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Lower Extremity Shingles Complicated by Varicella Zoster Viral Meningitis

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Abstract Varicella zoster viral infection commonly presents as "chickenpox" in children and "shingles" in adults which may be complicated by meningitis in the immunocompromised but very rarely in the immunocompetent. Also, most reported cases of zoster meningitis were associated with the development of crops of vesicular rash at the cranial or cervical dermatomal levels. Here, we present a case of a 55-year-old African man with history of chronic low back pain who presented with frontal headache, fever and rash of the left lower extremity of two days' duration. He had no neck stiffness, neck pain or mental status changes on presentation. Brain imaging revealed no significant findings but Cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis and patient was promptly started on IV acyclovir. Biofire CSF analysis detected presence of Varicella Zoster virus (VZV). In this clinical encounter, leg rash and non-specific symptoms of fever and headache in the absence of meningism, confusion or focal neurologic deficits is an unusual presentation of VZV meningitis which may delay diagnosis. Hence, a high index of suspicion and early treatment for neurologic complications of VZV like meningitis is required in order to prevent lethal or severe long-term neurologic deficits in patients.

Keywords: *Varicella Zoster virus, meningitis, shingles, rash, headache*

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1. Background

The primary clinical manifestation of Varicella zoster virus (VZV) infection is chicken pox which presents as rash, low grade fever and malaise. It is usually benign in an immunocompetent patient. However, VZV may infect neurons directly as a result of viremia or infect nerve endings in the skin from the lesions on the skin and move retrograde along sensory axons to establish latency in neurons within the regional ganglia.

Herpes zoster (shingles) is a sporadic disease that results from reactivation of the latent virus from dorsal root ganglia resulting in a dermatomal rash preceded by pain. CNS involvement such as encephalitis, meningitis or meningoencephalitis may follow the localized skin eruption.

Our report tries to emphasize that early consideration for lumbar puncture and CSF analysis should be made in cases of shingles associated with fever and neurologic symptoms.

2. Case Presentation

55-year-old African man who migrated from Senegal 20 years before, presented to the emergency room on account of moderate and throbbing frontal headache of two days' duration with left hip shooting pain of five days' duration radiating to the left leg. There was associated subjective fever, he denied neck stiffness, neck pain, visual blurring, hearing loss, focal weakness, confusion, nausea or vomiting. He also denied cough, shortness of breath, abdominal pain or diarrhea. He was unaware of tick bites or sick contacts. He has no history of recent travels and no childhood history of rash. His past medical history is significant for chronic back pain. He had not received the shingle's vaccine.

On examination, vital signs revealed fever (101.9F). He was a well-developed and well-nourished man, not in obvious distress. Neurological exam showed that he was alert and oriented in time place and person, GCS was 15/15, cranial nerves were grossly intact, no neck stiffness, Kernig and Brudzinski signs were negative, bilateral tympanic membranes were clear, no gait abnormalities. A cluster of tiny vesicular rash which he was previously not aware of was noted at the lateral left leg (L4 dermatome).

2.1. Initial Investigations

Brain CT was done and showed no acute abnormalities. CBC, chemistry, blood cultures, urinalysis and chest X-ray as part of work up for fever were unremarkable.

CSF samples were drawn and he was started on empiric broad spectrum antibiotics consisting of vancomycin, ceftriaxone, ampicillin, acyclovir and dexamethasone added for possible meningoencephalitis. CSF analysis revealed clear and colorless sample, WBC 100, RBC 8, Polys 1, Lymphocytes 80, Monocytes 17, Eosinophils 2. CSF Glucose 91 and Serum glucose 177. CSF Protein 72. CSF Gram stain showed polymorphonuclear leukocytes and no organisms. Based on evidence of lymphocytic pleocytosis on CSF, patient was continued on intravenous acyclovir and other antibiotics were de-escalated. As it was COVID-19 pandemic era, COVID-19 testing was conducted and was negative.

2.2. Days 2-5

Symptoms remained unchanged despite symptomatic treatment of headache and neuropathic pain with acetaminophen and gabapentin respectively, he developed mild neck stiffness, more clusters of vesicular rashes developed on the lateral aspect of left lower leg (Figure 1) and another cluster on the medial aspect. Remaining results of investigations obtained were serum HSV 1/2 Ig M and HSV1/2 CSF PCR which were negative (Table 1), Respiratory Syncytial Virus (RSV) screen was negative, Influenza virus A/B negative, 4th generation HIV testing negative, Treponema pallidum Ab screen was also negative. Brain MRI was negative for any acute findings, left hip X-ray showed mild degenerative joint disease.

2.3. Day 6

In the absence of remarkable improvement in symptoms and inadequacy of initial CSF samples for further analysis, repeat lumbar puncture was done, opening pressure was 270 mmH2O. BioFire meningitis /encephalitis panel PCR detected Varicella zoster virus, CSF West Nile IgM antibodies negative, West Nile IgG positive, Serum Varicella zoster Ab IgM Positive with titer of 2.29, Serum Varicella zoster IgG positive with titer of >4000. Lyme total Ab IgG and IgM serum were Negative (Table 1).

2.4. Day 7

Headache improved significantly and skin rashes were crusted and dry (Figure 2). Dose of gabapentin was increased to 300mg q8 hours to further suppress postherpetic neuropathic pain in the left lower extremity. He was discharged to outpatient follow up on completing 10 days of IV Acyclovir with resolution of all symptoms.

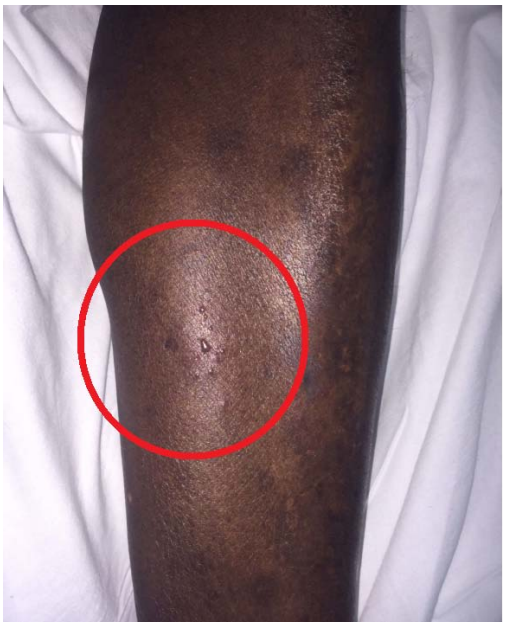

Figure 1. Vesicular rash over the lateral aspect of left lower leg

Table 1. CSF and Serology studies reports

	Serum	CSF	
	Antibodies	Antibodies	PCR
Herpes simplex virus Type 1 and 2	Ig M: Negative		Not detected
Varicella zoster	Ig M : Positive (2.29) Ig G : Positive (>4000)		Detected
West Nile virus		Ig M: Negative Ig G: Positive	
Lyme disease	Ig M : Negative Ig G : Negative		

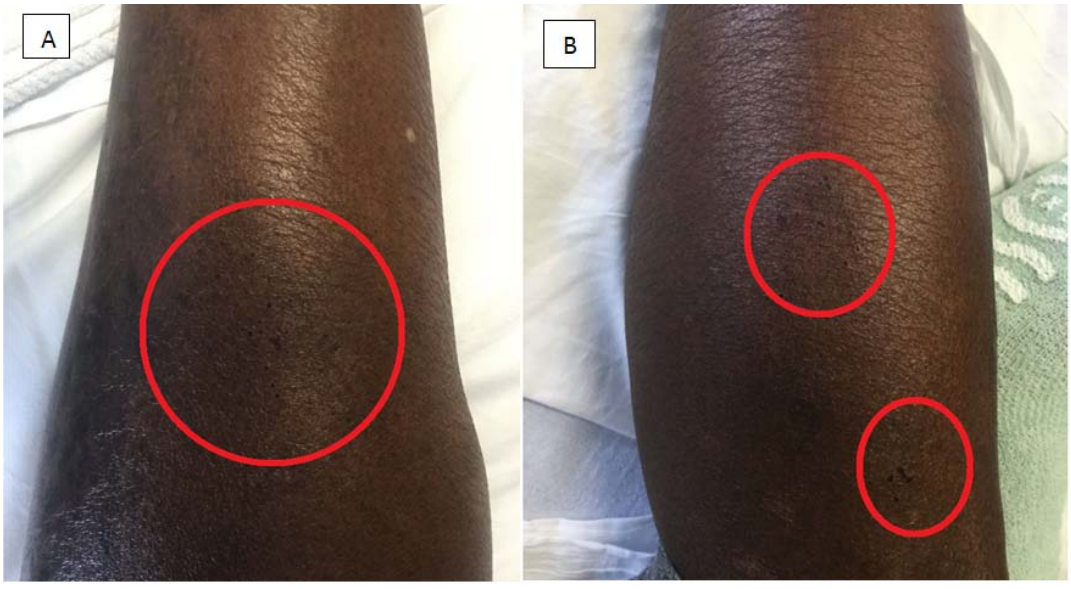

Figure 2. Crust and dry rashes over lateral aspect (A) and medial aspect (B) of left lower leg on Day 8

3. Discussion

Varicella Zoster virus (VZV), a member of the Herpesviridae family, is an enveloped, double stranded, linear DNA virus with a capsid arranged in an icosahedral form. VZV is a neurotropic virus that infects nearly all humans. It causes two unique diseases which are chicken pox (varicella) and shingles (herpes zoster). Chicken pox characterized by vesicular lesions at different stages of development on the face, trunk, and extremities is due to primary infection by VZV while shingles, characterized by a dermatomal, unilateral vesicular eruption is due to reactivation of a latent VZV that gained access to the sensory ganglia during an episode of chicken pox.

The site of initial VZV entry in the naïve host is the mucosal epithelia of the upper respiratory tract after transmission of the virus by aerosolized respiratory droplets or by direct contact with the virus in a chicken pox or shingles skin lesion. The virus subsequently infects local immune system cells and those in adjacent lymphoid tissues with a resultant viremia. Infected Mononuclear cells especially T cells transports the virus to the skin causing rash. Free virus presents in the skin vesicles infect nerve endings and move retrograde along axons to establish latency within neurons in the regional ganglia. VZV specific cell mediated immunity that develops in the host stops the infection. It also helps to control VZV latency limiting its potential for reactivation to cause shingles. If VZV reactivation occurs and is not limited, VZV spreads within the ganglion involving multiple neurons then continues anterograde down the sensory nerve to cause infection in the skin and on occasions, retrograde to the CNS. The involved sensory ganglion develops intense inflammation which may sometimes involve the meninges or brain parenchyma with hemorrhagic necrosis of the nerve cells. This neuronal damage explains the neuropathic pain of shingles. Some cases have been reported of reactivation of VZV with direct invasion of cranial nerves [1] in otherwise immunocompetent patients. In particular, one case exhibited involvement of CN VI with increased intracranial pressure and bilateral papilledema [2].

Varicella (chicken pox) occurs worldwide, with developing countries hardest hit, especially in absence of routine vaccination programs. It typically affects persons by mid-adulthood. In the United States, more than 1.2 million people contract the disease annually. The United States Centers for Disease Control and Prevention (CDC) estimates that approximately 30 percent of Americans will experience herpes zoster during their lifetime [3].

Herpes Zoster (shingles) incidence increases with age and reaches approximately 10 cases per 1,000 patient-years by age 80. This is because cell-mediated immunity (CMI) has been noted to decline with aging as part of immunosenescence with potential for VZV reactivation [4]. The epidemiology may be related to the properties of VZV (known to be sensitive to heat, climate, population density, and risk of exposure) [5].

The major clinical features of herpes zoster (shingles) are usually rash and acute neuritis, with thoracic and lumbar dermatomes most commonly involved. The rash typically starts as erythematous papules, typically in a single dermatome but may involve contiguous sites. Within several days, grouped vesicles or bullae form and transform to pustular rashes within 3 to 4 days. In immunosuppressed patients and elderly, they can however be hemorrhagic. In immunocompetent individuals, the lesions crust by 7 to 10 days and are no longer infectious. Scarring and hypo- or hyperpigmentation may persist months to years after herpes zoster has resolved

Approximately 75% of patients have prodromal pain preceding the rash in the affected dermatome. This pain can be constant or intermittent and usually precedes the rash by 2 to 3 days and is frequently mistaken for another disease, such as angina, cholecystitis, appendicitis, spinal disc diseases, or renal colic, depending on the involved dermatome [6].

Reports have been made of VZV cases with dermatomal pain of herpes zoster preceding dermatomal rash by as much as 7-10 days described as preherpetic neuralgia [7]. The patient in our case had his rash preceded by 4-5 days of neuropathic pain. His meningeal signs also presented much later in the course of his illness which can delay diagnostic testing and initiation of treatment without a high index of suspicion. The location of his pain in the lower extremity can also cause a diagnostic dilemma given his history of chronic back pain and radiculopathy. This case also underlines the importance of prompt CSF analysis in neurological emergency situations.

Aseptic meningitis is one of the neurologic complications of VZV infection which occurs more in immunocompromised patients than immunocompetent individuals with vesicular eruptions preceded or followed by meningeal symptoms and signs.

The most common complication of herpes zoster is Post-herpetic Neuralgia (PHN) defined as significant pain (rated more than 3/10) persisting for 90 days after the rash onset. Individuals older than 60 years of age account for 50% of these cases [8]. Immunosuppressed patients also have a higher incidence. By contrast, patients who receive the live attenuated herpes zoster vaccine are less likely to develop PHN, even if herpes zoster occurs. Other complications include Acute retinal necrosis, Ramsay Hunt syndrome (herpes zoster oticus) and neurologic complications such as Peripheral Neuropathy, Myelitis, Guillain Barre Syndrome, Stroke Syndromes, cranial neuropathies, VZV vasculopathy (e.g. Giant Cell Arteritis) and Encephalitis. Notably, all neurologic VZV complications may develop in the absence of rash, as confirmed by the detection of VZV DNA or anti-VZV antibody (or both) in CSF.

Our patient presented with unique diagnostic challenge which could be easily missed with fatal consequences. His rash was located atypically distant from the head and neck region, HIV was negative and he had no meningeal symptoms or signs on presentation. In conclusion, previously healthy patients with dermal irritation and fever may be in an early phase of what could turn out to be meningitis with potentially serious consequence if early diagnosis and treatment is not instituted.

Statement of Competing Interests

The authors have no competing interests.

References

[1] Pasedag, T., Weissenborn, K., Wurster, U., Ganzenmueller, T., Stangel, M. and Skripuletz, T., "Varicella Zoster Virus Meningitis in a Young Immunocompetent Adult without Rash: A Misleading Clinical Presentation", *Case reports in neurological medicine*, 2014: 686218. Dec 2014.

[2] Ibrahim, W., Elzouki, A., Husain, A. and Osman, L., "Varicella Zoster Aseptic Meningitis: Report of an Atypical Case and Literature Review", *The American journal of case reports*, 16: 594-597. Sep 2015.

[3] Harpaz, R., Ortega-Sanchez, I.R. and Seward, J.F., "Prevention of Herpes Zoster: Recommendations of the Advisory Committee on Immunization Practices (ACIP)", *MMWR. Recommendations and reports: Morbidity and mortality weekly report. Recommendations and reports / Centers for Disease Control*, 57(RR-5):1-30. Jun 2008.

[4] Gershon, A.A, Gershon, M.D., Breuer, J., Levin, M.J., Oaklander, A.L., and Griffiths, P.D., "Advances in the understanding of the pathogenesis and epidemiology of herpes zoster", *Journal of clinical virology*, 48 (1). S2-S7. May 2010.

[5] Ashour, A., Obeidat, K., Azrieh, B., Alsaud, A., and Yassin, M., "An Association of Varicella Zoster Virus, Facial Palsy, and Meningitis in a Young Immunocompetent Male", *Case reports in neurology*, 12 (1). 136-139. Jan-Apr 2020.

[6] Wareham, D.W., and Breuer, J., "Herpes zoster", *British medical journal / British Medical Association*, 334(7605): 1211-1215. Jun 2007.

[7] Sanguankeo, A., Upala, S., Sornprom, S., and Thamcharoen, N., "Varicella-zoster meningitis with a late-onset of skin eruption", *BMJ case report*, 2015: bcr2014208056. Feb 2015.

[8] Choo, P.W., Galil, K., Donahue, J.G., Walker, A.M., Spiegelman, D. and Platt, R., "Risk Factors for Postherpetic Neuralgia", *Archives of internal medicine*, 157(11):1217-24. Jun 1997.