CASE REPORT

Convulsions with Gastroenteritis in a Toddler: A Case Report and Literature Review

Emily M. Beydler, BS[1]; Jaclyn Otero, MD2; Molly Posa, MD[2]; Alexandra M. Stern MD[2]
[1]University of Florida College of Medicine
[2]University of College of Medicine, Department of Pediatrics

ABSTRACT

Gastroenteritis can cause seizures in children through a variety of mechanisms. One underrecognized etiology is convulsions with gastroenteritis (CwG) which are seizures in the presence of a normal neurological exam, serum electrolytes, glucose, and cerebral spinal fluid in a previously healthy child with normal neurological development. We present the case of a 15-month-old previously healthy male with vomiting and diarrhea who developed tonic-clonic seizures within 36 hours of gastroenteritis symptoms. He presented to the Emergency Department for seizure activity and was hospitalized. Continuous electroencephalogram monitoring revealed focal seizure origin in the right central parietal region. After unsuccessful trials of lorazepam and levetiracetam, the patient progressed to status epilepticus, requiring fosphenytoin administration. During hospitalization, his gastrointestinal pathogen PCR panel detected norovirus: given his unsuccessful response to typical anti-epileptic medications, CwG was considered. Previous case reports discussing CwG patients have demonstrated seizure resolution with carbamazepine; therefore, lorazepam and levetiracetam were discontinued, and the patient was started on carbamazepine at 12 mg/kg/day. After the initiation of carbamazepine treatment, the patient had no additional seizures. He was discharged after four days. He has regularly scheduled follow-up appointments with Neurology and remains seizure-free on carbamazepine treatment. The long-term neurodevelopmental prognosis for patients with CwG is highly favorable and has not been shown to increase the risk for future neurological disorders, including epilepsy.

BACKGROUND

Seizures in children are commonly associated with gastroenteritis through multiple etiologies, including fever, metabolic abnormalities, or brain inflammation resulting in encephalitis or encephalopathy.[1–3] Another distinct cause is convulsions with gastroenteritis (CwG). Though no formal definition exists, CwG is diagnosed clinically as mild gastroenteritis with afebrile seizures in the absence of electrolyte imbalance, acidosis, or hypoglycemia, with viral detection in the stool and normal electroencephalogram (EEG) and cerebrospinal fluid (CSF), if collected, in previously healthy children with normal neurological development and neurological exam.[4]

PRIMARY OBJECTIVE

Pediatricians should recognize the unique presentation, diagnosis, and treatment of CwG and its favorable neurodevelopmental prognosis.

SUBJECT PRESENTATION

A 15-month-old male with no past medical history presented to the emergency department (ED) with generalized tonic-clonic seizures. He had been seen 36 hours prior in the ED for recurrent episodes of non-bloody, non-bilious emesis. At that time, the patient was afebrile, tolerated oral hydration, and was discharged with a prescription for ondansetron 2 mg every 8 hours to manage his emesis. The following day, he remained afebrile but developed non-bloody diarrhea. Two days after his gastrointestinal symptoms started, he collapsed while playing followed by shaking of his extremities for approximately one minute, with a brief episode of apnea and perioral cyanosis from which he recovered spontaneously. The patient's parents immediately brought him to the ED for evaluation. The patient was not taking any medications other than the prescribed ondansetron, and his immunizations were up to date. He had no personal or family history of allergies nor a family history of seizures. His review of systems was negative for fever, anorexia, sleep disturbance, hematochezia, hematuria, abdominal distension, irritability, rash, cough, or congestion.

On arrival to the ED, vital signs were obtained: blood pressure, 98/59 mm Hg; pulse, 109 beats/min; respiratory rate, 22 breaths/min; and SpO2, 95% on room air. His examination demonstrated no focal neurological deficits, and he displayed normal tone and strength.

Laboratory studies showed no electrolyte abnormalities or abnormal blood counts. While in the ED, he had another episode with tonic-clonic movements in the extremities, right eye deviation, and perioral cyanosis, followed by hypersomnolence. The child was given intravenous (IV) levetiracetam 20 mg/kg (later increased to 30 mg/kg) and oral acetaminophen. He was hospitalized for further evaluation and management of new-onset seizures in the setting of gastroenteritis.

While admitted, the child continued to have recurrent seizures. He was placed on continuous EEG monitoring and required a one-time IV dose of lorazepam 0.1 mg/kg for persistent seizure activity. The EEG demonstrated that the patient's seizures lasted an average of 50 seconds, with spikes arising in the right central parietal region with contralateral spread followed by generalized spread. No interictal abnormalities were found, and the rest of the EEG was normal for his age. Given the focality of the seizures, an MRI was obtained, which was normal without structural abnormalities.

The child's seizures progressed to status epilepticus, requiring bag-mask ventilation and IV fosphenytoin (20 mg/kg). A stool sample was sent, and the gastrointestinal pathogen PCR panel detected norovirus. At this point, CwG was suspected, prompting a change in his anti-epileptic medication to carbamazepine 5 mg/kg. There is medical literature supporting the efficacy of carbamazepine in CwG patients.[5] At a Neurology follow-up appointment as a 27-month-old, the patient has remained seizure-free since discharge and remains on carbamazepine.

DISCUSSION

Convulsions with gastroenteritis (CwG) were first reported in Japan in 1982 and are predominantly diagnosed in Asia in children with norovirus or rotavirus.[4] The first reported cases in the United States occurred in 1994 and were of three patients in California, with later cases in Arizona and Maryland.[6,7]

CwG has been identified in children ages one month to six years, with an average age between one and two years old.[8] In a study of 140 patients diagnosed with CwG, the average interval between the development of enteric symptoms and seizure onset was 2.11±1.14 days.[9,10] Most seizures in CwG are generalized, but complex partial seizures and focal features such as lateral eye deviation, which occurred in our patient, have also been reported.[4] Typically, EEG findings in CwG are benign, but slow waves, focal spikes, and cortical epileptiform discharges have been observed.[2] The majority of patients with CwG have no imaging abnormalities.[3] Lumbar puncture is considered unnecessary and not recommended in suspected CwG patients.[2]

Several studies have demonstrated the efficacy of low-dose carbamazepine in treating patients with CwG: unlike most cases of childhood seizures, treatment with benzodiazepines, phenobarbital, and levetiracetam is typically less effective.[3,11] In a prospective observational study of 126 CwG patients in Japan, carbamazepine was the most effective treatment, with all patients remaining seizure-free who received it.[5] While the mechanism for this effect is unknown, other studies have corroborated this finding.[3] Furthermore, the pathogenesis of CwG is not currently understood. Some studies have proposed that a genetic mechanism may be involved. However, no mutations or single nucleotide polymorphisms have yet been identified, including sodium channelopathies, given carbamazepine's inactivation of voltage-gated sodium channels.[12]

Additionally, children diagnosed with CwG typically have no family history of epilepsy.[8] Another proposed mechanism in patients with CwG is the direct or indirect central nervous system infiltration by the virus. Both norovirus and rotavirus can cross the blood-brain barrier resulting in encephalitis and encephalopathy in susceptible individuals. Since CwG has not been identified in children older than six, further research is needed to investigate the relationship between CwG and the vulnerability of the developing brain.[8]

The long-term neurological prognosis for patients with CwG is highly reassuring. An Italian study followed 81 patients for at least three years, and none developed epilepsy.[13] Additionally, in most CwG cases, chronic anticonvulsant therapy is unnecessary.[13] On follow-up after discharge, all patients diagnosed with CwG had normal EEG findings.[2,3]

In conclusion, a previously healthy child with new-onset seizures following gastroenteritis who presents with normal vital signs, exam, and laboratory studies, CwG should be suspected. Treatment of CwG with carbamazepine is highly efficacious and yields a favorable neurodevelopmental prognosis.

REFERENCES

1. Nardone R, Brigo F, Trinka E. Acute symptomatic seizures caused by electrolyte disturbances. *J Clin Neurol*. 2016;12(1):21-33.
2. Castellazzi L, Principi N, Agostoni C, Esposito S. Benign convulsions in children with mild gastroenteritis. *Eur J Paediatr Neurol*. 2016;20(5):690-695.
3. Ueda H, Tajiri H, Kimura S, et al. Clinical characteristics of seizures associated with viral gastroenteritis in children. *Epilepsy Res*. 2015;109:146-154.
4. Kang B, Kim DH, Hong YJ, Son BK, Kim DW, Kwon YS. Comparison between febrile and afebrile seizures associated with mild rotavirus gastroenteritis. *Seizure*. 2013;22(7):560-564.
5. Higuchi Y, Kubo T, Mitsuhashi T, et al. Clinical epidemiology and treatment of febrile and afebrile convulsions with mild gastroenteritis: A multicenter study. *Pediatr Neurol*. 2017;67:78-84.
6. DiFazio MP, Braun L, Freedman S, Hickey P. Rotavirus-induced seizures in childhood. *J Child Neurol*. 2007;22(12):1367-1370.
7. Iyadurai S, Troester M, Harmala J, Bodensteiner J. Benign afebrile seizures in acute gastroenteritis: is rotavirus the culprit? *J Child Neurol*. 2007;22(7):887-890.
8. Kang B, Kwon YS. Benign convulsion with mild gastroenteritis. *Korean J Pediatr*. 2014;57(7):304-309.
9. Kim BR, Choi GE, Kim YO, Kim MJ, Song ES, Woo YJ. Incidence and characteristics of norovirus-associated benign convulsions with mild gastroenteritis, in comparison with rotavirus ones. *Brain Dev*. 2018;40(8):699-706.
10. Kim YO. Benign Convulsions with Mild Gastroenteritis. *Ann Child Neurol*. 2020;28(1):2-7.
11. Khosroshahi N, Rahbarimanesh A, Boroujeni FA, Eskandarizadeh Z, Zoham MH. Afebrile benign convulsion associated with mild gastroenteritis: A cohort study in a tertiary children hospital. *Child Neurology Open*. 2018;5:2329048X18773498.
12. Yamashita S, Okumura A, Yamamoto T, Shimojima K, Tanabe T, Shimizu T. SCN1B is not related to benign partial epilepsy in infancy or convulsions with gastroenteritis. *Neuropediatrics*. 2011;42(4):135-137.
13. Verrotti A, Moavero R, Vigevano F, et al. Long-term follow-up in children with benign convulsions associated with gastroenteritis. *Eur J Paediatr Neurol*. 2014;18(5):572-577.