ONLINE EXCLUSIVE

Persistent rash on the sole

The patient's immune status offered a clue to the diagnosis

Joel Hua-Liang Lim, MBBS, MRCP, MMed; Stephanie Sutjipto, MBBS, MRCP, MMed; Lucinda Siyun Tan, MBBS, MRCP, MMed
National Skin Centre, Singapore (Drs. Lim and Tan); Tan Tock Seng Hospital, Singapore (Dr. Sutjipto)

joellimhl@nsc.com.sg

DEPARTMENT EDITOR
Richard P. Usatine, MD
University of Texas Health at San Antonio

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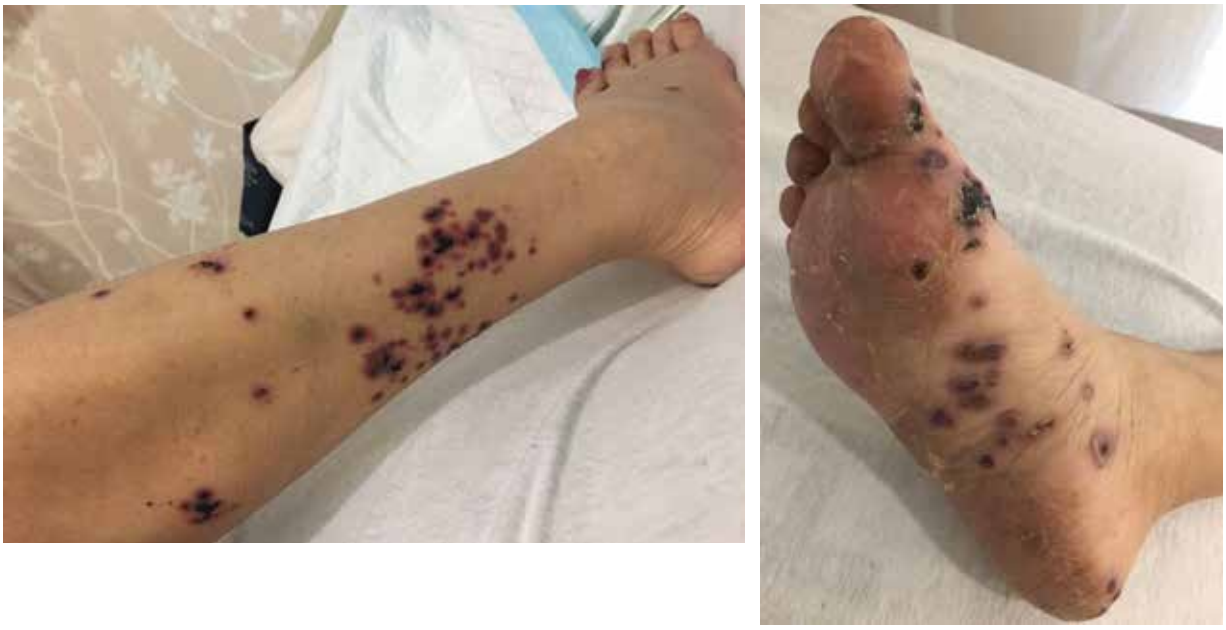
A 52-YEAR-OLD CHINESE WOMAN presented to a tertiary hospital in Singapore with a 3-month history of persistent and intermittently painful rashes over her right calf and foot (FIGURE). The patient had pancytopenia due to ongoing chemotherapy for metastatic nasopharyngeal carcinoma. She was systemically well and denied other dermatoses. Examination demonstrated scattered crops of tense hemorrhagic vesicles, each surrounded by a livid purpuric base, over the right plantar aspect of the foot, with areas of eschar over the right medial hallux. No allodynia, hyperaesthesia, or lymphadenopathy was noted.

A punch biopsy of an intact vesicle was performed.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE
Hemorrhagic vesicles over the right lateral calf and sole



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Diagnosis:

Herpes zoster

Histopathologic examination showed full-thickness epidermal necrosis with ballooning degeneration resulting in an intra-epidermal blister. Multinucleated keratinocytes with nuclear moulding were seen within the blister cavity. Grocott-Gomori methenamine-silver (GMS), acid-fast, and Gram stains were negative. Granular immunoglobulin (Ig) G, IgM, and C3 were seen intramurally. DNA analysis of vesicular fluid was positive for varicella zoster virus (VZV). A diagnosis of herpes zoster (HZ) of the right S1 dermatome with primary obliterative vasculitis was established.

Immunocompromised people—those who have impaired T-cell immunity (eg, recipients of organ or hematopoietic stem-cell transplants), take immunosuppressive therapy, or have lymphoma, leukemia, or human immunodeficiency virus (HIV) infection—have an increased risk for HZ. For example, in patients with acquired immunodeficiency syndrome (AIDS), HZ uniquely manifests as recurrent shingles. An estimated 20% to 30% of HIV-infected patients will have more than 1 episode of HZ, which may involve the same or different dermatomes.[1,2] Furthermore, HZ in this population is more commonly associated with atypical presentations.[3]

It's been proposed that in atypical presentations, the reactivated VZV spreads from adjacent nerves to the outermost layer of the arterial wall, giving lesions a vasculitic appearance.

What an atypical presentation may look like

In immunocompromised patients, HZ may present with atypical cutaneous manifestations or with atypical generalized symptoms.

Atypical cutaneous manifestations, as in disseminated zoster, manifest with multiple hyperkeratotic papules (3-20 mm in diameter) that follow no dermatomal pattern. These lesions may be chronic, persisting for months or years, and may be associated with acyclovir-resistant strains of VZV.[2,3] Another dermatologic variant is ecthymatous VZV, which manifests with multiple large (10-30 mm) punched-out ulcerations with a central black eschar and a peripheral rim of vesicles.[4] Viral folliculitis—in which infection is limited to the hair follicle, with no associated blisters—has also been reported in atypical HZ.[5]

Our patient presented with hemorrhagic vesicles mimicking vasculitic lesions, which had persisted over a 3-month period with intermittent localized pain. It has been proposed that in atypical presentations, the reactivated VZV spreads transaxonally from adjacent nerves to the outermost adventitial layer of the arterial wall, leading to a vasculitic appearance of the vesicles.[6] Viral-induced vasculitis may also result either directly from infection of the blood vessels or secondary to vascular damage from an inflammatory immune complex–mediated reaction, cell-mediated hypersensitivity, or inflammation due to immune dysregulation.[7,8]

Differential includes vesiculobullous conditions

There are several important items to consider in the differential.

Cutaneous vasculitis, in severe cases, may manifest with vesicles or bullae that resemble the lesions seen in HZ. However, its unilateral nature and distribution distinguish it.

Angioinvasive fungal infections in immunocompromised patients may manifest with scattered ulceronecrotic lesions to purpuric vesiculobullous dermatoses.[9] However, no fungal organisms were seen on GMS staining of the biopsied tissue.

Atypical hand-foot-and-mouth disease tends to affect adults and is associated with Coxsackievirus A6 infection.[10] It may manifest as generalized vesiculobullous exanthem resembling varicella. The chronic nature and restricted extent of the patient's rash made this diagnosis unlikely.

Successful management depends on timely identification

Although most cases of HZ can be diagnosed clinically, atypical rashes may require a biopsy and direct immunofluorescence assay for VZV antigen or a polymerase-chain-reaction (PCR) assay for VZV DNA in cells from the base of blisters. Therefore, it is important to consider the diagnosis of HZ in immunocompromised patients presenting with an atypical rash to avoid misdiagnosis and costly testing.

Our patient was treated with oral acyclovir 800 mg 5 times/day for 10 days, with prompt resolution of her rash. JFP

CORRESPONDENCE
Joel Hua-Liang Lim, MBBS, MRCP, MMed, 1 Mandalay Road, Singapore 308205; joellimhl@nsc.com.sg

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