CASE REPORT

Varicella-zoster meningitis with a late-onset of skin eruption

Anawin Sanguankeo,^{1,2} Sikarin Upala,^{1,2} Suthanya Sornprom,¹
Natanong Thamcharoen¹

¹Bassett Medical Center, Columbia University College of Physicians and Surgeons, Cooperstown, New York, USA
²Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Correspondence to

Dr Anawin Sanguankeo,
anawin.sanguankeo@bassett.org

Accepted 27 January 2015

SUMMARY

Viral meningitis caused by varicella-zoster virus (VZV) is an uncommon neurological complication of herpes zoster. It may occur before or after the onset of the vesicular rash along the dermatomal distribution, which is the classic presentation of herpes zoster. We describe a case of a 51-year-old immunocompetent Caucasian man who presented with neck and severe right-sided facial pain. Eight days later, he had photophobia and papular rash on his forehead. Cerebrospinal fluid (CSF) examination confirmed aseptic meningitis and CSF PCR detected the presence of VZV DNA. Neurological complications of VZV infection, such as aseptic meningitis, may be difficult to diagnose and can cause delay in treatment, especially in cases with late onset of dermatological manifestations of herpes zoster. Definite diagnosis requires evidence of acute VZV infection in blood or cerebrospinal fluid.

BACKGROUND

Varicella-zoster virus (VZV) reactivation within the cranial nerve or dorsal root ganglia that causes herpes zoster is associated with a wide range of neurological presentations and complications. The usual presentation comprises a dermatomal vesicular eruption, often preceded by prodromal pain, itching or tingling for 2–3 days. Prodromal pain can be atypically severe and long-lasting before the eruption, in some cases, thus delaying the diagnosis. We present a case of varicella-zoster meningitis with late cutaneous manifestation in a 51-year-old immunocompetent Caucasian man, in whom the diagnosis was not suspected until the rash erupted.

CASE PRESENTATION

A 51-year-old Caucasian man presented with neck pain and severe throbbing right-sided headache for the past 6 days. Initially, the patient developed neck pain, headache and pain in the right preauricular area, which was also mildly swollen. Three days later, he developed fever and chills and presented to the emergency department. He underwent CT of the head and sinuses, but there were no relevant findings to account for his symptoms. The severe constant headache persisted and extended over the right parietal region. He also had vomiting and photophobia. He denied any visual changes, hearing loss, cough, chest pain or shortness of breath. He was unaware of any tick bites or contact with ill individuals. Aside from a history of chicken-pox during childhood, the patient had no history of serious illnesses or infections.

On physical examination, his vital signs were as follows: blood pressure 113/81 mm Hg, pulse 67/min, T 36.4°C (97.5°F), Respiratory Rate 20/min. He presented mild right preauricular swelling and tenderness. The neck was supple without stiffness, Kernig or Brudzinski signs. Other aspects of the neurological examination were intact.

INVESTIGATIONS

A CT of the head was performed and showed no acute intracranial abnormalities. The cerebrospinal fluid (CSF) examination was carried out 6 days after onset and showed a protein level of 130 mg/dL, glucose level of 45 mg/dL (serum glucose 112 mg/dL) and white cell count of 532/mm³ with lymphocytic predominance (98%). CSF for herpes simplex virus and mumps was negative. One day after hospitalisation (7 days after onset), the patient developed a painful erythematous papular rash on the right side of his forehead and right upper eyelid (figure 1). CSF examination by PCR for VZV DNA was positive. Results of HIV and hepatitis C antibody were negative.

TREATMENT

After CSF examination revealed lymphocytic pleocytosis, the patient was initially treated with

Figure 1 Erythematous papular eruption on the right side of the forehead and right upper eyelid (herpes zoster ophthalmicus).

CrossMark

To cite: Sanguankeo A, Upala S, Sornprom S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-208056

acyclovir intravenously. The patient refused to stay in the hospital after 2 days of therapy and was given a high dose of valacyclovir orally for 1 week with significant improvement on follow-up.

DISCUSSION

There have been reports that dermatomal-distribution pain of herpes zoster may precede skin lesions (preherpetic neuralgia) by 7–10 days¹ or 3 weeks.² In one case series of zoster patients whose pain preceded rash by 7 to more than 100 days,³ half the patients had been taking long-term steroids or had metastatic cancer. No patient presented with meningitis. Since PCR for detection of VZV DNA in the CSF have become more readily available, there have been an increasing number of reports of VZV-cause aseptic meningitis with a delay-onset or absence of skin manifestation.⁴ Persson *et al*⁵ found that some participants developed blisters concurrently or after symptoms of meningitis.

The present case illustrates a neurological complication of herpes zoster: aseptic meningitis with an atypical late-onset zoster ophthalmicus. Habib *et al*⁶ reported herpes zoster meningitis with hypoglycorrhachia in an immunocompetent patient, similar to our case, except that in our case the patient had late-onset zoster rash. Primary infection of VZV causes varicella (chickenpox), after which the virus can remain latent in a cranial nerve or dorsal root ganglia at any point of the neural axis. Years later, VZV may reactivate and cause zoster (shingles), a syndrome usually characterised by pain along an affected dermatome, followed by the typical vesicular eruption 2–3 days later.⁷ Our patient presented with facial pain that lasted about 1 week before he developed multiple papules on the dermatomal distribution of the trigeminal nerve (V1). The cause of atypical skin manifestation might be due to intravenous acyclovir administered, which interfered with rash eruption.

Aseptic meningitis is one of the neurological manifestations of VZV infection that can occur in immunocompetent^{8,9} as well as in immunocompromised¹⁰ patients. It has been recorded in association with the classic vesicular eruption, which could be preceded or followed by meningeal irritation, and also in the absence of the cutaneous eruption (zoster sine herpete). In a case of meningitis caused by VZV without antecedent skin rash, its pathogenesis involves the reactivation of viral particles in the ganglion with a relatively low viral load. They inflict direct damage to the CNS tissue, which is followed by the viral spread to the rest of the CNS and skin via axonal transport, causing a delayed skin manifestation.¹¹ This may lead to a delay in diagnostic test and initiation of antiviral treatment. Severe complications with high morbidity and mortality rate that may occur preceding skin rash include encephalitis, myelopathy and cerebrovascular disease.¹² Intravenous acyclovir should be given to patients who have herpes zoster meningitis, and especially to those with severe neurological complications or immunocompromised status.⁷ If there is a reason intravenous acyclovir should not be used, a high dose of valacyclovir (8 g/day) may be given to achieve an area-under-the-curve (AUC) approximate to that of intravenous acyclovir.¹³

Aseptic meningitis associated with VZV infection in immunocompetent patients is relatively rare (with an incidence of 0.5%).¹⁴ Its incidence could be underestimated in the literature because of under-reporting secondary to lack of direct viral detection from CSF. The CSF profile in VZV meningitis is clinically indistinguishable from other types of viral meningitides. However, aseptic meningitis associated with VZV may present a CSF profile characterised by a higher white cell count, lymphocyte and monocyte percentages, and protein levels, compared

with that in enterovirus-causing meningitis.¹⁵ Definite diagnosis of VZV meningitis, especially in cases without skin manifestation of herpes zoster, requires virological confirmation. Evidence of active VZV infection is supported by the presence of anti-VZV IgM in serum or CSF, anti-VZV IgG in CSF and VZV DNA in blood mononuclear cells or CSF.¹²

Learning points

- ▶ Varicella-zoster meningitis may be present in immunocompetent patients without risk factors.
- ▶ Treatment for varicella-zoster virus (VZV) meningitis should be started before receiving a confirmation test in case of high suspicion to prevent severe neurological complications.
- ▶ Intravenous antibiotics should, if possible, be given in every VZV meningitis case.
- ▶ Late cutaneous or atypical presentation of zoster may cause a delay in diagnosis and initiation of treatment.
- ▶ Diagnosis of zoster meningitis requires virological or serological confirmation.

Contributors SU and NT were directly involved with the patient care and analysed and interpreted the patient data. AS and SS were major contributors in writing the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Burgoon CF Jr, Burgoon JS, Baldrige GD. The natural history of herpes zoster. *J Am Med Assoc* 1957;164:265–9.
- 2 Juel-Jensen B. Shingles: a belt of roses from hell. *BMJ* 1979;1:818.
- 3 Gilden DH, Dueland AN, Cohrs R, *et al*. Preherpetic neuralgia. *Neurology* 1991;41:1215–18.
- 4 Bergstrom T. Polymerase chain reaction for diagnosis of varicella zoster virus central nervous system infections without skin manifestations. *Scand J Infect Dis Suppl* 1996;100:41–5.
- 5 Persson A, Bergstrom T, Lindh M, *et al*. Varicella-zoster virus CNS disease—viral load, clinical manifestations and sequelae. *J Clin Virol* 2009;46:249–53.
- 6 Habib AA, Gilden D, Schmid DS, *et al*. Varicella zoster virus meningitis with hypoglycorrhachia in the absence of rash in an immunocompetent woman. *J Neurovirol* 2009;15:206–8.
- 7 Cohen JL. Clinical practice: herpes zoster. *N Engl J Med* 2013;369:255–63.
- 8 Cooper CJ, Said S, Teleb M, *et al*. An immunocompetent patient with a vesicular rash and neurological symptomatology. *Case Rep Med* 2013;2013:168943.
- 9 Goyal H, Thakkar N, Bagheri F, *et al*. Herpes zoster meningitis with multidermatomal rash in an immunocompetent patient. *Am J Emerg Med* 2013;31:1622.e1–2.
- 10 Takayama N, Yamada H, Kaku H, *et al*. Herpes zoster in immunocompetent and immunocompromised Japanese children. *Pediatr Int* 2000;42:275–9.
- 11 Echevarria JM, Casas I, Martinez-Martin P. Infections of the nervous system caused by varicella-zoster virus: a review. *Intervirology* 1997;40:72–84.
- 12 Echevarria JM, Martinez-Martin P, Tellez A, *et al*. Aseptic meningitis due to varicella-zoster virus: serum antibody levels and local synthesis of specific IgG, IgM, and IgA. *J Infect Dis* 1987;155:959–67.
- 13 Gnann JW Jr. Antiviral therapy of varicella-zoster virus infections. In: Arvin A, Campadelli-Fiume G, Mocarski E, *et al*. eds. *Human herpesviruses: biology, therapy, and immunoprophylaxis*. Cambridge: Cambridge University Press, 2007. Chapter 65. <http://www.ncbi.nlm.nih.gov/books/NBK47401/>
- 14 Cohen JL, Brunell PA, Straus SE, *et al*. Recent advances in varicella-zoster virus infection. *Ann Intern Med* 1999;130:922–32.
- 15 Hong HL, Lee EM, Sung H, *et al*. Clinical features, outcomes, and cerebrospinal fluid findings in adult patients with central nervous system (CNS) infections caused by varicella-zoster virus: comparison with enterovirus CNS infections. *J Med Virol* 2014;86:2049–54.

Copyright 2015 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