Prevalence of Neurological Complications Caused by Shigellosis in Children Hospitalized at Qom Children Hospital

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ABSTRACT: This descriptive cross-sectional study attempted to determine the prevalence of neurological complications caused by shigellosis at Qom Children Hospital. The study was conducted March 2010 to June 2012 on 1 month to 12-year old children with diarrhea hospitalized at Qom Children Hospital in whose stool culture Shigella was detected. Results were analyzed by using SPSS 13. Of 312 patients with shigellosis admitted to Qom Children Hospital within the March 2010 to June 2012, 55 (16.7%) had neurological complications, of whom 54 experienced seizures and one was diagnosed with acute encephalopathy caused by Shigellosis with Ekiri syndrome. The male and female prevalence ratios were identical, and nearly the same ratios were observed among the patients with respect to neurological complications. Results revealed that seizures were the most common neurological complication caused by shigellosis at Qom Children Hospital, and demanded serious attention in order to prevent the seizure-related complications.

Keywords: Shigellosis, neurological complications, seizure, children

INTRODUCTION

Many microorganisms can cause diarrheal diseases; however, Shigella has been identified by the World Health Organization (WHO) as the most important cause of diarrhea (1-2). Shigella refers to facultative anaerobic gram-negative bacteria from the Enterobacteriaceae family. The swallowing of as few as 100 basillus can cause infection (3). Shigella is also the most common cause of bacterial dysentery, which accounts for half a million
deaths among children under 5 years of age, and causes growth disorders and malnutrition (4-7). It is estimated that 164.7 million people worldwide become infected with Shigella, and approximately 1.1 million death develop from shigellosis every year (4-5).

Shigella is a highly prevalent disease among children aged 6 months to 10 years living in tropical regions including Iran (8). Since the pathogenic Shigella bacillus can produce two types of toxins (i.e. intestinal toxin and Shiga toxin), there is a wide range of complications such as gastroenteritis and extra digestive system manifestations (seizures, encephalopathy, paraplegia and eventually lethal toxic encephalopathy) (9-10). Neurological complications are the most common extra-intestinal manifestations caused by shigellosis (10-11). They cover a broad range of symptoms such as headache, memory impairment, confusion, lethargy, delirium and hallucination, seizures, reduced awareness, and coma, all of which can be signs of acute encephalopathy caused by Shigellosis. Seizures and cognitive disorders are well-known events that occur during Shigella infection. Previous studies suggested that a history of seizures and cognitive disorders were associated more with Shigellosis than with other pediatric infections (11-12).

Studies show that increased temperature and Shigelllosis-caused metabolic disorders set the ground for seizures. Moreover, hyponatremia, hypoglycemia, hyperkalemia, and increased creatinine levels have been suggested as factors contributing to cases of encephalopathy caused by Shigelllosis. The duration of Shigelllosis-caused acute encephalopathy has been reported to range from 12 hours to 12 days. Full neurologic recovery is often attainable, even though a fatal form of encephalopathy called Ekiri syndrome may occur in certain cases. This form is often very acute, and is usually accompanied by reduced awareness, coma and, sometimes, death (12-13). Considering the remarkable prevalence of Shigellosis in children admitted at hospitals and children's wards, and given its coincidence with a variety of neurological complications, this study intended to examine the prevalence of shigellosis-caused neurological complications and factors that influence them.

METHODS AND MATERIALS

This was a descriptive cross-sectional study conducted from March 2010 to June 2012 (for 26 months) on children aged 1 month through 12 years, hospitalized because of diarrhea at Qom Children Hospital, and in whose stool culture shigella was detected.

Having submitted their consent to participate in the study, the patients were examined in terms of age, history of seizures, family history of seizures, body temperature at onset of seizures, incidence rates of neurological symptoms prior to intestinal symptoms and prevalence of leukopenia or leukocytosis.

The stool samples taken from the patients were collected in special disposable containers to isolate the Shigella bacteria, and were put in Cary Blair transport medium in anticipation of delays in sending the samples to the laboratory.

After collection, the samples were microscopically examined for consistency, color, mucus, and blood, and the wet mount technique was employed to check the presence of five red and white blood cells per high-power field (14). The samples were then placed on a growth-expanding broth medium, and after 6 hours were transferred to selective and differential media such as MacConkey agar (MAC), XLD, Salmonella Shigella agar, and Hektoen enteric agar. After incubation for one day at 37°C, the samples were evaluated in terms of bacterial growth and colony formation (15).

The cultured bacteria were examined using morphological assessment, Gram staining, oxidase, catalase, mobility, citrate, TSI, indole, methyl red, Voges–Proskauer (VP), urea, ornithine decarboxylase, lysine decarboxylase and arginine dehydrogenase tests (13). The results were finally analyzed by SPSS 13.

RESULTS

Of the 312 patients with shigellosis admitted to Qom Children Hospital within the 26 months, 55 (16.7%) had neurological complications, of whom 54 experienced seizures and one was diagnosed with acute encephalopathy caused by Shigelllosis who exhibited the Ekiri syndrome.

The mean age of the children under study was 3.5 years (17.6% under 1 year, 64.8% between 1 and 5 years, and 17.6% over 5 years of age).

The mean age of children with seizures was 2 years: 1.5 years lower than the average for children without neurological symptoms (3.5 years). The majority of children with seizures (56%) were less than 1 year old (between 6 months and 1 year old), 29.5% over 5 years old, and 14.5% from 1 to 5 years old.

The male and female prevalence ratios were almost identical (F/M=1.1), with nearly the same ratio in relation to neurological complications (F/M=0.9).
Among children with neurological complications, there were 14 (25%) with a history of focal seizures (FC), and 10 (18%) with a positive family history.

All the children with seizures, except one with body temperature of 36.5°C, had fever and body temperature ranging from 37.5 to 41 °C (38.6 °C on average).

In 18 out of 55 cases (33%), seizures started prior to intestinal symptoms, and were regarded as the initial manifestation of the disease. The interval between seizures and the onset of diarrhea in this group varied from approximately 6 hours to 48 hours. In three of the 55 cases (5%), focal seizures were the only manifestation of the disease and no cases of diarrhea were observed.

The WBC count showed a wide range, from leukopenia to leukocytosis (2200-34000), but the white blood cell count was in the normal range in most patients. Moreover, the prevalence of leukopenia was 31 out of 257 (12%) among children unaffected by neurological complications, and 6 out of 55 (11%) among children with seizures: there was no significant difference between the two groups with regard to prevalence of leukopenia.

**DISCUSSION**

In a study conducted at Mofid Hospital (in Tehran) in 1991, diarrhea and fever occurred in 98.4 percent and seizure in 36.5 percent of patients, which were consistent with the findings of the current study and with international statistics (16). Furthermore, the rate of neurological complications was 80%, of which seizures were more prevalent (43.08%). Moreover, given that history of seizure or febrile seizure was reported in only 21.14% of the subjects, it could be concluded the major causes of such complications in children with shigellosis were the presence of Shiga toxin (and its elevated levels) in peripheral blood (16).

The rate of acute epileptic encephalopathy with continuous spike-waves in our study was 15.38%, which is different from the statistics presented in the relevant literature. The reasons for this difference were the fact that only hospitalized patients were studied in this research, and suspicious movements of children were misinterpreted by their parents and by the medical personnel. Therefore, the medical personnel must be trained to recognize the various forms of this type of encephalopathy (16).

In an eight-year study carried out in Thailand during 1895-1993 on a total of 694 children with positive culture Shigella, about 45% of patients were children less than 4 years old. Moreover, the most frequent neurological symptom was fever (70%), febrile diarrhea (40%), and accompanying neurological symptoms (20%), which was lower than what we observed in our study (17). Moreover, 15 of the children died (12 with Ekiri syndrome, while in our study one child who exhibited the Ekiri syndrome died, and 3 from other causes). It should be noted there was no significant relationship between Ekiri syndrome and a history of seizures or cerebral palsy observed in this study (P>0.05) (17).

Our results suggest that seizures were the most common neurological complication caused by Shigellosis. Moreover, the mean age of the affected children and the high body temperature in almost all of them (98% over 37.5 °C and 77% over 38 °C) indicate the probable role of both factors in the occurrence of seizures. This confirms the results of previous research. As for the history of seizures and a positive family history, however, these two risk factors seemingly did not aggravate Shigellosis because the majority of patients with seizures lacked such medical history.

Thirty three percent of the patients showed the neurological symptoms prior to the intestinal symptoms (particularly the 5 percent in whom previous focal seizures were the only clinical sign of Shigellosis), and the rate of Shigellosis was relatively high. Therefore, it is important that initial stool culture be performed for all patients who visit hospitals and complain of focal seizures to better diagnose the potential cases and prevent incorrect diagnoses.

Concerning the possible relationship between leukopenia and the prevalence of neurological symptoms in patients with shigellosis, the results of this study revealed no significant differences in the prevalence of leukopenia between the groups with neurological symptoms and the group without them. The WBC approach is probably an unreliable measure for predicting the probability of occurrence of neurological complications in these patients. However, some studies point out that time plays an effective role in the extensive variations observed in WBC counts of patients with Shigellosis. Moreover, they suggest there is a natural course of immunological responses in the body against the gradual penetration of Shiga toxins into the bloodstream that is identical in almost all patients and varies from leukopenia to leukocytosis. Furthermore, they attribute the different results obtained for samples taken from the patients to differences in the time the CBC test is requested for them.

Considering what was said above, it is recommended that further studies with larger sample sizes be conducted to study more accurately the relationship between factors causing complications resulting from...
shigellosis, and the relationships between demographic factors, race, economic status of the family, levels of personal hygiene, etc., and development of shigellosis.

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