IDCases 28 (2022) e01502

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Herpes vegetans on the shoulder mimicking nonmelanoma skin cancer

Bao Vincent K. Ho[a,b,*], Neha K. Puar[a], Edward W. Seger[a], Anand Rajpara[a]

[a] Division of Dermatology, University of Kansas Medical Center, Kansas City, KS, USA
[b] School of Medicine, University of Kansas Medical Center, Kansas City, KS, USA

ARTICLE INFO

Article history:
Received 5 April 2022
Received in revised form 7 April 2022
Accepted 8 April 2022

Keywords:
Herpes simplex virus (HSV)
Herpes vegetans
Dermatology
Infectious Disease
Nonmelanoma skin cancer (NMSC)

ABSTRACT

Atypical morphologic and anatomic presentations of herpetic infection can be a diagnostic and therapeutic challenge. Although herpes simplex virus type 2 (HSV-2) infections primarily occur in the oral or anogenital region, our patient presented with ulcerated vegetative plaques on the shoulder sharing clinical features with nonmelanoma skin cancer (NMSC). Depending on the clinical appearance and anatomical site, proper workup including biopsy can be pivotal to arrive at a correct diagnosis as lesions can mimic a broad spectrum of cutaneous diseases, particularly if the lesion occurs in an atypical location. Dermatology providers should include HSV-2 in the differential diagnosis when challenged with unusual ulcerated or verrucous lesions.

Introduction

Herpes vegetans is a rare variant of cutaneous herpes simplex virus (HSV), more commonly caused by HSV-2 than HSV-1 that primarily affects immunocompromised patients predominantly in mucocutaneous transition zone areas, such as the oral or anogenital region [1,2]. Immunosuppressed patients with herpes virus infection can have an atypical cutaneous manifestation and present a diagnostic and therapeutic challenge. Clinically, lesions appear as vegetating hyperkeratotic, verrucous, eroded, or ulcerated plaques and nodules that can mimic malignancy [1–4]. The published case reports of atypical herpes vegetans infection have been reported to occur on hand, genitalia, oral mucosa, and eyelid [5–7]. We report a case of herpes vegetans in a patient with metastatic renal cancer on chronic immunosuppression presenting as ulcerated vegetative plaques on the shoulder.

Case report

A 65-year-old male presented with asymptomatic lesions on the right posterior shoulder during a hospital stay for a critical pain crisis related to his advanced malignancy. The patient's medical history was notable for type 2 diabetes mellitus, chronic kidney disease, metastatic renal cell carcinoma on cabozantinib plus nivolumab combination therapy, and medication-induced pneumonitis on chronic oral steroid use with trimethoprim/sulfamethoxazole prophylaxis. Dermatology was consulted for the evaluation of two painless well-demarcated, purulent vegetative plaques with central brown/black eschar and surrounding erythema, 1–2 cm in diameter, located on the right posterior (Fig. 1). The lesions developed several months before and were slowly enlarging, which raised the concern for nonmelanoma skin cancer (NMSC). The patient denied fever, chills, night sweats, or having had any oral or genital lesions in the past.

The remainder of the physical exam revealed small uniform asymptomatic inflammatory papules on the chest, back and shoulders, likely related to the patient's long-term prednisone use. Laboratory testing prior to dermatology consultation revealed mild hyponatremia (131 mmol/L), but no other major hematologic or electrolyte abnormalities. A comprehensive metabolic panel revealed mildly elevated aspartate aminotransferase (51 U/L), elevated alkaline phosphatase (490 U/L), and a mild elevation in serum creatinine concentration of 1.28 mg/dL (baseline 1.20 mg/dL) and serum glucose (165 mg/dL). Human immunodeficiency virus (HIV) testing was not obtained during the hospital course.

A punch biopsy was performed and showed epithelial hyperplasia, ulceration, eosinophilic intranuclear inclusions and focal multinucleated keratinocytes surrounded by a dense inflammatory infiltrate (Fig. 2A and B) with no evidence of malignancy. Immunoperoxidase stain was strongly positive for HSV 1 and 2 (Fig. 3). Tissue cultures for aerobic/anaerobic and acid-fast bacteria, and fungal etiologies were unremarkable. Superficial swabs were

Abbreviations: NMSC, nonmelanoma skin cancer; HSV, herpes simplex virus; HIV, human immunodeficiency virus; VZV, varicella zoster virus; PCR, polymerase-chain reaction

* Correspondence to: 3901 Rainbow Blvd, Kansas City, KS 66160, USA.
E-mail address: b425h553@kumc.edu (B.V.K. Ho).

https://doi.org/10.1016/j.idcr.2022.e01502
2214-2509/

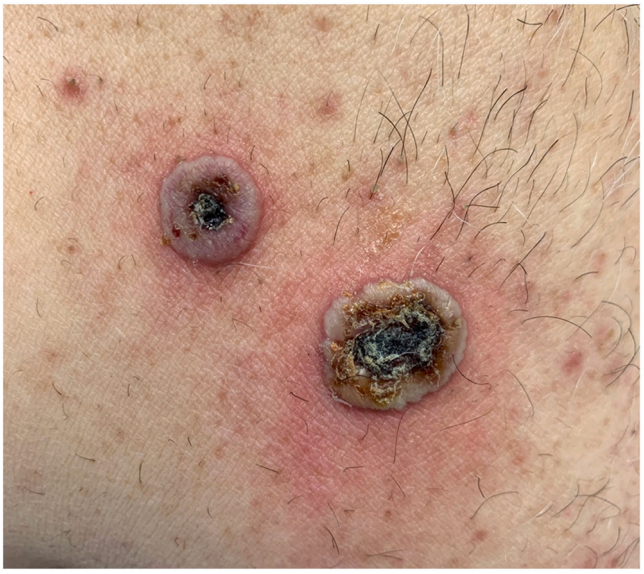

Fig. 1. Well-demarcated, purulent vegetative plaques with central brown/black eschar and surrounding erythema, 1–2 cm in diameter, located on the right posterior shoulder.

positive for HSV-2 and negative for varicella zoster virus (VZV) on polymerase-chain reaction (PCR). Given the clinicopathologic findings, herpes vegetans was diagnosed.

The patient was started on intravenous acyclovir 10 mg/kg, given every 8 h, but then developed an acute kidney injury given the abrupt rise in serum creatinine (1.5 mg/dL) shortly thereafter. Intravenous fluid resuscitation and maintenance therapy was administered with adequate improvement in kidney function. The treatment was then transitioned to oral valacyclovir 1 g, given three times daily for 14 days. After discussion with palliative care and medicine providers, the patient ultimately decided to be discharged with home hospice care. Upon remote follow-up after completing the antiviral therapy, the patient reported improvement in the size of the lesions but denied complete resolution with valacyclovir. Further treatment was deferred after discussion regarding his goals of care given his advanced malignancy.

Discussion

Herpes vegetans is a rare presentation of HSV-2 that primarily affects the anogenital region in patients with immunosuppressive conditions, including those with HIV, organ transplants, congenital immunodeficiency disorders, and malignant neoplasms [1–4,6,8].

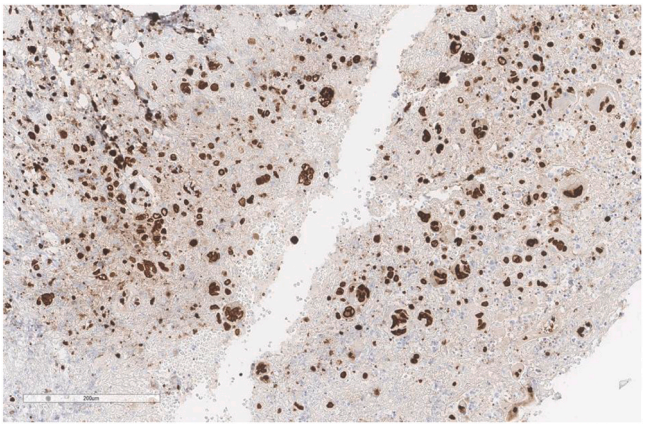

Fig. 3. Immunohistochemical analysis demonstrates strong positivity of a polyclonal antibody against herpes simplex virus 1 and 2. Immunoperoxidase stain; Original magnification: x200.

Atypical presentations of HSV-2 infection can manifest as generalized papular eruptions, hyperkeratotic verrucous lesions, eroded vegetating plaques, or as persistent and extensive ulcerations [1–4]. To our knowledge, this is the first reported case of herpes vegetans presenting as ulcerated vegetative plaques on the shoulder.

Depending on the clinical appearance and anatomical site, proper workup including biopsy can be pivotal to arrive at a correct diagnosis as lesions can mimic a broad spectrum of cutaneous diseases, particularly if the lesion occurs in an atypical location. In our case, a skin biopsy and tissue culture were performed to distinguish it from a deep bacterial or fungal infection and NMSC. Other differential diagnoses of herpes vegetans can consist of condyloma acuminata, pyogenic granuloma, pyoderma vegetans, and malignancy [1,3].

Histopathological features typical of herpes infection include multinucleated keratinocytes containing molded nuclei surrounding ulcers, eosinophilic intranuclear viral inclusions, often with extensive necrosis and inflammatory infiltrate consisting of lymphocytes, histiocytes, plasma cells and eosinophils [1]. Immunostaining for HSV is used to confirm the diagnosis in junction with PCR analysis to enhance the sensitivity HSV-2 detection and differentiation from other viral etiologies, such as HSV-1 and VZV.

HSV-2 infection in immune-competent patients can also present differently from the characteristic grouped vesicular presentation typically seen in the general population and may be an initial sign of previously undiagnosed HIV infection. Therefore, prompt identification and treatment are necessary to mitigate risk of HIV acquisition or transmission in individuals with HSV-2 infection [9]. Although acyclovir is the first-line therapeutic agent for herpetic

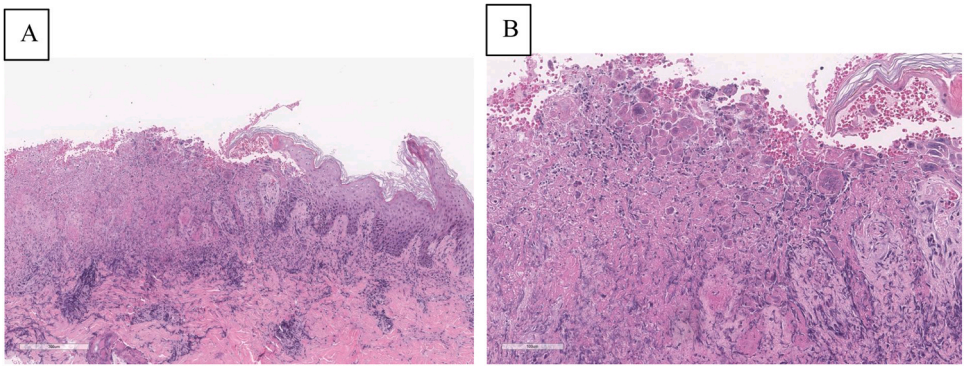

Fig. 2. Punch biopsy obtained from the periphery of the lesion shows epithelial hyperplasia, ulceration, eosinophilic intranuclear inclusions, and multinucleated keratinocytes surrounded by a dense inflammatory infiltrate, typical of herpes simplex virus. (H&E); Original magnifications: A, x40; B, x200.

infections, valacyclovir has been proposed as an effective alternative in cutaneous herpes vegetans infections because of its higher bioavailability [2].

Drug resistance to acyclovir is not uncommon with HSV-2 infection and may contribute to atypical presentations with more frequent and severe recurrences. Prophylactic acyclovir may not be sufficient for HSV suppression in the setting of immunodeficiency and treatment is often prolonged until clearance of all lesions. Other treatment modalities include intravenous or intralesional cidofovir, foscarnet, and topical imiquimod [10]. Surgical excision may be considered for refractory lesions; however, new lesions may still develop at adjacent sites even when used in combination with oral or topical antiviral therapy [1–3].

Atypical morphologic and anatomic presentations of herpetic infection can be a diagnostic and therapeutic challenge. Although HSV-2 infections primarily occur in the oral or anogenital region, our patient presented with ulcerated vegetative plaques on the shoulder sharing clinical features with NMSC. Dermatology providers should include HSV-2 in the differential diagnosis when challenged with unusual ulcerated or verrucous lesions. Biopsy and other diagnostic methods should be considered to aid in diagnosis as lesions can mimic a broad spectrum of cutaneous diseases.

CRediT authorship contribution statement

Bao Vincent Ho: Writing – original draft, Writing – review & editing. **Neha Puar**: Visualization, Investigation, Writing – review & editing. **Edward Seger**: Supervision, Writing – review & editing. **Anand Rajpara**: Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

Acknowledgements

The authors would like to thank Hongyan Dai, MD, PhD, a dermatopathologist in the Department of Pathology and Laboratory Medicine at the University of Kansas Medical Center, for providing the dermatopathology images.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author statement

All authors discussed the results and contributed to the final manuscript.

Funding

This article has no funding source.

References

[1] Beasley KL, Cooley GE, Kao GF, Lowitt MH, Burnett JW, Aurelian L. Herpes simplex vegetans: atypical genital herpes infection in a patient with common variable immunodeficiency. J Am Acad Dermatol 1997;37(5 Pt 2):860–3. https://doi.org/10.1016/s0190-9622(97)80012-6

[2] Simonsen M, Nahas SC, Silva Filho EV, Araújo SE, Kiss DR, Nahas CS. Atypical perianal herpes simplex infection in HIV-positive patients. Clinics 2008;63(1):143–6. https://doi.org/10.1590/s1807-59322008000100024

[3] Rashid A, Nanjappa S, Dessureault S, Messina JL, Greene JN. Herpes vegetans and review of verrucous lesions of the anogenital region. Infect Dis Clin Pract 2017;25:294–300. https://doi.org/10.1097/IPC.0000000000000537

[4] 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(3):224–6. https://doi.org/10.1111/j.1365-2230.1994.tb01171.x

[5] Gross G, Doerr HW. Atypical herpes simplex virus type 2 manifestations on the hand. Hautarzt 2001;52(9):807–11. https://doi.org/10.1007/s001050170071

[6] Koushk-Jalali B, Oellig F, Wieland U, Kreuter A. Herpes simplex vegetans in a patient with primary myelofibrosis. Infection 2019;47(5):877–8. https://doi.org/10.1007/s15010-019-01329-y

[7] Blieden LS, Chévez-Barrios P, Yen MT. Herpes simplex vegetans presenting as an eyelid mass. Ophthalmic Plast Reconstr Surg 2011;27(3):e58–9. https://doi.org/10.1097/IOP.0b013e3181e97922

[8] Boix-Vilanova J, Montis MC, Giacaman A, Corral-Magaña O, Bauza A. Herpes vegetans in a human immunodeficiency virus-negative kidney transplant patient. Clin Exp Dermatol 2019;44(1):92–4. https://doi.org/10.1111/ced.13748

[9] Looker KJ, Welton NJ, Sabin KM, et al. Global and regional estimates of the contribution of herpes simplex virus type 2 infection to HIV incidence: a population attributable fraction analysis using published epidemiological data. Lancet Infect Dis 2020;20(2):240–9. https://doi.org/10.1016/S1473-3099(19)30470-0

[10] Lolis MS, González L, Cohen PJ, Schwartz RA. Drug-resistant herpes simplex virus in HIV infected patients. Acta Derm Croat 2008;16(4):204–8.