Reichl A, Yao M, Spiker M. Hemorrhagic Herpes Zoster as a Harbinger of Malignant Transformation.
Brown Hospital Medicine. 2023;2(4). doi:10.56305/001c.87786

Images in Hospital Medicine

Hemorrhagic Herpes Zoster as a Harbinger of Malignant Transformation

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Journal of Brown Hospital Medicine
Vol. 2, Issue 4, 2023

Article Information

Keywords: hepes zoster, varicella, infectious disease, hematology, transformation

https://doi.org/10.56305/001c.87786

Submitted: August 04, 2023 EDT

Accepted: September 05, 2023 EDT

Abstract

A 61 year old male with a history of B-cell lymphoma presented with hemorrhagic vesicles and bullae in the C8-T2 distribution. He was diagnosed with disseminated hemorrhagic varicella zoster. Given persistent thrombocytopenia, a bone marrow biopsy was performed that revealed transformation to acute myeloid leukemia. Hemorrhagic herpes zoster may be a marker of occult cancer, especially hematologic malignancies.

A 61-year-old man presented to the emergency department with a week of hemorrhagic bullae involving his right chest, arm and back (Figure 1a-c) associated with "shock-like" pain. Medical history was notable for small B-cell lymphoma and subsequent therapy-related myelodysplastic syndrome (t-MDS), last receiving decitabine-cedazuridine 4 months prior to presentation. His exam demonstrated innumerable hemorrhagic vesicles and bullae on an erythematous base in the C8-T2 distribution. Scattered hemorrhagic vesicles were appreciated throughout the face, head, torso, and lower extremities. Upon presentation, he was febrile to 102.8 degrees Fahrenheit and tachycardic to 131 beats per minute. Home medications included atorvastatin, metoprolol tartrate, and triamcinolone cream.

Initial labs were pertinent for a hemoglobin of 9,000/mm^3 and platelets of 3,000/mm^3. Creatinine was 1.26 mg/dL (baseline ~0.8 mg/dL). An urgent peripheral smear did not demonstrate schistocytes or blasts. Coagulation studies, liver enzymes, bilirubin, and haptoglobin were normal. Highest concern was for disseminated hemorrhagic varicella zoster virus (VZV) and he was started on intravenous acyclovir. Vesicular fluid returned positive for VZV DNA and negative for herpes simplex virus. Serum polymerase chain reaction demonstrated VZV viremia (313,000 copies/mL).

After two weeks of intravenous acyclovir, the patient was transitioned to oral valacyclovir with significant improvement in his lesions. Given his persistent and severe thrombocytopenia (< 10,000/m^3) requiring daily platelet transfusions, a bone marrow biopsy was obtained demonstrating transformation to acute myeloid leukemia (AML). The patient underwent induction chemotherapy with azacitadine and venetoclax.

Primary infection with VZV typically results in uncomplicated varicella (chickenpox), allowing the virus to seed sensory ganglia and establish lifelong latency. Herpes zoster (HZ) is caused by reactivation of latent VZV along a sensory nerve within the dermatome.[1] There are more than 1 million cases of HZ in the United States yearly, and immunocompromised persons are at increased risk for disseminated disease involving noncontiguous dermatomes or extracutaneous sites.[1,2] Hemorrhagic HZ (HHZ) is a rare presentation and is typically described in the setting of immunosuppression, severe thrombocytopenia (<10,000/m^3), or anticoagulation.[3] Typically, burning in the affected dermatome precedes cutaneous eruptions by roughly two days.[2] The diagnosis is mainly clinical, but VZV PCR can provide clarity in patients with unusual presentations.[1,2] The standard therapy for HZ is acyclovir and its prodrug valacyclovir, which are processed to nucleoside analogues that block DNA replication in affected cells.[2] Intravenous acyclovir is reserved for immunocompromised patients with severe HZ.

A recent meta-analysis suggested that HZ may be a marker of occult cancer, including hematologic malignancies. The reported pooled relative risk for hematologic malignancy within 1 year of herpes zoster infection was 2.26 (95% CI 1.58, 3.22).[4] It is not the standard of care to screen for underlying immunologic phenomena in otherwise healthy patients with HZ. For patients presenting with HHZ, obtaining a complete blood count, and considering disorders of the immune system is prudent given the association with severe thrombocytopenia and the possibility for an underlying hematologic disorder.[3] Given our patient had known t-MDS with elevated risk of transformation to AML, obtaining a bone marrow biopsy proved to be diagnostically useful.

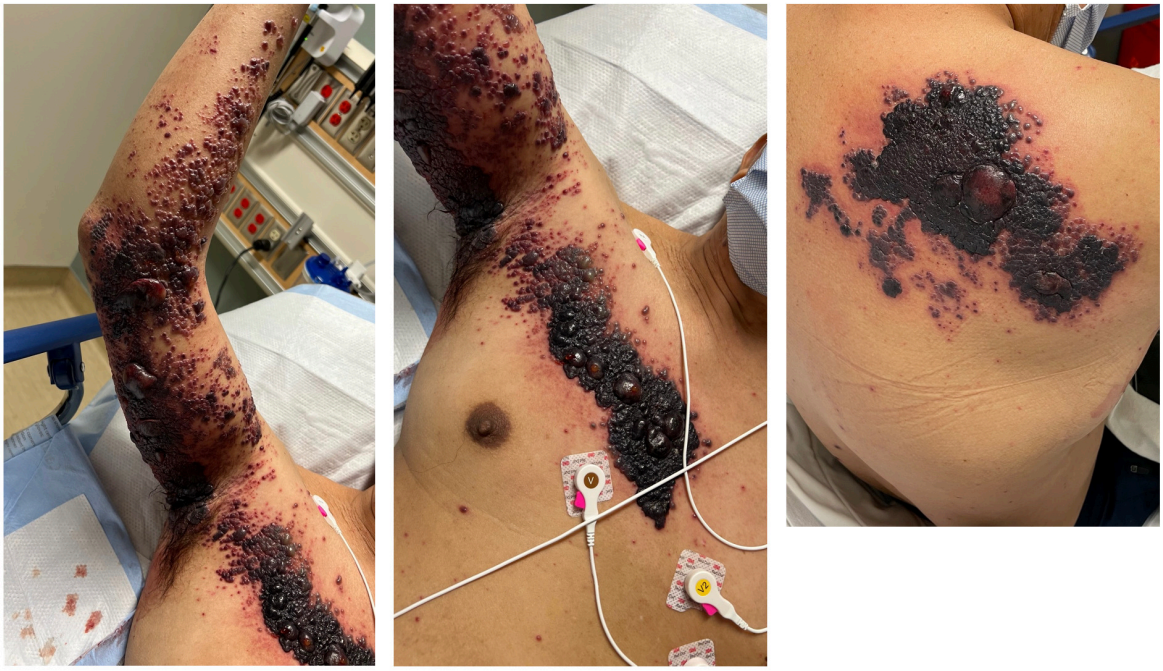

Figure 1. Rash comprised of hemorrhagic vesicles and bullae on the patient's right (a) arm (b) chest and (c) upper back

Author Contributions

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures/Conflicts of Interest

The authors declare they have no conflicts of interest

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