International Journal of Research in Dermatology
Devaraj Y et al. Int J Res Dermatol. 2024 Sep;10(5):277-281
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20242361

Original Research Article

Beyond dermatomes disseminated Herpes zoster in the immunocompetent: two rare cases

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Received: 05 June 2024
Revised: 15 July 2024
Accepted: 18 July 2024

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ABSTRACT

Herpes zoster is typically a localized reactivation of the varicella-zoster virus (VZV) that occurs in individuals following a primary varicella infection (chickenpox). Disseminated herpes zoster, characterized by widespread vesicular lesions beyond the primary dermatome, is uncommon and usually associated with immunocompromised states. Till date only 25 immunocompetent patients with disseminated HZ have been reported in literature. We report two such cases of disseminated HZ in immunocompetent individuals. The 1st patient is a 53-year-old woman with painful, itchy multiple grouped erythematous papules, vesicles, and bullae over right T8-T9 dermatome and multiple papules, crusted papules, and vesicles over face associated with fever and fatigue. The 2nd patient is an 8-year-old boy with multiple grouped clear vesicles and bullae with erythematous base involving the left S1-S5 dermatome. Multiple discrete erythematous papules and vesicles (active and crusted) were noted over trunk, right forearm, left arm, bilateral thigh and left mandibular area. Routine laboratory investigations were within normal limits. Tzanck smears were done, and multinucleated giant cells were seen in both cases. They were treated with antivirals and showed improvement. We have reported these two cases of disseminated HZ due to their occurrence in immunocompetent patients, which is a very rare phenomenon.

Keywords: COVID19 vaccination, Disseminated herpes zoster, Immunocompetent

INTRODUCTION

Herpes zoster (HZ), or Shingles, is a viral infection that occurs due to reactivation of the varicella-zoster virus (VZV), also known as Herpes simplex virus 3 (HSV 3). Primary infection by this virus leads to chickenpox (varicella). The virus then remains dormant in the dorsal root ganglion of the patient.[1] Decades later, when the immunity of the patient becomes low either due to physical trauma, psychological stress, immunosuppression (HIV/malignancy), older age, transplant recipients and presence of comorbid conditions, the virus gets reactivated, resulting in Herpes zoster.[2] The exact factors that cause this reactivation are still not fully understood. The lifetime risk of developing herpes zoster is about 30%, and among individuals who reach the age of 85, at least 50% will have experienced the condition. Greater incidence has been noted in women and white race.[3]

Disseminated herpes zoster, an uncommon and severe variant of herpes zoster, is characterized by having over 20 vesicles outside the original or neighboring dermatome. It is usually seen in immunocompromised persons in older population.[4] We report two unique cases with disseminated zoster in a non-immunocompromised

state. To the best of our knowledge, there are only a limited number of documented cases of disseminated zoster in a non-immunocompromised patient and hence we are reporting these two cases.

CASE REPORT

Case 1

A 53-year-old housewife residing in Pandavapura, Karnataka, presented to the Dermatology OPD with the complaints of multiple painful and itchy fluid filled lesions over face and right side of abdomen since 2 days. Lesions initially started as grouped vesicles on right side of abdomen and the next day multiple papules were noticed over the face. There was also history of moderate grade fever and fatigue. There was no history of topical application and no history of oral medication. She was not a known case of diabetes mellitus, hypertension, thyroid disorders.

On examination multiple grouped erythematous papules, vesicles, and bullae over the right side of abdomen i.e right T8-T9 dermatome and multiple erythematous discrete papules, crusted papules, and vesicles over face were noticed (Figure 1 & 2). There was history of varicella in childhood. No history of similar complaints in the family was noted. Tzanck smear was done, and multinucleated giant cells were seen (Figure 3). All routine blood investigations were within normal limits. Patient was treated with oral Valaciclovir 1g TID and symptomatic management.

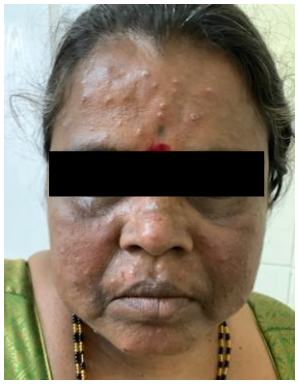

Figure 1: Multiple discrete erythematous papules, crusted papules, and vesicles over face.

Case 2

An 8-year-old boy residing in Karnataka, presented to us with multiple fluid filled lesions over left buttock, left side of scrotum, penis since 3 days. Over the next 2 days, new lesions occurred in the form of fluid filled lesion and red raised lesions over trunk, right forearm, left arm, bilateral thigh and left mandibular area. Lesions were associated with burning sensation, pain, and fever of moderate grade. There was history of varicella 3 years ago. There was no history suggestive of immunodeficiency and perinatal history was unremarkable.

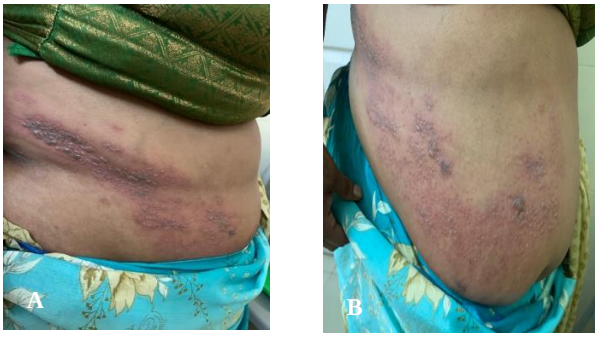

Figure 2 (A and B): Multiple grouped erythematous papules, vesicles, and bullae over the right side of abdomen.

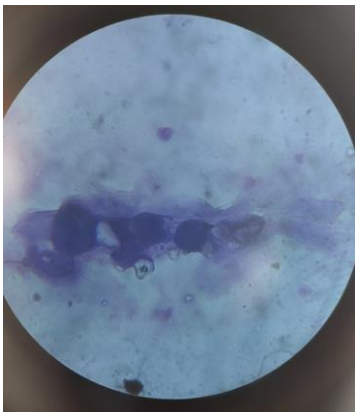

Figure 3: Tzanck smear showing multinucleated giant cells.

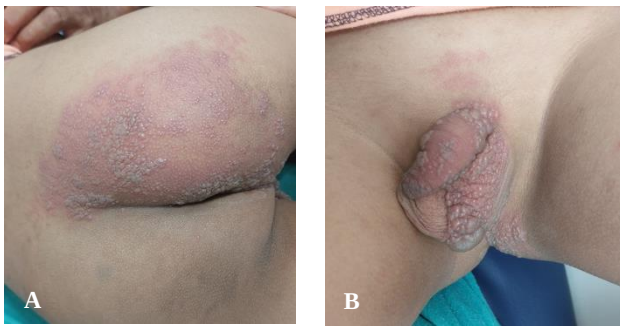

Figure 4 (A and B): Multiple grouped clear vesicles and bullae with erythematous base over left S1-S5 dermatome.

On examination multiple grouped clear vesicles and bullae with erythematous base noted over left S1-S5 dermatome (Figure 4). Multiple (24) discrete erythematous papules and vesicles (active and crusted) noted over trunk, right forearm, left arm, bilateral thigh and left mandibular area (Figure 5). Tzanck smear was done, and multinucleated giant cells were seen (Figure 6). Other routine investigations were normal. He was treated with IV acyclovir 30 mg/kg/day in three divided doses

for five days to which patient responded. Significant improvement was seen within 3 days and the patient was discharged on day 4 with all intravenous medications converted to oral medications. The patient was followed up 1 week later.

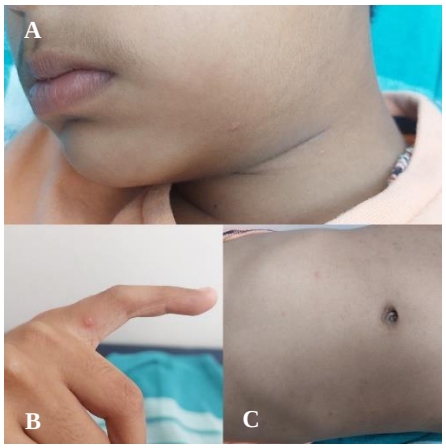

Figure 5 (A-C): Multiple discrete erythematous papules and vesicles (active and crusted) over trunk, right index finger, and left mandibular area.

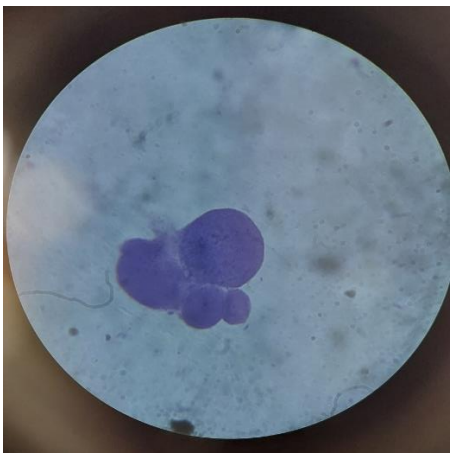

Figure 6: Tzanck smear showing multinucleated giant cells.

DISCUSSION

VZV is a double-stranded DNA virus. It is a highly neurotropic alpha herpesvirus that infects only humans. It causes varicella, also known as chickenpox, as an acute infection, and can later reactivate from the dorsal root ganglia to cause herpes zoster, or shingles (Figure 7).[1,5,6] The reactivated virus triggers a robust immune response, leading to inflammation of the affected nerves and surrounding tissues. This inflammatory response involves the release of pro-inflammatory cytokines and an influx of immune cells leading to the signs and symptoms i.e., typical herpes zoster lesions appearing as clusters of vesicles on an erythematous base, accompanied by pain, paresthesia, and itching along one or two adjacent dermatomes.[7]

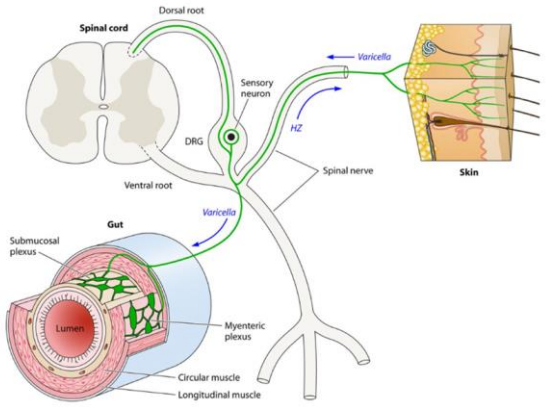

Figure 7: Potential routes taken by VZV during its life cycle.

Complications of herpes zoster can include postherpetic neuralgia (chronic pain that persists after the rash heals), secondary bacterial infections of the skin lesions, dissemination and ocular complications if the ophthalmic branch of the trigeminal nerve is involved. In severe cases, neurological complications such as encephalitis or myelitis may occur.[7] In disseminated herpes zoster, scattered herpetic lesions can be found on non-contiguous dermatomes (over 20 lesions). The diagnosis of disseminated herpes zoster can be made based on clinical presentation.[8] Disseminated HZ crossing dermatome boundaries may result from a viraemic spread, suggesting a more severe causative subtype in an immunocompetent patient.[9] VZV can also spread through fomites originating from skin lesions of varicella and HZ. Unlike varicella, HZ does not exhibit a seasonal pattern or occur in epidemics, as it arises from the reactivation of the patient's own latent virus. Consequently, the incidence rate of HZ tends to be more stable compared to that of varicella.[10]

VZV isolates from varicella (from external infection) and HZ (from internal reactivation) can be categorized into five genotypes based on specific geographical areas. These genotypes have stable distributions globally, with genotypes B and C prevalent in Europe and North America, J2 and A1 in Africa and Asia, and J in Japan. Both co-infecting genotypes can potentially enter a dormant state within the host and have the capability to reactivate. This indicates that immunity to the VZV acquired from chickenpox might not always prevent reinfection (though it may be subclinical) with a different strain., potentially contributing to up to 30% of HZ cases.[3] Diagnosis is typically based on clinical evaluation, but it can be confirmed through polymerase chain reaction, viral culture, or, less commonly, direct fluorescent antibody analysis.[5] The incidence of herpes zoster (HZ) tends to increase with age due to diminished cell-mediated immunity specific to varicella-zoster virus (VZV) in elderly individuals.[11] Disseminated HZ is rare and mainly occurs in cases of immunosuppression, such as in individuals with human immunodeficiency virus (HIV) infection, where there is impaired T cell immune

response to VZV, or in solid organ and stem cell transplant recipients, who exhibit reduced VZV cellular response and specific IgG antibody avidity.[12] Disseminated herpes zoster may be seen in healthy individuals when the virus accidentally escapes cellular immunity, which is even rarer, as seen in our case. However the exact mechanism by which some seemingly immunocompetent patients develop disseminated zoster is not clearly understood.[13,14] Recently Lin et al reported that disseminated herpes zoster (DHZ) can occur as a rare side effect in immunocompetent individuals following COVID-19 vaccination (mRNA or protein subunit) or COVID-19 infection, with SARS-CoV-2 spike proteins identified as triggers for VZV reactivation. Spike proteins in the virus activate the innate immune system via endosomal Toll-like receptors, leading to type I interferon production and naïve CD8+ T cell differentiation, disrupting VZV latency in ganglia and causing reactivation.[15] Zhang et al also documented a similar case of disseminated herpes zoster in a healthy elderly man following the administration of an inactivated SARS-CoV-2 vaccine.[16] Jacob et al documented a case of disseminated HZ in a 15 year old immunocompetent boy who presented with vesicles in the T2 dermatome of 1 week duration, which later spread to trunk, extremities and face. The only significant history was that his antenatal history revealed that his mother had varicella at 28 weeks' gestation and was treated with aciclovir.[17] In a recently published article by Moon et al. reported a total of twenty-two cases of disseminated herpes zoster in immunocompetent individuals. Therefore, a total of 25 immunocompetent patients with disseminated HZ are reported in literature so far (Table 1).[13] However, it is important to keep in mind that old age can be considered an immunocompromised state even without an underlying disease.

Table 1: Few of the recent documented cases of disseminated herpes zoster in immunocompetent individuals.[13]

Author	Age	Sex	Underlying disease	Initial symptoms	Skin lesion location	Treatment
Chakraborty et al[18]	60	M	None	Right upper limb vesicles and pain	Trunk, back, face, and right upper extremities	IV acyclovir
Chiriac et al[19]	67	M	Arterial hypertension	Erythematous rash	Trunk, face, and right inferior limb	Oral acyclovir
Oh et al[20]	86	M	Chickenpox	Confusion and right face swelling	Right face, trunk, and extremities	IV acyclovir
Sohal et al[21]	40	M	Hypertension Migraine	Headache	Right thigh and gluteal region	
Matsuo et al[22]	78	F	None	Lower abdominal pain	Head, chest, abdomen, and back	IV acyclovir
Matsumoto et al[23]	16	M	None	Left otalgia and spinning vertigo	Left earlobe, chest, abdomen, back, both arms and legs	famciclovir (1500 mg/day)

Early diagnosis and prompt treatment with antivirals is required in patients with disseminated HZ, as they are at a high risk of visceral organ involvement and other complications. These cases are typically treated with intravenous acyclovir at a dose of 10 mg/kg every 8 hours for 5-7 days. Other medications include oral acyclovir and oral valacyclovir.[24] Our first patient was treated with oral Valaciclovir 1g TID and our second patient was treated with IV acyclovir 30 mg/kg/day in three divided doses for five days which lead to complete resolution of lesions.

CONCLUSION

In recent years, increased awareness of this type of herpes zoster has led to more published cases, enhancing the recognition of the diagnosis, particularly in target populations. However, reports of disseminated herpes zoster in immunocompetent patients are rare as in our cases. Clinicians must still identify disseminated herpes zoster, implement prevention and treatment strategies, particularly for immunocompromised patients, and carefully monitor seemingly immunocompetent individuals.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Devaraj Y, Govindaraju N, Panigrahi S, Johnson RA. Beyond dermatomes disseminated Herpes zoster in the immunocompetent-two rare cases. Int J Res Dermatol 2024;10:277-81.