2세의 건강했던 여환에서의 노로바이러스 소뇌염 1예

고려대학교 의료원 소아청소년과

정유진 · 이광철 · 김건하 · 은소희 · 은백린 · 변정혜

Norovirus Associated Cerebellitis in a Previous Healthy 2-year-old Girl

Norovirus causes acute gastroenteritis, occasional afebrile seizures, and rarely encephalitis. We describe a child with cerebellitis due to norovirus that has not been reported previously. A previously healthy 2-year-old girl with a recent history of acute gastroenteritis, who presented with acute cerebellar ataxia. She exhibited marked truncal ataxia, was barely able to walk, and was prone to sitting or lying down. Multiplex PCR using stool samples revealed norovirus (genogroup II) and magnetic resonance imaging showed increased T2 signal in the hemi-cerebellum. Norovirus may be a potential pathogenic cause of acute cerebellitis in children.

Key Words: Norovirus, Child, Cerebellitis

Lindsey Yoo Jin Chung, MD, Kwang Chul Lee, MD, PhD, Gun-Ha Kim, MD, PhD, So-Hee Eun, MD, PhD, Baik-Lin Eun, MD, PhD, Jung Hye Byeon, MD, PhD

Department of Pediatrics, Korea University College of Medicine, Seoul, Korea

Introduction

Norovirus is the predominant viral etiological agent of acute gastroenteritis across all age groups, although it is most prevalent in young children and the elderly. Noroviruses are recognized as the second most frequent cause of diarrhea in children following rotaviruses, and are a common cause of food-borne disease worldwide. Among the central nervous system diseases, noroviral infection has been reported to be associated with meningitis and encephalitis; however, its association with pure acute cerebellitis has not been documented previously. The common infectious agents associated with acute cerebellitis are the Epstein-Barr virus (EBV), varicella zoster virus (VZV), rotavirus, *Mycoplasma*, and the human herpesvirus-6. Here we describe a case of acute cerebellitis associated with a noroviral infection and discuss its pathogenesis.

Case Report

A 2-year-old girl visited a local hospital due to fever, diarrhea, and rashes on her skin and mouth, and was managed conservatively. Her symptoms subsided after a few days. A day after the gastrointestinal symptoms, she developed ataxia and gait disturbance, she could barely use her right hand, she tended to sit or lay down, and she was less talkative. She still showed ataxia after 10 days, and was

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Correspondence to Jung Hye Byeon, MD, PhD
Department of Pediatrics, College of Medicine, Korea University, 73, Inchon-ro, Seongbuk-gu, Seoul 02841, Korea

Tel: +82-2-920-5090, Fax: +82-2-922-7476

E-mail: byeonagnes@naver.com

admitted to the Korea University Hospital, Anam, at this time for evaluation and management. She was born at 37 weeks by caesarean section owing to a placental abruption, weighting 2,740 g, and had no medical history except for a mild language delay with vocabulary of only 30 words.

A physical examination at the time of admission revealed that she was afebrile and alert, and poorly cooperative due to irritability. A general examination showed no abnormal findings. In a neurological examination, she showed no tremors of the upper extremities, but could barely use her right hand, and exhibited truncal ataxia along with a gait disturbance. She had a motor grade 3–4/5 (Medical Research Council scale)¹⁾ in the lower extremities. Reflex testing revealed normal deep tendon reflexes and a negative Babinski reflex.

Laboratory tests showed mild leukocytosis (13,500/mL) with 37.5% neutrophils, 2.2% eosinophils, 6.4% monocytes, 53.1% lymphocytes, and 0.8% basophils. Her electrolyte levels and liver function test results were normal. The inflammatory markers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were 9 mm/hr and 0.48 mg/L, respectively. A cerebrospinal fluid (CSF) analysis showed 2 leukocytes/ μ L, a protein level of 21.6 mg/dL, and a glucose level of 58 mg/dL. A multiplex real time PCR with anyplex TM II RV16 detection kit (V1.1, Seegene, Seoul, Korea) that can detect sixteen viruses (human adenovirus, bocavirus 1/2/3/4, corona virus OC43/229E/NL63, enterovirus, influenza A/B, metapneumovirus, parainfluenza 1/2/3/4, rhinovirus A/B/C and RSV A/B) on a CSF sample revealed all negative results. Results of serological tests for *Mycoplasma pneumoniae*-specific immunoglobulin M revealed negative and EBV viral capsid antigen (VCA)-IgM, and VZV IgM were negative. While a herpes simplex virus (HSV) IgM test result was equivocal (0.97, positive >1.2, negative <0.8), results of CSF PCRs for HSV type I and II were negative. A multiplex-PCR with a Seeplex Diarrhea-V ACE Detection kit (Seegene, Seoul, Korea) that can detect four viruses (rotavirus, norovirus, enteric adenovirus, and astrovirus) on a stool sample revealed positive results for norovirus (genogroup II), suggesting a noroviral infection. Magnetic resonance imaging (MRI) of the brain showed asymmetrically high T2 signal intensity with leptomeningeal enhancement of the right cerebellar folia, suggestive of acute cerebellitis (Fig. 1). In diffusion imaging, high signal intensity was showed on B-1000 image but normal on ADC may be T2 shine through effect which means cerebellar edema other than diffusion restriction.

The patient was diagnosed with acute cerebellitis associated with a norovirus infection and was administered steroid pulse therapy with IV methylprednisolone (30 mg/kg/day) for 3 days and maintained with PO prednisolone (2 mg/kg/ day) for 3 more

days, which was then tapered off. Her physical and neurological symptoms improved and she was discharged two weeks later. A follow-up MRI performed 2 months after discharge showed improvements (Fig. 2).

Discussion

Acute cerebellar ataxia is a syndrome characterized by the acute onset of ataxia ranging from a few days to a few weeks after an acute febrile illness²⁾. Gait disturbance is the primary symptom, and associated symptoms may include nystagmus, slurred or garbled speech, vomiting, dysarthria, and headache. Ataxia is observed following many infectious diseases including infections due to varicella zoster virus, EBV, enterovirus, rubella, parvovirus, and *Mycoplasma*. However, reports of ataxia following vaccinations are rare. Varicella zoster virus is most often involved among these infections. The pathogenesis of ataxia remains unclear, although emerging evidence suggests that an autoimmune mechanism may be involved as antiviral antibodies and autoreactive antibodies against brain tissue have been detected in CSF of patients^{3–5)}. In contrast, in some cases, viral nucleic acids have

Fig. 1. Magnetic resonance imaging (MRI) of the brain axial revealed asymmetry T2 high signal intensity with leptomeningeal enhancement at the right cerebellar folia, suggestive of acute cerebellitis (Black arrowheads).

Fig. 2. Follow up brain MRI improved 2 month later (White arrowheads).

been detected in the CSF, suggesting a direct viral invasion of the central nervous system²⁾. Our case is compatible for postinfectious cerebellitis which is one of the causes of acute cerebellar ataxia.

Central nervous system manifestations including encephalopathy and seizures have been reported in association with norovirus infection⁶⁻⁸⁾; however, acute cerebellitis associated with norovirus infection has not been reported before. In a few cases of norovirus-associated neurological disorders, viral RNA has been detected in the CSF with PCR^{6,7)}. In acute cerebellar ataxia, however, results of CSF examination are oftentimes normal or non-specific, usually showing only mild lymphocytic pleocytosis and elevated protein content⁹⁾.

In our patient, norovirus was detected in a stool specimen by a multiplex-PCR test. No other abnormal findings were detected even in the CSF sample. Even though we did not perform a multiplex-PCR test on the CSF for norovirus, results of other CSF analyses were well within the normal range indicating that the mechanism for acute cerebellar ataxia may not involve direct viral invasion. Furthermore, the detection rate of noroviral RNA in CSF is very low. A recent investigation reported that the sialic acid-containing glycosphingolipids (gangliosides) are ligands for human noroviruses, suggesting a new mechanism of human

norovirus-host interaction that may affect the gangliosides in the brain¹⁰⁾. Some other studies have reported the pathophysiology of acute cerebellar ataxia based on MRI and single-photon emission computed tomography findings that are comparable with our MRI findings here¹¹⁻¹³⁾.

We treated the patient with high dose steroid because symptoms lasted more than 10 days. Conventional treatment for acute cerebellar ataxia is supportive and clinical re-evaluation should be done two to three weeks after the initial presentation. There are a few case reports of treatment of refractory cases with glucocorticoid¹⁴⁻¹⁶⁾ or intravenous immune globulin (IVIG)^{17,18)} but prospective clinical trials are lacking. Our patient showed good prognosis, high dose steroid could be one of the consideration for treatment however, there should be more studies needed.

요약

노로바이러스는 급성 위장관염을 일으키는 바이러스로써, 간헐적으로 비열성 경련을 일으키며 드물게 뇌염을 발생시킨다. 하지만 노로바이러스에 의한 급성 소뇌염은 보고된 바가 없다. 우리는 발병 전 건강했던 급성 장염의 병력이 있던 2세 여환에서 보인 급성 소뇌 실조증에 대하여 보고하고자 한다. 환아는 명확한 체간 운동 실조(truncal ataxia)를 보였고, 거의 걷지 못하였으며, 앉거나 누워있으려는 성향을 보였다. 병원 입원 기간 동안 흔하게 알려진 바이러스 및 세균 검사에서 음성소견이나 환아의 변으로 시행한 Multiplex-PCR 상 Norovirus (genogroup II) 소견을 확인하였다. 또한 뇌의 자기공명영상 소견 상 소뇌 반구에서 T2 high signal을 보였다. 노로바이러스는 소아에 있어 급성 소뇌염의 잠재적인 발병원인으로 고려해볼 수 있다.

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