had no residual pain

following the infection. Disseminated herpes zoster should be included in the differential diagnosis if there are multiple vesicles and pustules, even in the absence of dermatomal skin lesions, in a setting of immunosuppression. Consideration of disseminated herpes zoster allows for prompt treatment, thereby reducing the risk of serious complications related to visceral dissemination, as well as improving the prognosis for the patient.

References

1. Arvin AM. Varicella-zoster virus. *Clin Microbiol Rev* 1996;9:361-381. [PMID: 8809466].
2. Ellis DL, Barsell A, Riahi RR, Stumpf B. Varicella zoster virus encephalitis in a patient with disseminated herpes zoster: report and review of the literature. *Dermatol Online J* 2015;21(3):16. [PMID: 25780972].
3. Gomez E, Chernev I. Disseminated cutaneous herpes zoster in an immunocompetent elderly patient. *Infect Dis Rep* 2014;6:5513. [PMID: 25276332].
4. Weber DM, Pellecchia JA. Varicella pneumonia: a study of prevalence in adult men. *JAMA* 1965;192:572-573. [PMID: 14284857].
5. Gnann JJW. Varicella-zoster virus: atypical presentations and unusual complications. *J Infect Dis* 2002;186 Suppl 1:S91-8. [PMID: 12353193].
6. McCrary ML, Severson J, Tyring SK. Varicella zoster virus. *J Am Acad Dermatol* 1999;41:1-14. [PMID: 10411403].
7. Nahass GT, Goldstein BA, Zhu WY, Serfling U, Penneys NS, Leonardi CL. Comparison of Tzanck smear, viral culture, and DNA diagnostic methods in detection of herpes simplex and varicella-zoster infection. *JAMA* 1992;268:2541-2544. [PMID: 1328700].
8. Cohen PR. Tests for detecting herpes simplex virus and varicella-zoster virus infections. *Dermatol Clin* 1994;12;51-68. [PMID: 8143385].
9. Binkhamis K, Al-Siyabi T, Heinstein C, Hatchette TF, LeBlanc JJ. Molecular detection of varicella zoster virus while keeping an eye on the budget. *J Virol Methods* 2014;202:24-27. [PMID: 24607430].
10. Sauerbrei A. Optimal management of genital herpes: current perspectives. *Infect Drug Resist* 2016;9:129-141. [PMID: 27358569].
11. Beutner KR. Valacyclovir: a review of its antiviral activity, pharmacokinetic properties, and clinical efficacy. *Antiviral Res* 1995;28:281-90. [PMID: 8669888].
12. Gershon AA, Gershon MD. Pathogenesis and current approaches to control of varicella-zoster virus infections. *Clinical Microbiol Rev* 2013;26:728-43. [PMID: 24092852].
13. Tyring SK, Plunkett S, Scribner AR, Broker RE, Herrod JN, Handke LT, et al. Valomaciclovir versus valacyclovir for the treatment of acute herpes zoster in immunocompetent adults: a randomized, double-blind, active-controlled trial. *J Med Virol* 2012;84:1224-32. [PMID: 22711350].
14. Chakrabarty A, Anderson NJ, Beutner R, Tyring SK. Valacyclovir for the management of herpes viral infections. *Skin Therapy Lett* 2005;10:1-4. [PMID: 15776202].
15. Bader MS. Herpes zoster: diagnostic, therapeutic, and preventive approaches. *Postgrad Med* 2013;125:78-91 [PMID: 24113666].
16. Forbes HJ, Thomas SL, Smeeth L, Clayton T, Farmer R, Bhaskaran K, et al. A systematic review and meta-analysis of risk factors for postherpetic neuralgia. *Pain* 2016;157:30-54. [PMID: 26218719].
17. Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. Herpes zoster recurrences more frequent than previously reported. *Mayo Clin Proc* 2011;86:88-93. [PMID: 21220354].