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NEUROLOGIC MANIFESTATIONS OF ACUTE GASTROENTERITIS: A REVIEW OF 45 PATIENTS IN THE INTENSIVE CARE SETTING

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ABSTRACT

Acute gastroenteritis (AGE) is a serious disease and is one of the most important causes of early childhood mortality in developing countries. The neurologic manifestations can be propounded as primary symptoms of AGE.

In order to determine the rate, clinical presentations, and outcome of patients with AGE who presented with neurologic manifestations and compare them with patients without neurologic symptoms, we reviewed the records of children 1 month to 14 years of age having AGE along with neurologic presentations, i.e. either convulsion or encephalopathy alone or together who had been admitted to the pediatric intensive care unit (PICU) of the Children's Hospital Medical Center (CHMS) from September 1996 till August 1998.

Among all the patients admitted at that time, 7% (75 patients) had AGE, of which 60% (45 patients) had concomitant neurologic symptoms including 4% who had convulsion alone, 20% had encephalopathy alone, and 36% showed both of the symptoms.

Of the patients who had AGE with neurologic symptoms, 36% initially presented with neurological manifestations without gastrointestinal symptoms. The duration of admission at PICU and the mortality rate among patients with AGE were significantly more in the patients with neurologic symptoms in comparison to those without neurologic symptoms.

According to our findings, neurologic symptoms may be the first manifestation of AGE and are likely to increase the risk of mortality in AGE.

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Keywords: Gastroenteritis; acute, convulsion, encephalopathy.

INTRODUCTION

AGE has a global distribution. It remains one of the major causes of childhood morbidity and mortality in developing countries.[1,2,3] The neurologic symptoms are among the frequent manifestations of AGE reported in 5% to 45% of children with AGE.[4,5,6,7] Neurologic symptoms include lethargy, confusion, irritability, headache, convulsion, and stupor or coma.[4,5] The neurologic manifestations often precede the appearance of diarrhea and can mislead the clinician to diagnose primary central nervous system (CNS) diseases.[4] In this study, we reviewed 75 patients who were severely ill enough to be hospitalized due to AGE at the PICU with focus on neurologic manifestations.

MATERIAL AND METHODS

We retrospectively evaluated records of the patients,

between 1 month of age to 14 years of age, admitted during the period of September, 1996 to the end of August 1998 at the PICU of CHMC who were diagnosed with AGE. Seventy-five patients had AGE of whom 45 had neurologic symptoms. Neurologic manifestations were divided into three groups: convulsion alone, encephalopathy alone, and encephalopathy and convulsion together. Encephalopathy was defined as a complex of at least two of the following symptoms on admission: irritability, severe headache, lethargy, and decreased level of consciousness. Convulsions were verified either on the basis of the history taken on admission or during the course of hospitalization. None of the patients had a previous history of any kind of neurological disorders. Demographic data, presenting sings and symptoms, laboratory results and the final outcome were reviewed and compared between the patients with neurologic symptoms and the patients without neurologic symptoms.

RESULTS

Among the 1040 patients who were admitted at the PICU of CHMC, 75 cases (7%) were affected by AGE; 45 of them had neurologic symptoms. In other words, 60% of the patients with AGE had neurologic manifestations: 4% had convulsions alone, 20% had encephalopathy alone, and 36% had both convulsions and encephalopathy. Most of the patients in this group (48%) were within one to four years of age who were admitted more frequently during the summer (51%). The mean age of children with neurologic manifestations was less than the other group (2.5 vs. 3.1), without a statistically significantly difference (P value= 0.08) (Table I). It seems that the mean age of children with convulsions alone was significantly lower in comparison with patients without neurologic symptoms and those with encephalopathy alone but the number of the patients was too little for further conclusion. The mean duration of encephalopathy was 2.8 days and there were 2 episodes of seizures in average among the patients with convulsions. The length of PICU admission was significantly less among patients without AGE (3.2±2.1; 1-7 days) in comparison to children with neurologic symptoms (5.6±3.4; 1-16), but no differences were detected within the former groups. By contrast, no significant differences in terms of sex, mean age, or laboratory findings were recorded between patients with neurologic symptoms and without neurologic symptoms (Table I and II). The clinical manifestations of the patients are summarized in Table II.

The duration of illness was less among the children with neurologic symptoms in comparison with the groups without neurologic presentations and was most likely less than 48 hours in the groups with convulsion alone compared to the group with encephalopathy alone. 69% of the patients with AGE had fever above 39°C at the time of admission. This character was seen more in the group with neurologic findings and also in the children with convulsion alone, but statistical analysis wasn't significant among them (P value= 0.12).

Bloody diarrhea and signs of dehydration were detected in 5% and 59% of the patients respectively, which were not significant among the children with or without neurologic symptoms and also within the three groups of patients with neurologic symptoms.

The paraclinical findings of these patients are summarized in Table III. The biochemical and hematologic findings were not significantly different among the patients without neurologic symptoms and the group of patients with neurologic symptoms. Although CSF (cerebal spinal fluid) examination was abnormal in 12% of the patients, the CSF culture was positive in only one case which was Klebsiella, and blood culture was also positive for the same organism. This patient was a six-month-old boy who was admitted with convulsions and encephalopathy without response to supportive therapy who died on the second day of admission.

7% of the patients had positive stool cultures with Shigella spp. All of this group of patients had neurologic symptoms and were slightly more prominent in the group with convulsion and encephalopathy. They were also in the younger age group, i.e. less than 4 years of age.

Table I. Main characteristics of patients with acute gastroenteritis with and without neurologic symptoms.

Main Characteristics	Patients without neurologic symptoms No= 30 40%	Patients with neurologic symptoms No= 45 60%	P value
Mean age (yr)	3.1±4.2	2.5±4.7	NS*
Duration of illness before hospitalization (day)	3.3±4.1	1.8±2.3	<0.05
Length of PICU stay (day)	3.2±2.1	5.6±3.4	<0.05
Final outcome (death)	2(3%)	13(17%)	<0.05

*NS: not significant, *p* value >0.05

Although all patients had received antibiotic and supportive therapy, the mortality rate was significantly different among the patients without neurologic symptoms in contrast to the other groups (2 vs. 13) (p value= 0.01). The mortality rate was also higher among the young children with either convulsion alone or convulsion with encephalopathy who had positive cultures.

DISCUSSION

AGE is usually characterized by diarrhea, abdominal pain, fever, and vomiting. Other manifestations such as sepsis, acute abdomen, seizure, and encephalopathy are also reported.[4,8,9] Neurologic manifestations have often been reported in the course of AGE.[4,5,10] In particular, convulsions and encephalopathy have been the first presentations of young children affected with infectious organisms such as *Shigella* spp, *Salmonella* spp, *Rotavirus*, *Echovirus* infection, and during *Escherichia coli* 0157 associated hemolytic uremic syndrome.[11] Their incidence, however, ranges in different reviews as varying from 5% to 45%.[4,5,6] Our survey of children with AGE includes only the patients who were admitted to the hospital with clinical symptomatlogy severe enough to be hospitalized in the intensive care unit. Therefore, the study is limited to selected patients with AGE. In this group of 75 patients, 4% had convulsions and 56% had different neurologic manifestations that we defined as encephalopathy either with or without convulsion. The rate of convulsion alone was less in our study in comparison with the report from the Middle East, in which among 117 patients with AGE, 53% had neurologic symptoms: 11% had convulsion alone, 22% had encephalopathy alone, and 20% had convulsion and encephalopathy.[4]

The mechanism involved in the development of convulsion and encephalopathy in gastroenteritis is poorly understood. Direct invasion of the central nervous system by the organism is very rare and was positive in only one of our paitents.[4,12] Fever itself has been implicated as a cause of neurologic manifestations, with rapidly in-

Table II. Comparison between patients with acute gastroenteritis with and without neurologic symptoms regarding neurologic manifestations.

Main Features	Patients without neurologic symptoms		Patients with neurologic symptoms							
			Convulsion alone		Encephalopathy alone		Convulsion & Encephalopathy		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Patients	30	40	3	4	15	20	27	36	75	100
Sex										
Male	18	24	2	3	9	12	15	20	44	59
Female	12	16	1	1	6	8	12	16	31	41
Age (yr)										
<1	9	12	2	3	3	4	7	9	21	28
1-4	14	19	1	1	9	12	13	17	37	49
5-10	7	9	-	-	2	3	7	9	16	22
>10	-	-	-	-	1	1	-	-	1	1
Duration of Illness (hr)										
<48	13	17	3	4	5	7	14	19	39	52
>48	17	23	-	-	10	13	13	17	43	57
Fever (39°C)	17	23	3	4	11	15	21	28	51	69
Dehydration	16	21	2	3	10	13	16	21	44	59
Bloody diarrhea	1	1	1	1	-	-	2	3	4	5
Final outcome (death)	2	3	2	3	4	5	7	9	15	20

Table III. Paraclinical findings among the patients with acute gastroenteritis with and without neurologic symptoms regarding neurologic manifestations.

Main Features	Patients without neurologic symptoms		Patients with neurologic symptoms							
			Convulsion alone		Encephalopathy alone		Convulsion & Encephalopathy		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
WBC; 15000(mm³)	10	13	3	4	6	8	15	20	34	45
Na (mEq/L)										
<130	3	4	1	1	2	3	3	4	9	12
>150	2	3	1	1	1	1	4	5	9	12
Blood sugar (mg/dL)										
<50	1	1	-	-	-	-	1	1	2	3
>150	2	3	1	1	-	-	1	1	4	5
Abnormal LP*	1	1	2	3	2	3	4	5	9	12
Positive culture										
Blood	1	1	-	-	-	-	1	1	2	3
CSF	-	-	-	-	1	1	-	-	2	3
Stool	-	-	1	1	1	1	3	4	5	7

*LP; Lumbar puncture was done only for 34 cases. (Abnormal LP was defined as at least one of these findings: CSF sugar<2/3rds blood sugar, CSF protein>45 mg/dL or CSF leukocyte count>5).

creasing temperature causing convulsions in susceptible children.[4,11,13]

High fever was the most common presenting symptom in our study where the mean age of the children with convulsion was less than the mean age of the patients with encephalopathy alone (1.9 yr vs. 5.4 yr). However, the possibility of encephalopathy accompanying AGE, due to neurotoxin secreted by the organism directly affecting the nervous system without invasion, may play a major role in the development of gastroenteritis especially in the younger age group with a relatively large absorptive area of the gastrointestinal tract.[14,15] Nearly 2/3rds of our patients with neurologic symptoms were less than four years old. Disturbances of electrolytes and blood sugar are often mentioned as the possible contributing factors in the neurologic mainfestations of AGE which had been seen occasionally in our patients without any difference between the two groups with or without neurologic manifestations.

The neurologic manifestations preceded the gastrointestinal symptoms in 36% of our patients, which was reported to be 24-30% in other studies.[4,9,11] This emphasizes the difficulty in making the correct diagnosis during the admission.

Finally, the duration of symptoms before hospitalization was less and the length of the intensive care unit stay was more in the patients with neurologic symptoms than in those without. Furthermore, the mortality rate was higher among patients with neurologic symptoms. This number was greater in our study than other studies due to the severity of the illness among our patients who were admitted to the PICU.[4,6,16,17]

In conclusion, our data show the importance of neurologic symptoms in children with AGE. Physicians should be alert to the relatively high frequency of neurologic manifestations in childhood AGE, as it may be the initial presentation, requiring early diagnosis and appropriate management to improve the outcome.

REFERENCES

1. Hoeklman RA: Diarrhea happens, a lot. Pediatr Annals 23: 523-4, 1994.
2. Glass RI, Lew JF, Gangarosa RE, et al: Estimates of mortality and morbidity rates for diarrheal diseases. J Pediatr 188: 527-533, 1991.
3. Hifshitz F: Introduction to management of acute diarrheal disease. J Pediatr 118: 525-526, 1991.
4. Avital A, Maayan C, Goiten KJ: Incidence of convulsions and encephalopathy in childhood shigella infections. Clinical Pediatr 21: 645-648, 1982.
5. Ashkenazi S, Dinari G, Wietz R, et al: Convulsions in

shigellosis: evaluation of possible risk factors. Am J Dis Child 137: 985-987, 1983.
6. Wong V: Acute gastroenteritis-related encephalopathy. J Child Neurol 16: 906-910, 2001.
7. Teka T, Fruque ASG, Fuchs GJ: Risk factors for deaths in under-age-five children attending a diarrhea treatment center. Acta Paediatr Inf 85: 1070-1075, 1996.
8. Lubis NU, Sinuhaji AB, Sutanto AH: Factors influence the mortality of children with gastroenteritis at the pediatric ward of Dr. Pringadi hospital, Medan. Paediatr Indones 31: 1-8, 1991.
9. Cimolai N, Morrison BJ, Carter JE: Risk factors for central nervous system manifestations of gastroenteritis associated hemolytic-uremic syndrome. Paediatr 90: 6116-21, 1992.
10. Bennish LM, Harris RJ, Wojthniak BJ, Struelens M: Death in shigellosis: incidence and risk factors in hospitalized patients. J Infect Dis 161: 500-506, 1990.
11. Tositti G, Fabris P, de Lalla F: Incidence, risk factors, and clinical significance of neurologic symptoms in patients with acute gastroenteritis. AJG 94: 3078-3079, 1999.
12. Bhutta ZA, Punjwani N, Lindblad BS: Concomitant bacteraemia as a risk factor for diarrheal disease; mortality in Karachi. Acta Pediatr 85: 8099-113, 1996.
13. Hanato CF, Huttly SK, Yeager BAC: Diarrhea: reflections from studies in a shanty town. Pediatr Infect Dis J 17: 7-9, 1998.
14. Ashkenazi S, Dinari G, Zevulunov A, et al: Convulsions in childhood shigellosis: clinical and laboratory features in 153 children. Am J Dis Child 141: 208-210, 1987.
15. Goren A, Freier S, Passwel JH: Lethal toxic encephalopathy due to childhood shigellosis in a developed country. Pediatr 89: 1189-1193, 1992.
16. Bennish CM: Potentially lethal complications of shigellosis. Rev Infect Dis 13 (Suppl 4): 5319-5324, 1991.
17. Plotz FB, Arets HG, Fleer A, et al: Lethal encephalopathy complicating childhood shigellosis. Eur J Pediatr 158: 550-552, 1999.