CASE REPORT

Varicella zoster meningitis: an atypical case of zoster reactivation in immunocompetent young adult

Muhammad Farhan Khaliq, Tanureet Kochar, Molly John

Internal Medicine, Charleston Area Medical Center, West Virginia University, Charleston, West Virginia, USA

Correspondence to

Muhammad Farhan Khaliq, muhammadfarhankhaliq@gmail.com

Accepted 14 December 2017

SUMMARY

Varicella virus is a neurotropic virus that can reactivate later in life to cause zoster or shingles. Typically, it affects elderly, immunocompromised population. We report an unusual case of an immunocompetent young adult presenting with occipital headache and zoster rash, without preherpetic and postherpetic neuralgia, who was diagnosed with varicella meningitis on Polymerase chain reaction (PCR). He was treated with intravenous acyclovir and later discharged on famciclovir. Diagnosis of varicella meningitis is difficult in the absence of typical features of zoster rash and requires high index of suspicion. Rapid diagnostic tests including varicella PCR and antithelial antibody testing can help in the confirmation of varicella zoster meningitis.

BACKGROUND

Varicella-zoster virus can reactivate to cause shingles. Rarely, reactivation can present as meningitis with or without dermatomal rash making it a diagnostic challenge. Absence of preherpetic neuralgia further adds to complexity of the condition. Accurate diagnosis is important for appropriate treatment and optimal neurological outcomes. Fortunately, no short-term poor outcomes are reported in the available literature. We present a case of 28-year-old immunocompetent male who presented with occipital headache and was diagnosed with varicella aseptic meningitis on the basis of cerebrospinal fluid (CSF) Polymerase chain reaction (PCR). He was treated successfully with acyclovir and did not develop any postherpetic neurological complications. Our case is atypical as it presented in young immunocompetent patient with rash appearing after the headache and not associated with preherpetic and postherpetic neuralgia.

CASE PRESENTATION

Our patient is a healthy 28-year-old Caucasian man presented to emergency room for severe occipital headache, nausea, vomiting, dizziness and subjective fevers. His nausea was preceded daily by several episodes of non-bilious, non-bloody vomiting with dizziness. His symptoms were intermittent, worst in the morning and intensified over the week course. On the third day of his illness, he visited urgent care facility where he was diagnosed with migraine and discharged on acetaminophen, Ibuprofen, cyclobenzaprine. With worsening symptoms, the patient directed himself to emergency room same evening, where CT scan of the brain revealed no

signs of bleed or increased intracranial pressure. He was advised bed rest and non-steroidal anti-inflammatory agents. On the fourth day, he developed non-itchy rash on the right side of the chest around the nipple area (see [figure 1](#)). Similar rash appeared on the back. He developed high grade fever on the seventh day that prompted him to visit our facility emergency room.

On arrival to the hospital, the patient was afebrile and his vitals were stable. He appeared weak and in mild distress because of his pain. He was alert and oriented with no nuchal rigidity or focal neurological deficits. No oropharyngeal rash was seen. Respiratory, cardiovascular and abdominal examinations were unremarkable. Skin examination revealed sharply demarcated area of vesicular rash in different stages of development in T4 dermatomal distribution. Overlying area of the rash was non-tender, and non purulent.

Review of the patient's social history revealed that he was originally from a rural village near Charleston, West Virginia, USA. He was an avid hiker and goes in the woods very often. The patient denied any sick contacts, travel outside state or animal exposure. He denied exposure to ticks. He had no history of smoking or drinking. He had no personal or family history of meningitis however, he reported being infected with varicella at 3 years of age but recovered without any complications. He was up to date on immunisations. Professionally, he is a graphic designer. The patient had no known history of congenital or acquired immunodeficiency and had never been treated with any immunosuppressant.

INVESTIGATIONS

Complete blood count and comprehensive metabolic panel were within normal limits. Inflammatory markers including C-reactive protein, procalcitonin and lactic acid were unremarkable. Due to the high index of suspicion, lumbar puncture was performed that revealed elevated opening pressure (>55 mmHg). High leucocyte count of $429 \text{ cells } 10^9/\text{L}$ with lymphocytic predominance (88%), CSF glucose level of 44 mg/dL, total CSF protein level of 164 mg/dL was noted. Cytology of the CSF showed large lymphocytes and occasional histiocytic cells with normal morphology.

PCR testing was positive for varicella zoster virus. CSF tested negative for herpes simplex 1 and 2, enterovirus, parechovirus, human herpes 6, cytomegalovirus, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*,

CrossMark

To cite: Khaliq MF, Kochar T, John M. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-223257

Figure 1 Herpes zoster rash in T4 dermatomal distribution on day 1.

Streptococcus agalactiae, *Listeria monocytogenes*, *Escherichia coli* K1 and *Cryptococcus neoformans*. Due to regional high prevalence, our patient was also tested for CSF *Borrelia burgdorferi* serology, histoplasmosis, arbo virus serology including La Crosse IgG and IgM, St Louis IgG and IgM, Eastern Equine IgG and IgM, Western Equine IgG and IgM and West Nile virus which remained negative.

PCR done on nasopharyngeal swab remained negative for adenovirus, *Bordetella pertussis*, *Chlamydia pneumoniae*, coronavirus 229E, coronavirus HKU1, coronavirus NL63, coronavirus OC43, parainfluenza 1, 2, 3 and 4, picornavirus, influenza A and B, metapneumovirus, *Mycoplasma pneumoniae* and respiratory syncytial virus. His HIV testing was negative. His skin swab from the rash tested positive for varicella zoster virus.

TREATMENT

Empirically, patient was started on intravenous ceftriaxone, vancomycin and acyclovir. His headache improved after lumbar puncture and intravenous acyclovir. His antibiotics were stopped after PCR came positive for varicella. Within 48 hours, his rash started improving. Given the favourable outcome, patient was discharged on famciclovir 500 mg every 8 hours for 5 days.

Figure 2 Herpes zoster rash improved after acyclovir administration on day 3.

OUTCOME AND FOLLOW-UP

He completed the course of antiviral therapy. His rash cleared up without development of any postherpetic neuralgia (see figure 2). On follow-up, there was no short-term neurological complication reported.

DISCUSSION

Varicella zoster virus is a neurotropic virus that belongs to Herpesviridae. It becomes latent after primary infection. Reactivation is observed with advancing age and immunosuppressed conditions. Reactivation manifests as zoster or shingles followed by postherpetic neuralgia, cranial nerve palsies, zoster paresis, meningoencephalitis, cerebellitis, myelopathy, multiple ocular disorders and vasculopathy that can resemble giant cell arteritis.^{1 2} All neurological complications can occur in the absence of rash. Rapid and accurate diagnosis of central nervous system infections is crucial to determine appropriate treatment. Delay in the empiric therapy has the potential to increase morbidity and mortality. Our case is unique as meningitis presented atypically in a relatively younger immunocompetent male with no preherpetic neuralgia.

Overall, aseptic meningitis is relatively rare. Galil *et al* reviewed herpes and its complications in 859 patients and reported varicella meningitis incidence to be 0.5% within 60 days of diagnosis.³ We believe incidence of varicella meningitis is higher. It is underdiagnosed due to the lack of availability of PCR and intrathecal testing of varicella zoster virus compared with herpes simplex virus (HSV) testing which is readily available in healthcare facilities.⁴ Because of its low incidence, atypical presentation and unavailability of testing, diagnosis requires high index of suspicion. Isolated neurological symptoms presenting without dermatomal rash can be easily missed once HSV meningitis is ruled out and can result in premature cessation of antivirals. Cases have been reported where meningitis has present solely with rash without preherpetic or postherpetic neuralgia as occurred in our case.⁴ If dermatomal pain is the only finding, it is known as zoster sine herpete (ZSH).

Our patient predominantly complained of occipital headache and never developed meningeal signs including neck rigidity, Brudzinski or Kernig sign. His symptoms responded to the diagnostic lumbar puncture. We attribute the symptoms mainly to elevated intracranial pressure. His vesicular rash disappeared within 48 hours of initiation of acyclovir. It also reflects patient's strong immune response as immunocompromised patients tend to develop severe and prolong disease. This was similar to other reported cases in literature. Early administration of acyclovir results in resolution of acute pain, dermatomal rash, prevents the virus from spreading throughout

Learning points

- ▶ Varicella meningitis can present in any age group, regardless of immunological status.
- ▶ Absence of dermatomal rash or preherpetic neuralgia does not exclude varicella meningitis.
- ▶ Cerebrospinal is the key to diagnosis. PCR varicella virus helps in confirmation. If suspicion is higher, intrathecal antibody testing should be done.
- ▶ Intravenous acyclovir therapy should be started empirically and should be stopped when both herpes and varicella zoster are negative on molecular testing.

the patient's body with higher rate of remission.^{5–7} Majority of cases reported in the literature were treated with intravenous acyclovir for longer durations ranging from 10 to 21 days.^{5 8} Our patient had clinical improvement in 48 hours. Patient was switched to oral famciclovir therapy which he tolerated very well. On follow-up, patient had no deficits on neurological exam. This indicates that patient with similar presentation and good clinical response to initial therapy can be discharged on oral therapy with close follow-up. However, efficacy of this approach needs to be determined by prospective studies to see long-term neurological outcomes.

Contributors MFK and MJ was involved in the care of the patient. MFK and TK came up with the initial plan. MFK prepared the first draft that was further modified by TK. All three authors contributed in literature search equally. Manuscript was critically reviewed for intellectual content and proofread by MJ. MFK and TK revised the manuscript. In the end, all authors read and approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Amlie-Lefond C, Jubelt B. Neurologic manifestations of varicella zoster virus infections. *Curr Neurol Neurosci Rep* 2009;9:430–4.
- 2 Nagel MA, Gilden D. Complications of varicella zoster virus reactivation. *Curr Treat Options Neurol* 2013;15:439–53.
- 3 Galil K, Choo PW, Donahue JG, *et al*. The sequelae of herpes zoster. *Arch Intern Med* 1997;157:1209–13.
- 4 Kangath RV, Lindeman TE, Brust K. Herpes zoster as a cause of viral meningitis in immunocompetent patients. *BMJ Case Rep* 2013. doi: 10.1136/bcr-2012-007575. [Epub ahead of print 9 Jan 2013].
- 5 Gupta P, Ranjan R, Agrawal CS, *et al*. Meningitis with polymerase chain reaction for varicella zoster positivity in cerebrospinal fluid of a young immunocompetent adult. *J Neurosci Rural Pract* 2016;7:591.
- 6 Kim MA, Yu RM, Kim KH, *et al*. A case of acute aseptic meningitis associated with herpes zoster. *Korean J Pediatr* 2009;52:705–9.
- 7 Gross G, Schöfer H, Wassilew S, *et al*. Herpes zoster guideline of the German dermatology society (DDG). *J Clin Virol* 2003;26:277–89.
- 8 Pasedag T, Weissenborn K, Wurster U, *et al*. Varicella zoster virus meningitis in a young immunocompetent adult without rash: a misleading clinical presentation. *Case Rep Neurol Med* 2014;2014:1–4.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>. BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow