

Clustering seizures associated with rotavirus gastroenteritis in a two-month-old infant

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Abstract. We present a case of 2-month-old infant with clustered convulsions and transient lactic acidosis associated with mild gastroenteritis caused by rotavirus. This is an unusual age for infection-related seizures. Rotavirus RNA was detected by RT-PCR in both fecal and cerebrospinal fluid (CSF) samples and were genotyped as G1 and G1(P8), respectively.

Key words: rotavirus, gastroenteritis, seizures, infant.

1. Introduction

Rotavirus A, the most common cause of diarrhea in children worldwide, is responsible for high morbidity and mortality rates (1). On the other hand, benign infantile seizures associated with mild gastroenteritis were first described in Japan by Morooka (2) in 1982. Since then several series of cases have been reported both in Asia and elsewhere (3-7) and it is now recognized as a clinical entity characterized by non-febrile convulsions, usually in clusters without dehydration or electrolyte imbalance. It generally occurs in previously healthy children between 6 months and 4 years old within the first 48 hours of the infectious process. However, in up to 40% of cases convulsions may be present before the onset of gastroenteritis (7). Laboratory findings including blood glucose level, serum electrolytes,

and cerebrospinal fluid analysis are typically normal, as are electroencephalography and other neuroimaging studies. The disease has a benign prognosis and only occasionally has required anticonvulsant therapy (8).

2. Case report

He was a previously healthy, single son, 2-month-old male infant. Parents were healthy. He was admitted to the hospital with a history of two episodes in the last three hours of abnormal eye movements, inward deviation of the eyes, and generalized hypotonicity with no response to stimuli, lasting three to four minutes each. While in the emergency room, he developed two more episodes consisting of forced eye deviation, generalized hypotonicity and lack of response for two minutes. The crisis finished without treatment. Physical examination between episodes was otherwise normal and he had no fever. He was admitted to the pediatric unit where 12 hours later he developed diarrhea without vomiting or fever.

Laboratory investigations found his white cell count, level of electrolytes and C reactive protein, as well as blood biochemistry, to be normal. The urine analysis showed pH= 8 with negative toxic detection. The cerebrospinal fluid (CSF) sample, obtained by lumbar puncture, revealed a cell

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count of 6/ μ L, protein 53 mg/dL, glucose 64 mg/dL and lactic acid of 3.1 mmol/L (normal range: 0.6-2.2 mmol/L). Blood lactic acid was 6.7 mmol/L (normal range 0.5-2.2 mmol/L), confirmed with two measurements, but was normal in a few hours (value prior to discharge of 1.3 mmol/L). Venous blood gas values were pH 7.28, bicarbonate 19 mmol/L and pCO₂ 26. The serum ammonia levels and the anion gap, as well as the aminoacids and organic acids in the CSF, were all normal as were the cranial ultrasonography and the electroencephalogram findings. As we suspected infection-related convulsions, a long term anticonvulsant therapy was considered unnecessary. The patient had no fever throughout his hospital stay and no further seizures occurred. He was discharged five days after admission. The disease outcome was satisfactory with normal neurological development during follow-up over the next six months.

2.1. Microbiological study

Group A rotavirus antigen was detected in a stool sample by an immunochromatographic assay (ICT, Vikia®, BioMérieux, France) in the hospital Microbiology laboratory. No enteropathogenic bacteria (*Salmonella sp*, *Shigella sp*, *Campylobacter sp* and *Aeromonas sp*) were detected by conventional culture methods. Fecal and CSF samples were sent to the reference laboratory (Viral Gastroenteritis Unit, Spanish National Centre for Microbiology, ISCIII, Madrid) to be tested for rotavirus by using RT-PCR. RNA was initially extracted from 140 μ L of clarified 20% -PBS stool suspensions or undiluted CFS with the QIAamp Viral RNA Extraction kit (QIAGEN GmbH, Germany) and strictly following product manufacturer instructions. The 60- μ L RNA eluates were stored at -20°C until the amplification of nucleic acids was performed. PCR were realized as described previously by Iturriza-Gomara et al (9). The CSF sample yielded a positive result for rotavirus genotype G1P(8). In the stool sample the G1 genotype was also identified, while the result for the P genotype was non-conclusive.

3. Discussion

Rotaviruses are the most common agents associated with benign seizures, although noroviruses have also been implicated as an important trigger of this condition (2). The prevalence of neurological manifestations has been estimated in 2-5% of children with rotavirus gastroenteritis, including encephalitis, encephalopathy and epileptic seizures (10). These

complications may reflect the high frequency of rotavirus gastroenteritis and fever in young children at risk of seizures or be the result of a direct invasion of central nervous system (7-11). The fact that two-thirds of children with seizures and rotavirus gastroenteritis present without fever, hypoglycemia or electrolyte abnormalities confirm that this virus can invade the CNS (9). This theory is also supported by the detection of virus RNA or antigens in the blood, stools and CSF of children with rotavirus gastroenteritis accompanied by seizures (12,13). These authors suggest that rotavirus may spread from the gastrointestinal tract into the blood and then to the CNS. However, the pathophysiology of the extra-intestinal rotavirus dissemination and the significance of RNA virus detection in CSF is not well understood and more studies are needed (14-16).

Other authors have attempted to explain how rotavirus could damage the CNS without direct invasion. Inflammation is known to be responsible for a growing number of acute and chronic neurological diseases. Although the role of inflammation in the pathogenesis of epilepsy and epileptic seizures has only been recognized recently, the production of cytokines and related molecules has already been implicated in experimental animal models and in humans (11,13). Further, the response of catastrophic epilepsy to steroids has been attributed to the pathogenic role of the inflammation, and several infectious and autoimmune diseases are associated with epileptic seizures. Although encephalitis can not be demonstrated, our case supports direct invasion of the rotavirus in the CSF as the main pathophysiological explanation for the seizures. Nevertheless, we think that in the future more studies must be done in order to explain the pathogenic mechanism of this type of crisis.

In any case, the prognosis of these seizures is favorable and, in the majority of patients, long term anticonvulsant treatment is not necessary to control the convulsions. This process must be recognized and suspected in very young infants like our patient (two months old) in order to avoid unnecessary studies and treatments. This is one of the youngest children reported with seizures and mild gastroenteritis. Only recently, a baby of 1 month of age has been described (17). Both cases support the idea that this type of crisis could also appear in very young infants.

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