ACTA MEDICA SALINIANA

CASE REPORT

VARICELLA-ZOSTER MENINGITIS

Dilista Piljić, Humera Porobić-Jahić, Medina Mujić

ISSN 0350-364X

DOI: 10.5457/742

Dilista Piljić
Humera Porobić-Jahić
Medina Mujić

ABSTRACT

Varicella-zoster virus (VZV) belongs to the group of alpha herpesviruses, and causes two epidemiologically and clinically distinct diseases, chickenpox or varicella as the primary VZV infection, while shingles respresents the endogenous reactivation of latent VZV infection, typically occuring in older individuals and rarely in younger ones. This is a case report of a 12-year-old boy who was hospitalized at the Clinic for Infectious Diseases at the University Clinical Center Tuzla, diagnosed with meningitis from February 20, 2023, to March 7, 2023. Cerebrospinal fluid analysis upon admission showed moderate pleocytosis with mild proteinorrhoea and hypoglycorrhoea. Cerebrospinal fluid was also subjected to microbiological analysis, which returned a positive PCR result for varicella-zoster virus. Laboratory findings showed stable parameters of inflammation throughout the hospitalization. Parenteral antiviral therapy (acyclovir ampoules) was initiated upon admission and continued for 14 days. Follow-up cerebrospinal fluid analysis showed significant improvement. The boy was discharged home in a recovered state with recommendations for follow-up tests and examinations. Varicella-zoster meningitis is a rare but serious and potentially life-threatening complication following primary infection with the varicella-zoster virus, particularly in immunocompromised patients with symptoms of CNS involvement.

Key words: Varicella-zoster virus, meningitis, immunological tests

Affiliations:
Clinic for Infectious Diseases,
University Clinical Center Tuzla,
Bosnia and Herzegovina

Received:
17.10. 2023.

Accepted:
14.01.2024.

Corresponding author:
Medina Mujić, MD
Clinic for Infectious Diseases
Tel: 38761424884
E mail: medina.mujic1@hotmail.com or
medina.mujic@ukctuzla.ba

Funding: none

Competing interests: none

INTRODUCTION

Varicella-zoster virus (VZV) belongs to the group of alpha herpesviruses and causes two epidemiologically and clinically distinct diseases, chickenpox or varicella as the primary VZV infection, while shingles represents the endogenous reactivation of latent VZV infection, typically occuring in older individuals and rarely in younger ones. [1] The course of the disease can be complicated by skin infection, neurological complications, pneumonia and hepatitis. [2] Central nervous system complications most commonly manifest as cerebral ataxia, meningoencephalitis and Reye's syndrome. Compared to enteroviruses and herpes simplex virus 1 (HSV-1) and 2 (HSV-2), which are among the most common causes of viral meningitis / encephalitis, VZV is one of the agents responsible for CNS infection. [3]

CASE REPORT

A 12-year-old boy was hospitalized at the Clinic for Infectious Diseases at the University Clinical Center Tuzla on February 20, 2023, with a diagnosis of meningitis, suspected to have a viral etiology. The illness began five days before admission with a headache, and two days before admission, he developed a fever, with the highest measured temperature being 38°C, along with vomiting. He did not have a cough, but his nose was congested. He had a reduced appetite, and his bowel movements and urination were normal. No other complaints were reported, and the boy had been relatively healthy until now. He had previously had chickenpox at the age of 3 and was regularly vaccinated. On admission, the boy was 12 years old, weighed 72 kg, was conscious, afebrile (36.5°C), had normal breathing, was hydrated, hypodynamic, and mobile. His skin was of normal color, with no rash. Palpable lymph nodes were not enlarged. His nostrils were only slightly congested. His lips and tongue were slightly dry, with no coating. His throat and tonsils were hyperemic but without exudates. Lung auscultation revealed normal breath sounds, with no pathological findings. Cardiac auscultation showed rhythmic

heart action, clear tones, and no murmurs. His abdomen was soft, non-tender upon palpation, and not enlarged above the level of the chest. The liver and spleen were not palpably enlarged. Kernig's sign was positive, but other meningeal signs were negative.

A lumbar puncture was performed on admission, which showed moderate pleocytosis with mild proteinorrhoea and hypoglycorrhoea (Table 1). Cerebrospinal fluid was collected for microbiological analysis, which returned a positive PCR result for varicella-zoster virus. Laboratory findings showed stable parameters of inflammation throughout the hospitalization, with leukocyte counts ranging from 6-8 x 10^9/L and CRP levels ranging from 3-8 mg/L. Parenteral antiviral therapy (acyclovir ampules) was initiated upon admission and continued for 14 days, along with symptomatic therapy.

During hospitalization, specifically on the second day after admission, the boy developed herpes zoster in the area of the right lumbar dermatome, which was not accompanied by severe pain, and the clinical picture of herpes zoster was milder (Figure 1). The boy was afebrile from the third day onwards, in good spirits, and without vomiting. An MRI of the brain showed no abnormalities, and the EEG showed moderately irregular alpha-type activity, with no focal findings or signs of current epileptic electrocortical activity. Cerebrospinal fluid analysis before discharge showed significant improvement (Table 1).

The boy was discharged home in a recovered state with recommendations for follow-up tests and examinations. He returned for a follow-up examination two weeks after discharge without complaints and with a normal physical examination. Considering that herpes zoster in children under 15 years is rare, it was decided to check the boy's immune status. Immune status tests were recommended in three months, all of which returned normal results (ANA screen, C3, C4, CIC, Beta2M, Ig - all fractions).

Table 1. Findings of cerebrospinal fluid.

Substance	Normal range	CSF on admission to the hospital	CSF before discharge from the hospital
Number of cells (x 10*6/ L)	0-5	826.00	80.00
Total proteins (g/L)	0.15-0.40	0.95	0.36
Glucose (mmol/L)	3.30-4.40	2.70	3.00
Chlorides (mmol/L)	110-130	127.00	127.00

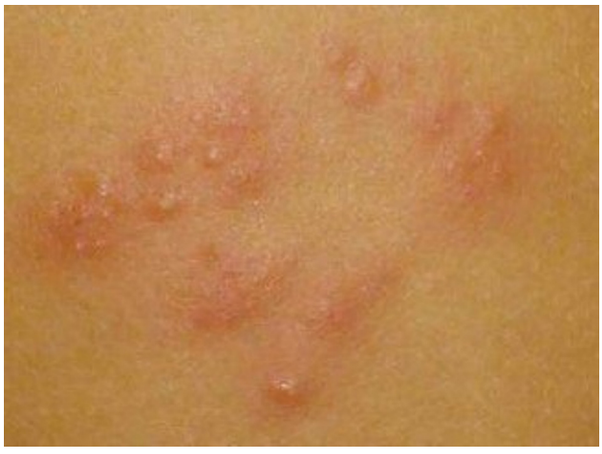

Figure 1. Herpes zoster.

DISCUSSION AND CONCLUSION

VZV is a virus that is widely distributed woldwide and is a common cause of CNS infection. The increasing incidence is likely due to improved diagnostic capabilities and more frequent clinical suspicions, even in the absence of skin lesions. Neurological consequences are not rare and can be serious even after proper treatment and recovery. [4] It is estimated that 0.01% to 0.25% of patients with chickenpox develop obvious neurological complications such as cerebellar ataxia, encephalitis, transverse myelitis, aseptic meningitis, polyneuritis, cranial neuropathies and Reye's syndrome. Neurological complications are more common during the herpes zoster phase. [5] Reactivation of VZV as a CNS infection is associated with a wide range of serious and potentially life-threatening complications, both in immunocompetent and immunocompromised patients, although it was initially considered a mild disease that only affected immunocompromised individuals. In the 1990s, complications of VZV CNS were considered rare. [6] VZV remains latent in sensory ganglion cells and can reactivate if cell-mediated immunity declines due to the patient's aging or the presence of immunosuppressive conditions. Therefore, VZV reactivation is rare in children. Eighty percent of patients with VZV encephalitis or meningitis have underlying immunosuppression. [7] Diagnosis required both typical skin lesions and specific neurological symptoms. However, VZV PCR in cerebrospinal fluid has led to a significant increase in cases, playing an essential role in CNS infections, especially in patients without skin lesions. [8] The incidence increases with age: 2.5 cases per 1000 patients in the 21–50 age range compared to 10.1 cases per 1000 patients in the >80 age range. Complications of VZV or herpes zoster CNS infection are poorly studied. Nevertheless, VZV has been reported as the main viral agent of CNS infection in the Swedish population, following tick-borne encephalitis. In patients with VZV CNS infection, VZV DNA has been detected in 0.5%-11.2% of CSF samples via PCR. [9-10]

VZV CNS infection is a progressive disease that is rarely fatal. [11] Reactivation of CNS presents a challenge for physicians. Clinical characteristics are diverse, nospecific and do not differ from other viral CNS infections. For every patient with encephalitis or suspected viral meningitis, the detection of VZV through PCR is recommended to appropriate antiviral treatment. [12-13] Polymerase chain reaction (PCR) allows for the detection of viral DNA and RNA in CSF samples with high sensitivity and specificity. Since isolating the virus and detecting intrathecal antibody production usually takes at least 10 days after symptom onset, PCR is the best technique for a rapid diagnosis and the initiation of correct treatment. [14]

Intravenous acyclovir at a dose of 10-15 mg/kg every 8 hours is the treatment of choice for VZV infection. The recommended duration of treatment is 14 days, but if there is suspicion or knowledge of compromised immune system function, treatment should be extended to 21 days. [15] In our case, intravenous acyclovir was administered for a total of 14 days, after which the child was discharged with a recommendation for symptomatic therapy.

VZV CNS infections are generally more common in immunocompromised individuals but do not exclude infections in immunocompetent individuals. In children, the most common CNS complication is cerebellitis, which can develop during primary infection. In adults, encephalitis and meningitis have a higher incidence than in children and usually occur after VZV reactivation. [9]

Reactivation of VZV in immunocompetent patients is not common, especially in childhood. Most cases reported in the literature involve adults, both for encephalitis [16] and meningitis, often associated with vesicular rash. [17, 18] The absence of vesicular rashes before or after CNS symptoms is rare. In one study of CNS complications of VZV in 84 children with neurological symptoms related to VZV infection, only two patients did not have a rash, despite a diagnosis of VZV meningitis confirmed by PCR analysis of CFS. [19]

In the case we described, we had a case of meningitis caused VZV reactivation in an immunocompetent child who did not exhibit the typical rash before but after CNS symptoms. Consequently, we decided to assess the complete immune status of the child, which returned normal results. In the available medical literature, we found three reported cases of meningitis due to VZV reactivation in the pediatric population in the absence of a weakened immune system, as described by Esposito S. and others in 2013., Yasuda R. and others in 2019., Oliveira K. and others in 2016. [20-22]The monovalent vaccine against the Oka/Merck strain of VZV was developed by Takahashi in Japan in the 1970s. The vaccine was registered in Germany and Sweden in 1984. In the United States, VZV vaccination was introduced into the national program in 1995, leading to a significant reduction in the incidence of VZV cases and the number of hospitalized patients (from 2.4 to 4.2/100,000 during 1995-1998 to 0.8/100,000 in 2005). [23] The average precentage of children vaccinated against VZV in the United States is around 80%, providing significant herd immunity, which also reduces the incidence of VZV cases. [24]

Therefore, we hope that with by introduction VZV vaccination in our region, the incidence of both primary infections and complications resulting from VZV infection, as well as the incidence and morbidity of CNS VZV infection, will decrease.

REFERENCES

1. Al- Turab M, Chehadeh W. Varicella infection in Middle East: Prevalence, complications, and vaccination. J Res Med Sci. 2018;23:19.
2. Gnann JW Jr. Varicella-zoster virus: atypical presentations and unusual complications. J Infect Dis 2022; 186 Suppl 1:S91
3. Alvarez JC, Alvarez J, Tinoco H et al. Varicella-Zoster Virus Meningitis and Encephalitis: An Understated Cause of Central Nervous System Infections. Cureus 2020; 12(11): e11583
4. Ciancia S, Crisafi A, Fontana I, De Fanti A, Amarri S, Lughetti L. Encephalitis due to herpes zoster without rash in an immunocompetent 12-year-old girl: case report and review of the literature. BMC Pediatrics 2020; 348
5. Espiritu R, Rich M. Herpes Zoster Encephalitis: 2 case reports and review of literature. Infectious Diseases in Clinical Practice 2007; 15(4):p 284-288
6. Frantzidou F, Kamaria F, Dumaidi K, Skoura L, Antoniadis A, Papa A. Aseptic meningitis and encephalitis because of herpesviruses and enteroviruses in an immunocompetent adult population. Eur J Neurol. 2008;15:995–997.
7. Mirouse A, Sonneville R, Razazi K et al. Neurologic outcome of VZV encephalitis one year after ICU admission: a multicenter cohort study. Annals of Intensive Care 2022; 12:32
8. DeBiasi RL, Tyler KL. Molecular methods for diagnosis of viral encephalitis. Clin Microbiol Rev. 2004;17:903–925.
9. Grahn A, Studahl M. Varicella-zoster virus infections of the central nervous system - prognosis, diagnostics and treatment. J Infect. 2015;71:281–293.
10. Herlin H, Hansen H, Bodilsen B et al. Clinical Infectious Diseases. 2020
11. Gilden D, Nagel M, Cohrs R, Mahalingam R. Varicella zoster virus in the nervous system. Baird N. F1000Res. 2015;4:1356.
12. McGill F, Griffiths MJ, Bonnett LJ et al. Incidence, aetiology, and sequelae of viral meningitis in UK adults: a multicentre prospective observational cohort study. Lancet Infect Dis. 2018;18:992–1003.
13. Calleri G, Libanore V, Corcione S, De Rosa FG, Caramello P. A retrospective study of viral central nervous system infections: relationship amongst aetiology, clinical course and outcome. Infection.2017;1:227-231.
14. Takahashi T, Tamura M, Takasu T. Diagnostic value of a "wide-range" quantitative nested real-time PCR assay for varicella zoster virus myelitis.J Med Virol.2013;1:2042–2055.
15. Bookstaver PB, Mohorn PL, Shah A, Tesh LD, Quidley AM, Kothari R, et al. Management of Viral Central Nervous System Infections: A Primer for Clinicians. J Cent Nerv Syst Dis. 2017;9:1–12

16. Mpaka M, Karantanas AH, Zakynthinos E. Atypical presentation of varicella-zoster virus encephalitis in an immunocompetent adult. Heart Lung. 2008;37(1):61–6.
17. Goyal H, Thakkar N, Bagheri F, Srivastava S. Herpes zoster meningitis with multidermatomal rash in an immunocompetent patient. Am J Emerg Med. 2013;31(11):1622
18. Kangath RV, Lindeman TE, Brust K. Herpes zoster as a cause of viral meningitis in immunocompetent patients. BMJ Case Reports. 2013;2013:bcr2012007575–5.
19. Chiappini E, Calabri G, Galli L, Salvi G, De Martino M. Varicella-zoster virus acquired at 4 months of age reactivates at 24 months and causes encephalitis. J Pediatr. 2002;140(2):250–1.
20. Esposito, S, Bosis, S, Pinzani, R, Morlacchi L, Senatore L, Principi N. A case of meningitis due to varicella zoster virus reactivation in an immunocompetent child. Ital J Pediatr 39, 72 (2013)
21. Yasuda, R, Minami, K, Ogawa, A et al. Herpes zoster and meningitis in an immunocompetent child: a case report. J Med Case Reports 13, 182 (2019)
22. Oliveira K, Fonseca J, Moreira D, Vila Real M. Varicella-zoster virus meningitis in an immunocompetent paediatric patient. Neurologia (Engl Ed). 2018 Nov-Dec;33(9):623-624
23. Kimberlin DW, Brady MT, Jackson MA, Long SS. Report oF the Committee on Infectious Diseases. American Academy of Pediatrics; 2015.
24. Marin M, Meissner H.C, Seward JF. Varicella prevention in the United States: a review of successes and challenges. Pediatrics. 2008; 122 (3):e744–e751.