Case report

The case of a 2-year-5-month-old boy with aseptic meningitis caused by Enterovirus 71

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Abstract Aseptic meningitis is caused predominantly by non-polio human enteroviruses, including Enterovirus 71 (EV71). Physicians who treat children with aseptic meningitis should always consider the possibility of EV71 causing infection, even without the presence of skin and mucocutaneous lesions. The authors report the case of a 2-year-5-month-old boy who presented with high-grade fever, vomiting and developed seizure. A cerebrospinal fluid test and magnetic resonance imaging of his brain revealed that he had aseptic meningitis. Supportive treatment and various antibiotics were prescribed at first, but the fever persisted. Finally, a polymerase chain reaction (PCR) test of his stool found that the causative agent was EV71. The patient stayed in hospital for 17 days and fully recovered without any neurological deficits. **Chiang Mai Medical Journal 2015;54(3):147-50.**

keywords: Aseptic meningitis, Enterovirus 71, children

Background

Enterovirus type 71 (EV71) is a common human virus associated with various clinical presentations ranging from asymptomatic, mild respiratory tract infections to severe and potentially fatal conditions[1,2] (e.g., aseptic meningitis, brainstem encephalitis, encephalomyelitis, acute flaccid paralysis, pulmonary edema, myocarditis, and cardiopulmonary failure)[3]. Neurological manifestations of EV71 occur mostly following herpangina and hand-foot-and--mouth disease, and may occur even without mucocutaneous lesions. Aseptic meningitis can lead to lethal sequelae such as encephalitis and status epilepticus. More than 80%[1,4,5] of aseptic meningitis cases in children are caused by the non-polio human enterovirus. Pediatricians should therefore be aware of this, in order to provide early diagnosis and prompt treatment.

Case presentation

A 2-year-5-month-old boy from northern Thailand was referred to Chiang Mai University Hospital (CMUH) with the chief complaint of prolonged fever (14 days) and seizure. He had been admitted to a rural hospital ten days before admission to CMUH with high-grade fever (40 ^{o}C) and four days of vomiting. His clinical state did not improve after two days of symptomatic treatment, so he then received ampicillin (100 mg/kg/day) and gentamicin (5 mg/kg/day). Three days later, he suffered altered consciousness, stiff neck and seizure

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development. He was intubated, prescribed diazepam with valproic acid and referred to a provincial hospital. A brain computerized tomography (CT) scan was unremarkable and so a lumbar puncture was performed. Cerebrospinal fluid revealed a white blood cell count of 280 cells/mm^3 (neutrophils 5%, lymphocytes 95%), protein of 68 mg/dL, sugar of 73 mg/dL (blood sugar of 136 mg/dL), negative gram stain, negative latex agglutination for *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus agalactiae* and negative cerebrospinal fluid culture. The antibiotics were changed to ceftriaxone (100 mg/kg/day) only one day after intubation because his consciousness was good and the seizures had discontinued. Two days before admission to CMUH, a repeated CT brain scan result was unremarkable, and chloramphenical was added to his treatment. However, the fever persisted and he was therefore referred to CMUH.

The child had no underlying condition. His prenatal and perinatal history was unremarkable. He had received a complete routine vaccination up to age.

On the day of admission to CMUH, he was febrile (38 ^{o}C), had normal blood pressure of 101/79 mmHg, pulse rate of 77 beats/min and respiratory rate of 30 respirations/min. He had good consciousness. Both pupils reacted to light (pupil size: 3 mm). He did not have nystagmus, facial palsy, or stiff neck. The motor examination revealed hyperreflexia (3+) of all extremities, equal movement of all extremities, no muscle weakness, and normal gait. The Babinski sign was dorsiflexion bilaterally.

Investigations

Laboratory investigations performed at the rural hospital revealed a complete blood count that noted haemoblobin (9.8 g/dL), haematocrit (23%), white blood cell count of 34,100 cells/mm^3 (neutrophils 86%, lymphocytes 13%, monocytes 1%) and normal platelet count. The electrolyte levels, renal function, and urine analysis were normal.

In laboratory investigations performed at CMUH, the blood culture was negative, but cerebrospinal fluid (CSF) revealed a white blood cell count of 256 cells/mm^3 (neutrophils 66% and lymphocytes 34%), protein of 185 mg/dL, sugar of 140 mg/dL (blood sugar of 123 mg/dL), negative gram stain, negative latex agglutination for *S. pneumoniae*, *N. meningitidis*, *H. influenzae* and *S. agalactiae*, negative herpes simplex virus (HSV) by polymerase chain reaction (PCR) and negative bacterial, tuberculous and fungal cultures. Immunofluorescene antibody (IFA) tests for scrub typhus and murine typhus, IgM and IgG, were negative. The magnetic resonance imaging (MRI) of the brain showed leptomeningeal enhancement of both the frontal and parasagittal areas. The stool PCR for EV71 was positive.

Differential diagnosis

EV71 aseptic meningitis

Treatment

Empirical treatment (meropenem: 120 mg/kg/day, vancomycin: 60 mg/kg/day and acyclovir: 1,500 mg/m^2/day) was given to the child at CMUH on his day of admission.

Outcome and follow-up

The fever subsided three days after admission to CMUH. The authors prescribed acyclovir as empirical treatment for five days, but then discontinued it because no evidence of HSV infection was found (HSV-PCR; negative). Vancomycin was given for 10 days, but stopped because the child developed a rash. Meropenem was given for a total of 14 days. The child recovered completely without any neurological deficits. The total duration of the hospital stay was 17 days.

Discussion

The patient presented with non-specific symptoms such as fever and vomiting. He had no previous upper respiratory tract infections or diarrhea. The physical examination was unremarkable and there was no sign of meningeal irritation. Afterwards, the child developed alteration of consciousness and seizure, which is why he was thought to have possible meningoencephalitis.

A previous study in Taiwan documented that 37% of children with EV71 infection had central nervous system involvement, and 17% of culture-confirmed EV71 infected children with central nervous system involvement had no previous skin or mucosal lesions[6,7]. The most appropriate imaging for identifying neurological involvement is MRI of the brain. In this case, the CT scan was normal, but a later MRI test revealed leptomeningal enhancement, indicating inflammation of the meninges and brain tissue.

The authors prescribed empirical antibiotic treatment because the child was thought to be in a severe condition and have an abnormal cerebrospinal fluid (CSF) profile. A condition of partially treated bacterial meningitis besides aseptic meningitis was considered as well. Generally, children with aseptic meningitis relate to EV71 and recover well. However, around 5% of patients may develop delayed cognitive functions in cases of severe central nervous system involvement such as encephalitis, encephalomyelitis and poliomyelitis-like syndrome[6].

Pediatricians should take care in observing children who come to the hospital with clinical symptoms of herpangina and hand-foot-mouth syndrome such as high fever, vomiting, lethargy, convulsion and ataxia, because such symptoms may stem from EV71 infections that can lead to neurological conditions, for example, aseptic meningitis or encephalomyelitis and cardiopulmonary infections[8].

In general, pediatricians should consider promptly prescribing intravenous immunoglobulin to patients with severe symptoms of neurological and cardiopulmonary conditions. However, the authors did not prescribe immunoglobulin to their patient because he had aseptic meningitis only. They therefore considered that supportive care and close monitoring would suffice in this case, in accordance with World Health Organization guidelines[8].

Learning points/take home messages

1. EV71 is a common human virus associated with various clinical presentations ranging from asymptomatic, mild respiratory tract infections to severe and potentially fatal conditions.
2. Neurological manifestations of EV71 occur mostly following herpangina and hand-foot-mouth syndrome, and possibly without mucocutaneous lesions.
3. Pediatricians should take care in observing children who come to hospital with clinical symptoms of herpangina and hand-foot-mouth syndrome such as high fever, vomiting, lethargy and ataxia, because such symptoms may stem from EV71 infections that can lead to severe neurological and cardiopulmonary infections.

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เด็กชายอายุ 2 ปี 5 เดือน เป็นเยื่อหุ้มสมองอักเสบจากเชื้อเอนโทโรไวรัส 71

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ภาวะเยื่อหุ้มสมองอักเสบ เป็นภาวะหนึ่งซึ่งสามารถเกิดขึ้นได้จากเชื้อเอนเทอโรไวรัส 71 สามารถพบได้ในเด็กเล็กที่มาด้วยภาวะมือเท้าปาก ผู้นิพนธ์รายงานเด็กชาย 1 ราย อายุ 2 ปี 5 เดือน มีอาการไข้สูง อาเจียน และชัก ผลการตรวจน้ำไขสันหลังและภาพถ่ายรังสี เข้าได้กับภาวะเยื่อหุ้มสมองอักเสบ ผู้ป่วยได้รับการรักษาจนหายเป็นปกติ และผลการตรวจพิเศษจากอุจจาระของผู้ป่วย พบเชื้อเอนเทอโรไวรัส 71 ผู้ป่วยรายนี้ได้รับการรักษาอยู่ในโรงพยาบาลเป็นเวลา 17 วัน และหายเป็นปกติ **เชียงใหม่เวชสาร 2558;54(3):147-50.**

คำสำคัญ: เยื้อหุ้มสมองอักเสบ เอนเทอโรไวรัส 71 เด็ก