Varicella Zoster Virus reactivation causing meningitis in a 12-year-old immunocompetent girl, a case report

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Abstract

Varicella-zoster virus (VZV) presents as chickenpox during primary infection. The virus becomes dormant in the dorsal root ganglia and can reactivate. Neurological complications of VZV reactivation have been described and may present without the typical herpes zoster rash. We present a case of a 12-year-old girl with persistent headache, photophobia, nausea, and vomiting. Cerebrospinal fluid showed lymphocytic pleocytosis and positive PCR for VZV. VZV meningitis is a rare diagnosis in immunocompetent children. However, our case suggests that sudden onset and persistent headache may rarely be caused by reactivation of VZV, even in the absence of a typical rash.

Introduction

Varicella-zoster virus (VZV), along with herpes simplex viruses 1 and 2, is a member of the alphaherpesvirinae subfamily. VZV can be spread by droplets from the upper respiratory tract or by direct contact and causes chickenpox as a primary infection. After primary infection, the virus becomes dormant in the dorsal root ganglia and cranial nerve ganglia. VZV can reactivate and the most commonly described disease is shingles (herpes zoster), a (painful) vesicular dermatomal rash. Reactivation of VZV is most common in elderly or immunocompromised patients (1).

Neurological complications have been described in both primary infection and reactivation of VZV. Possible neurologic complications of VZV reactivation include meningitis, encephalitis, transverse myelitis, large vessel encephalitis, and cranial nerve palsies. VZV reactivation can occur without the typical shingles rash, making PCR testing an important diagnostic tool (2).

Central nervous system infection from VZV reactivation can be difficult to recognize, especially if the disease presents without the typical shingles rash. In addition, VZV is often not recognized as a possible pathogen in an immunocompetent child or young adult. We present a case of a 12-year-old girl who presented with acute headache without rash or fever. A lumbar puncture revealed signs of meningitis, and PCR testing confirmed VZV as the causative agent.

Case

A 12-year-old girl presented to the emergency department with a 3-day history of persistent headache. There was no significant past medical history. She described the pain as throbbing and localized it to the frontal region. The pain was associated with nausea, vomiting, sonophobia and photophobia. She was afebrile, had a normal neurological clinical examination and no nuchal rigidity. There were no skin lesions present. Laboratory values showed no elevated markers of infection.

She was admitted for observation and symptomatic treatment of her headache. Intravenous tramadol hydrochloride, acetaminophen, ketorolac and alizapride had little effect. Because she did not respond to any of the medications, further investigations were indicated. The ophthalmologic examination with fundoscopy and the CT scan of the brain were both normal and showed no evidence of increased intracranial pressure. A lumbar puncture was performed because of persistent symptoms without a known cause and to rule out a treatable infection. Measurement of the opening pressure showed an increased intracranial pressure of more than 50 cmH2O (N < 28 cmH2O). Cerebrospinal fluid (CSF) cell count showed a lymphocytic pleocytosis (589 WBC/µL and 86% lymphocytes), elevated protein (0.71 g/dL, reference rang 0.15-0.45 g/dL) and low glucose (47 mg/dL N 40-80 mg/dL). PCR meningitis-encephalitis panel identified Varicella-zoster virus as the cause of meningitis. Brain MRI scan with angiography and EEG were normal. Additional serologic tests showed the presence of varicella zoster virus IgG, but no IgM. In depth history revealed that she had a primary infection with VZV when she was two years old.

Acyclovir was started for a period of 12 days and a good clinical response was seen after a few days. A repeat lumbar puncture on day 10 showed negative PCR for VZV, but the opening pressure measurement was not repeated. Follow-up at 6 months showed no sequelae.

Discussion

We present the case of a 12-year-old immunocompetent girl with persistent and debilitating headache, in whom VZV reactivation was surprisingly found in the central nervous system. Central nervous system complications of VZV reactivation in immunocompetent children and adolescents have been described in the literature, but are uncommon (3-8). The best known presentation of VZV reactivation is shingles with the typical (painful) vesicular dermatomal rash. Central nervous system complications may occur without the typical rash. A recent review of 25 cases shows that 24% of these children with VZV reactivation meningitis presented without the typical rash (9). This review included both VZV reactivations after natural infection as well as after vaccination. Our patient presented without nuchal rigidity. In a retrospective case series describing 11 patients with central nervous infection due to varicella reactivation were described, only 27% of the patients had nuchal rigidity (10).

Studies estimating the prevalence of VZV meningitis and encephalitis have been performed in recent years, but most have been conducted in an adult patient population and include immunocompromised patients. In a prospective Finnish study, 8% of the cases of aseptic meningitis or encephalitis were positive for VZV (11). A retrospective study of adult patients with a clinical diagnosis of viral meningitis or encephalitis showed that 2.1% of the CSF samples were positive for VZV(10). Both

studies were conducted in an adult patient population and one of the studies included only immunocompetent patients (11). Data on pediatric patients are scarce and the prevalence cannot be estimated.

VZV central nervous system infections are mostly seen in the elderly with declining cell-mediated immunity or in immunosuppressed patients. With recent advances in PCR diagnostic testing, VZV central nervous system infections due to reactivation are also seen in immunocompetent patients and even children. One known risk factor for the development of childhood zoster is a varicella infection during the first year of life, but our patient had chickenpox at the age of 2 years (12). Although new insights have been gained into the latency and reactivation of VZV, more needs to be discovered to fully understand why the virus reactivates (13).

Vaccination against VZV is performed with a live attenuated vaccine and after vaccination, the vaccine strain of VZV also becomes dormant in the dorsal root and cranial nerve ganglia. A study conducted in California from 2000 to 2006 reported a decreased risk of herpes zoster in vaccinated children (14). However, VZV reactivation can still occur after vaccination. An article reviewing vaccine safety in the United States with data from 1995 to 2005 reported 52 cases of herpes zoster in vaccinated individuals, 10 of which were confirmed to be due to vaccine strain VZV and 7 of which were due to wild-type VZV (15). In the remaining cases, the VZV was not further specified. Two of these cases had herpes zoster and meningitis and were confirmed to have vaccine strain VZV in their CSF. A recent review article comparing VZV reactivation meningitis after natural infection and after immunization showed that the reactivation meningitis occurred at a younger age and at a shorter interval after immunization (9). Most of the children in the review received only one dose of the vaccine. A two dose schedule is currently recommended.

In our patient, lumbar puncture showed an elevated opening pressure of > 50 cmH2O, but fundoscopy showed no signs of papilledema. Nitrous oxide was used during the procedure, which may cause an increase in intracranial pressure, especially in patients with altered intracranial compliance (16). There were no other factors that could increase the intracranial pressure during the procedure. The pronounced increase in intracranial pressure is unlikely to be entirely due to the use of nitrous oxide. An increase in intracranial pressure has been reported in the literature in patients with viral meningitis, particularly varicella and enterovirus meningitis (17, 18). In an observational retrospective study of patients with aseptic meningitis, 16 of the 116 patients had increased intracranial pressure, but only 40% had papilledema (18).

Cerebrospinal fluid (CSF- analysis showed lymphocytic pleocytosis with high protein and low glucose levels. This may also be associated with tuberculous meningitis. Therefore, the differential diagnosis may be more difficult, especially in regions where tuberculosis is endemic,. Although we expect lower CSF glucose levels in tuberculosis meningitis than presented in our case. However, low CSF glucose are also seen in other viral central nervous system infections such as West Nile virus, herpes simplex virus, cytomegalovirus and HIV infection (19).

The Infectious Disease Society of America recommends the use of acyclovir IV (10–15 mg/kg every 8 hours for 10-14 days) for VZV encephalitis (20). This recommendation is based on case reports and small case series, but no clinical trial has been conducted. There are no recommendations for VZV meningitis. However, the same therapy is initiated because of the potential morbidity and sequelae after a central nervous system infection with VZV. Data on the sequelae of VZV meningitis in the pediatric population are limited and further research is needed.

Conclusion

We have presented a case of an atypical presentation of meningitis with persistent headache, photophobia, nausea and vomiting, but without nuchal rigidity or vesicular rash. Our case highlights the need for further investigation in the setting of atypical, debilitating and persistent acute-onset headache. If no common cause is found in the initial investigations, PCR analysis must be performed. Our case shows that a sudden onset of persistent headache, even in absence of a typical rash is rarely caused by reactivation of VZV.

Conflict of interest

The authors have no conflicts of interest to declare with regard to the topic discussed in this manuscript.

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