Neurological Manifestations in Rotavirus Gastroenteritis in Children Under two Years of Age

Rotavirus infection is usually localized to the intestine but involvement of central nervous system (CNS) has been reported along with norovirus and adenovirus. The pre-valence of neurological manifestations is 2-5% in children with rotavirus gastroenteritis, which includes encephalitis, encephalopathy and epileptic seizure [1,2]. In addition, rotavirus is known to cause mild encephalopathy/encephalitis with a reversible splenial lesion (MERS), acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) and acute necrotizing encephalopathy (ANE) in children [3]. Convulsions associated with gastro-enteritis are yet to be recognized as an epilepsy syndrome or situation-related seizures by the International League Against Epilepsy (ILAE) [4]. In spite of high incidence of rotavirus gastroenteritis, there are very few reports on child-ren presenting with acute gastroenteritis (AGE) and neuro-logical symptoms, its etiology and clinical outcome from our country [5].

A total of 57 children with acute gastroenteritis and neurological manifestations were screened for rotavirus between October, 2013-May, 2016 and 12 were found to have rotavirus in stools. Of these, we report four children in whom rotavirus RNA was detected both in stool and (CSF) samples. The four children had history of convulsion and passage of loose watery stool 8-10 times in a day with no dehydration, but had (single/multiple) episodes of febrile/afebrile convulsions. Seizure semiology was sequential progression from non-motor (behavioral arrest) to motor (multi focal clonic) seizures. Sleep EEG showed genera-lized rhythmic high amplitude theta activity over a normal background. Three children under 6 months of age were exclusively breastfed; one child under 6 months of age had similar history of diarrheal episode in her family. All three children had normal anthropometric measures. Serum electrolytes were within the normal range in all the patients (**Table I**).

CSF was collected by lumbar puncture and examined for routine biochemistry, cell type, cell count and was also tested for rotavirus by nucleic acid based molecular assays (RT-PCR) for VP7 gene (G type). We collected stool samples in McCartney bottles using sterile catheters and examined the samples within 2 hours for enteric pathogens comprising bacterial, viral and parasitic pathogens using conventional, immunological and molecular methods. Stool samples were tested for bacteria (salmonella, shigella, aeromonas, vibrio, campylobacter, *E. coli*) parasites (Giardia and entameba) and viruses (group A and adenovirus 40/41). The samples negative for bacterial and parasitic pathogens were tested for viral pathogens. Both stool and CSF samples were screened by immune-chromatography for the presence of enteric adenovirus and group A rotavirus VP6 antigen. The presence of viral genome was confirmed by amplification of rotavirus VP7 gene (G genotype) by conventional RT-PCR method in both stool and CSF samples. Rotavirus RNA was present in stool and CSF of all four children.

All the patients were receiving oral rehydration solution at home, before admission, and did not have dehydration at presentation. Oral antibiotic was prescribed at primary health care level. Antipyretic and anti-emetic was given for fever and vomiting. Adequate hydration was maintained, the course was benign and longterm anti-seizure medicine was not required. All the patients improved within 5-7 days and no fatality was reported.

We also observed that 66.7% (8/12) children with rotavirus infection with negative rotavirus RNA in CSF did not have seizure during the second episode of fever. In this aspect an important hypothesis is the pathomechanism of low-grade inflammation (encephalopathy) by the Rotavirus itself. Minami, et al. [6] measured the elevation of serum IL-6 and TNF-α, CSF IL-6 and IL-8 levels and suggested encephalopathy as a consequence to systemic immune response to cytotoxicity. Another possible explanation is increased concentration of carnitine in CSF reported in some cases, which may damage blood brain barrier. Alternatively, shared peptide hormones between the brain and the gastrointestinal tract, associated with spontaneous electrical epileptogenic activity and lowered seizure threshold seen in some adults, could be a contributing factor to the occurrence of afebrile convulsions during gastroenteritis [7]. More studies are needed to understand the pathophysiology of afebrile seizures in gastroenteritis. Moreover, concomitance of febrile and afebrile convulsions to rotavirus gastroenteritis are reported as 1.2-6.4% [8]. Thus, it is important to identify other probable causes for convulsions, other than electrolyte imbalances, destruction of blood-brain barrier by fever or encephalopathy and encephalitis [8].

Further evaluation may be needed to understand the pathogenesis in our case, which could possibly be because of some inflammation due to systemic immune response to cytotoxicity. Rotavirus encephalitis is a complication that is not

Table I Clinical Characteristics of Children With Rotavirus Diarrhea and Neurological Manifestation With Detection of Group A Rotavirus (GARV) Gene in Stool and Cerebrospinal Fluid (CSF)

Case	*Age/sex*	*Presenting history*	*Fever*	*Biochemical test*	*Cerebrospinal fluid (CSF) analysis*	*Rotavirus VP7 (G type)*	
						Stool virology	*CSF*
1	4 mo/F	Diarrhea,vomiting, drowsiness	Afebrile	Na - 136 mmol/L K-3.8 mmol/L Ca- 9.2 mg/dL Glucose- 96 mg/dL	Glucose-64 mg/dL Protein-86 mg/dL Cells-10/µL	Positive G9	Positive (G Typing NT)
2	3 mo/F	Diarrhea, convulsion	Febrile	Na -142 mmol/L K-4.1 mmol/L Ca-9.5 mg/dL Glucose- 120 mg/dL	Glucose-80 mg/dL Protein-75 mg/ dL Cells-8/µL	Positive G1	Positive G1
3	5 mo/F	Diarrhea, convulsion	Febrile	Na -139 mmol/L K-4 mmol/L Ca-9.3 mg/dL Glucose-80 mg/dL	Glucose- 55 mg/dL Protein- 60 mg/dL Cells- 12/µL	Positive G1	Positive (G Typing NT)
4	14 mo/M	Diarrhea, convulsion	Febrile	Na-140 mmol/L K- 4.2 mmol/L Ca-9.6 mg/dL Glucose-95 mg/dL	Glucose-65 mg/dL Protein- 100 mg/dL Cells-20/ µL	Positive G1	Positive G1

M: male; F: female; Na: sodium; K: potassium; Ca: calcium; NT: non typable.

so rare as is evidenced from reports. We recommend that rotavirus etiology should be investigated for in children having seizures during episodes of gastroenteritis.

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