Disseminated varicella zoster virus presenting as large eschar in immunocompromised patient

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Introduction

A 74-year-old female with a medical history significant for rheumatoid arthritis managed with methotrexate, hydroxychloroquine, and abatacept, presented to the emergency department with exacerbation of a wound on her right thigh (see Figure 1). The wound was initially noticed one month prior and treated with doxycycline by primary care, who then referred to dermatology and was pending appointment.

On examination, the patient presented with a large eschar on her right thigh and buttock, exhibiting tenderness upon palpation. Additionally, there were eschars present on her abdomen, bilateral lower and upper extremities, along with some clustered blisters on her right foot and ankle.

The initial differential of the eschar included non-uremic calciphylaxis, vasculopathy, vasculitis, and infectious etiology. Laboratory workup included CBC, CMP, HIV, cryoglobulins, ANA panel, hepatitis B (sAg, sAb, cAb), hepatitis C antibody, RPR, lupus anticoagulant, anticardiolipin antibodies, anti-beta-2 glycoprotein antibodies, protein C and S, antithrombin III activity, protein electrophoresis and UA. Results revealed elevated CRP and ESR. However, non-uremic calciphylaxis was deemed less likely based on computed tomography (CT) imaging findings (no calcification present). Vasculopathy was ruled out with unremarkable lab findings, while the vasculitis workup was notable for the presence of Hepatitis B core antibody with undetectable Hepatitis B DNA. Tissue cultures revealed moderate growth of *Pseudomonas aeruginosa*, along with light growth of *Proteus mirabilis* and Group B *Streptococcus* (*Streptococcus agalactiae*).

Punch biopsies were obtained from the right thigh lesion for histopathological examination (H&E) and direct immunofluorescence (DIF). Histopathological examination revealed epidermal necrosis with viral cytopathic changes, and immunostaining with Varicella-Zoster Virus (VZV) was positive. DIF was positive for granular vessel wall staining with C3, as well as perivascular and diffuse fibrinogen staining (Figure 2).

These findings confirmed the diagnosis of VZV with associated leukocytoclastic vasculitis (LCV). The patient was diagnosed with disseminated VZV infection with LCV secondary to infection in the setting of immunosuppression. Antibiotic therapy was managed by infectious disease based on tissue culture results. The patient was started on Acyclovir at a dosage of 10 mg/kg/dose every 8 hours for 7 days. On day 10 of admission, the patient was found to have altered mental status. Subsequent CSF analysis was performed with detection of VZV in CSF, confirming VZV encephalitis. Despite medical intervention, the patient's medical status deteriorated, and she was intubated and transferred to MICU.

Discussion

The case report presented here underscores the importance of recognizing atypical presentations of VZV infection, particularly in immunocompromised patients. Literature review reveals a growing body of evidence linking VZV in immunocompromised individuals to a spectrum of unusual manifestations. Disseminated herpes zoster, characterized by more than 20 lesions outside of a dermatome, is highlighted as an uncommon but notable presentation, frequently observed in those with compromised immune systems [1]. Failure to promptly address disseminated VZV infections can lead to severe organ damage and an elevated risk of mortality, with reported rates ranging from 5% to 15% in non-HIV immunocompromised patients and up to 26% in HIV-positive individuals [3].

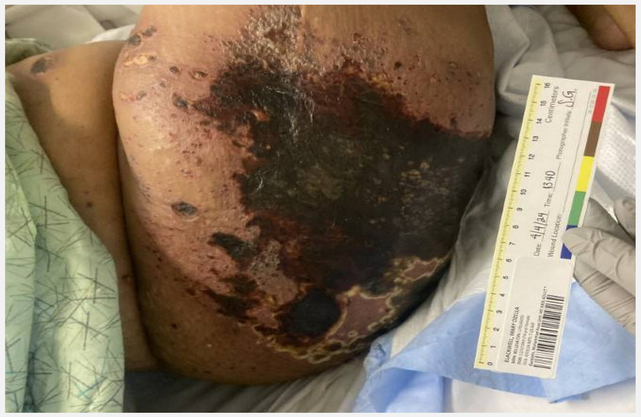

Figure 1. Right hip with large eschar with surrounding vesicles.

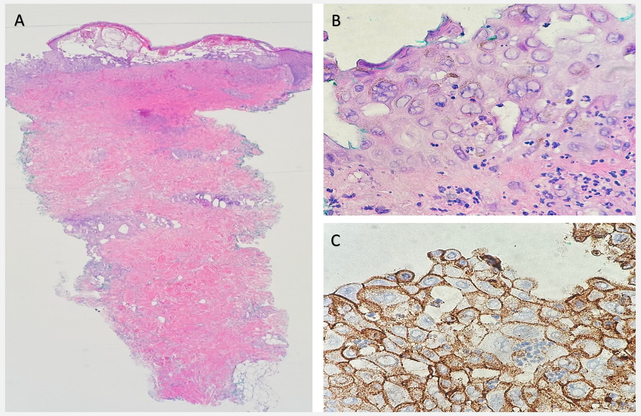

Figure 2. H&E – 2x (low power): intraepidermal blister (A), H&E – 40x (high power): multinucleated, enlarged keratinocytes with chromatin margination and molding, consistent with viral cytopathic changes (B), VZV IHC – 40x: positively highlighting keratinocytes (C).

Discussion

Of particular concern is the potential for disseminated VZV to progress to VZV encephalitis, as evidenced by at least 10 documented cases in the literature [4]. Immunocompromised status significantly increases the risk of such complications, highlighting the need for vigilance in this patient population. The case discussed here further underscores the diagnostic challenges posed by atypical VZV presentations. In one instance, a patient receiving immunosuppressive therapy for rheumatoid arthritis exhibited VZV infection diagnosed as vasculitis, leading to a delay in diagnosis and treatment [5]. Only after an extensive workup, including skin biopsy, was the accurate diagnosis made.

This case report serves as a reminder of the importance of considering VZV infection in the differential diagnosis of immunocompromised patients presenting with unusual clinical features. Early recognition and appropriate management are crucial in mitigating the potentially devastating consequences of disseminated VZV and its associated complications, including VZV encephalitis. Additionally, clinicians should maintain a high index of suspicion for VZV-related pathology, especially when dealing with diagnostic challenges or atypical clinical presentations, to ensure timely intervention and improved patient outcomes.

Conclusion

This is a case of atypical presentation of VZV leading to disseminated infection and ultimately VZV encephalitis. The lesions mimicked those of other diagnoses, such as calciphylaxis, resulting in a wide differential upon initial evaluation. The proper diagnosis was made on extended work up after skin biopsy and immunostaining revealed viral infection with VZV. It is crucial to consider atypical presentation of VZV in immunocompromised individuals and to obtain a full, appropriate work up to ensure timely diagnosis and management.

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