

Case Report

Fulminating Shigella Encephalopathy (Ekiri Syndrome): A Case Report

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Kuwait Medical Journal 2007, 39 (4): 369-372

ABSTRACT

Neurological manifestation, particularly seizures and encephalopathy, are common in childhood shigellosis. Fulminating shigella encephalopathy (Ekiri syndrome) is a rare form of shigella associated encephalopathy characterized by a rapid, severe and fatal course with few dysenteric symptoms. Brain edema is a common finding in patients presenting with severe shigella encephalopathy. Shiga toxin production is not essential for development of shigella-associated neurological symptoms. Early recognition and proper management

of cases of severe shigella encephalopathy may help to improve the outcome. We are reporting the case of a six and half year old male child with severe fulminating shigella-encephalopathy (Ekiri syndrome) who made a partial recovery. Brain magnetic resonance image (MRI) findings of this patient are reported. To the best of our knowledge, brain MRI studies were not reported before in the pediatric population with Ekiri syndrome; moreover, this is probably the first case of Ekiri syndrome to be reported in the Arab population.

KEY WORDS: brain edema, convulsions, Ekiri syndrome, encephalopathy, shigellosis

INTRODUCTION

Shigellosis is a common infectious disease especially in underdeveloped countries. The inflammatory process of acute shigella infection affects the colon and is characterized clinically by fever, cramping abdominal pain with frequent loose stools that might contain mucus, pus and blood.

Four serogroups (or species) of shigella have been described including group A (*Shigella dysenteriae*), group B (*Shigella flexneri*), group C (*Shigella boydii*) and group D (*Shigella sonnei*). These groups are further classified into serotypes and sub-serotypes.

Shigella organisms are highly virulent. A very small inoculum - as little as ten microorganisms - can cause disease in humans^[1].

Case history

A six and half year-old boy with unremarkable previous medical history presented with fever of 38.5 °C and repeated vomiting of one day duration.

During examination, he looked fully conscious, alert with stable vital signs (blood pressure of 105/60 mmHg and a heart rate of 110/min). His systemic review was unremarkable with no signs of meningeal irritation.

He was admitted to the hospital for observation and commenced on intravenous fluids and antipyretics.

Six hours later, the child started to pass frequent, loose, smelly motions that were not mixed with mucus or blood. By that time he was looking ill with depressed sensorium and high fever (39.5 °C).

Laboratory tests showed low serum sodium level of 129 mmol/l. Otherwise his electrolytes, sugar, liver enzymes, lactate and blood ammonia levels were all normal. Toxicology screening came negative.

Soon, the child developed two seizure episodes, 10 minutes apart; both were aborted by intravenous (iv) diazepam, and he was kept on continuous phenytoin infusion. Central nervous system (CNS) infection was suspected and the child was maintained on iv ceftriaxone and acyclovir. The child suddenly developed cardio-respiratory arrest. He was immediately resuscitated with endotracheal intubation and was shifted to the intensive care unit (ICU).

Brain computed tomography (CT) showed generalized brain edema (Fig. 1) that was managed with iv mannitol, hyperventilation and head elevation.

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Fig. 1: Non-enhanced CT brain at the level of mid-brain shows features of cerebral edema with effacement of CSF spaces

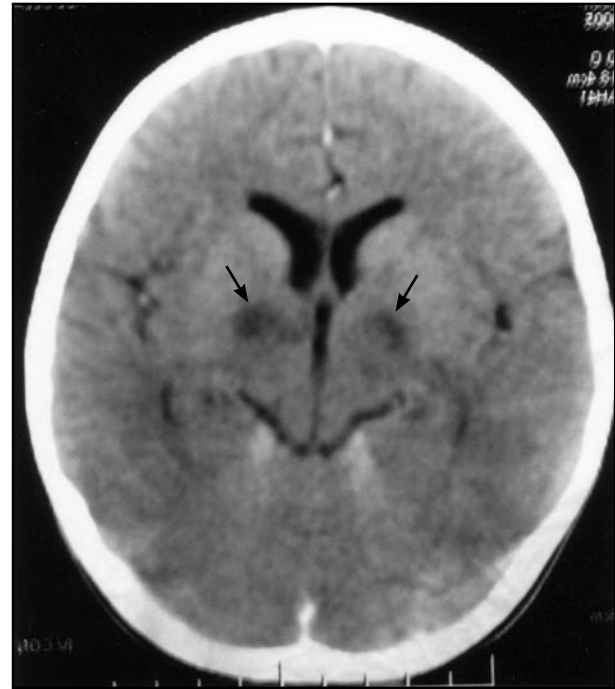


Fig. 2: Contrast-enhanced CT brain shows non-enhancing low attenuation areas in thalami and basal ganglia bilaterally

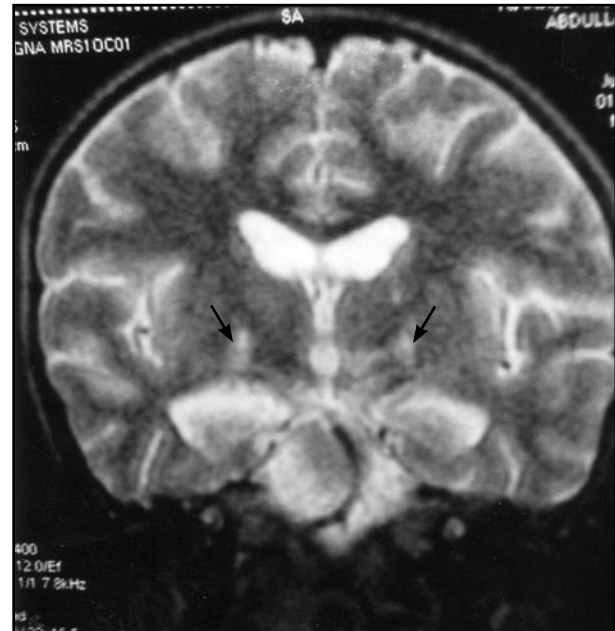
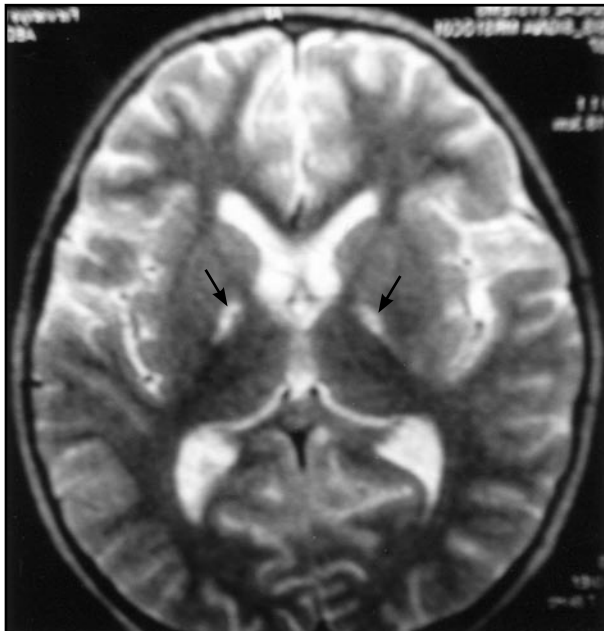


Fig. 3 (a & b): T2-weighted axial (3a) and coronal (3b) MRI brain images showing multiple lesions of high signal intensity in thalamic, basal ganglia and internal capsule regions bilaterally

Subsequent examination of the cerebrospinal fluid (CSF) was unremarkable with negative blood, urine and CSF cultures. Serology study for viruses was also negative. Stool cultures collected on admission grew *Shigella sonnei*.

Screening for metabolic disorders was negative. Electroencephalogram (EEG) showed a slow background activity with active focus of slow sharp waves in both temporo-parietal areas. *Shigella*-associated encephalopathy was assumed. CT brain

on the sixth day after admission showed resolution of the brain edema with bilateral hypodense areas in both thalami and basal ganglia (Fig. 2). The child could be extubated on the eighth day after admission.

His level of consciousness slowly improved. Two weeks after admission, he was able to open his eyes spontaneously and showed a good response to verbal stimuli. However, he developed hypertonia and hyperreflexia with very poor muscle power. By

that time he could be shifted to a general pediatric ward where an intensive physiotherapy program was started.

MRI brain done four weeks after admission showed multiple lesions in the area of basal ganglia, thalami and internal capsule bilaterally (Figs. 3 a & b).

Six weeks later, he was able to sit and stand with support, recognize his mother's face and swallow fluids and soft food without choking or aspiration. He was then discharged home.

Ten weeks later, he could recognize most family members; he was able to say few words. Both muscle tone and reflexes were increased in the four limbs and this was more evident on the left side, with some dystonic movements in the upper limbs.

Muscle power improved in the right upper and lower limbs (grade of 3/5) while it remained poor on the left side (grade of 1/5). The patient was then lost to follow up.

DISCUSSION

Complications of shigella infection include both intestinal and extra-intestinal manifestations^[2]. Hemolytic uremic syndrome and central nervous system (CNS) complications are among the most common extra-intestinal manifestations of shigellosis. Seizures and acute transient encephalopathy state (manifested by headache, delirium, lethargy, hallucinations, confusion, and depressed sensorium) are the most commonly reported neurological manifestations in pediatric population with shigellosis^[1,3]. These may accompany or even precede the development of intestinal symptoms. The case may be misdiagnosed as a primary CNS disease, if the neurological symptoms appeared first^[4].

Both seizures and shigella associated encephalopathy are usually benign, and are rarely followed by neurological sequelae^[5].

A particularly fulminant form of acute shigella-associated encephalopathy known as Ekiri syndrome (Japanese: epidemic diarrhea) was first described in Japanese patients in the early 1900's (before and immediately after the Second World War). The major clinical abnormalities were rapidly developing seizures and coma in patients with high fever and few dysenteric symptoms^[6].

Only few cases of fulminant shigella encephalopathy (Ekiri syndrome) have been described in the second half of the last century. The largest series of this rare complication of shigellosis was reported by Goren *et al*^[7], who studied 15 cases of fatal shigella encephalopathy during the years 1980 to 1990

Having ruled out all other causes, acute fulminating encephalopathy (Ekiri syndrome) secondary to *Shigella sonnei* infection was a logical explanation for the sudden and severe neurological deterioration in our patient.

Cerebral edema is a common finding reported in most patients with shigella-associated encephalopathy, either by CT brain or at autopsy^[2,7,8]. This was seen in the first CT brain of our patient (Fig.1). Focal or diffuse areas of low signal intensity were also reported in CT brain in cases of fulminating shigella encephalopathy^[9]. This was seen as areas of low attenuation in the thalamic and basal ganglia regions bilaterally in the second CT brain of our patient done six days after presentation (Fig. 2). The same lesions persisted in the follow up MRI brain a month later. (Figs. 3 a & b).

The pathogenesis of shigella associated neurological dysfunction is not well understood. Shiga toxin, which is produced in appreciable amount by *S. dysenteriae*, was proved to be a neurotoxin in animal models. It acts on the neurons indirectly by inducing vascular endothelial damage in the brain and spinal cord with secondary neurological dysfunction. It also has cytotoxic activity, probably related to its ability to inhibit protein synthesis in mammalian cells^[10].

The majority of shigella associated neurological findings were reported in patients with *Shigella sonnei* and *Shigella flexneri*^[11]. Both species do not usually produce shiga toxin, as both are lacking the structural gene encoding shiga toxin production^[12,13].

Moreover, shiga toxin was neither detected in the CSF of patients with shigella - associated neurological findings, nor produced *in vitro* by shigella strains isolated from these patients. These data suggest that the neurological manifestation of shigellosis in human may not be related to shiga toxin production^[12].

Balter *et al*^[14], studied the role of nitric oxide (NO) in shigella - related seizure in an animal models. NO is an important neurotransmitter in both peripheral and central nervous system. Overproduction of NO has been linked to neurotoxicity during ischemia. It also has a role in some form of neurodegenerative brain disease and in seizures induction^[15].

In their study, Balter *et al*^[14] found that *Shigella dysenteriae* infection elevate serum NO level, and this lowered the threshold of induced convulsions in mice. They hypothesized that NO may have a role in induction of neurological manifestation of human shigellosis by acting as a mediator to cytotoxins produced by different *Shigella* species and possibly by other enteric infections.

Khan *et al*^[11] in a large study discussed the prognostic factors that affect the outcome in children

with shigellosis who presented with neurological manifestation. They found that patients who were unconscious and with documented seizures at presentation were at great risk of fatal outcome in shigella associated encephalopathy.

Although the mechanism that underlies neurological dysfunction in some cases of shigella enteritis is unclear, yet the syndrome exists as a well recognized clinical entity. It needs to be considered by pediatricians as a differential diagnosis in children presenting with acute encephalopathy of obscure origin.

Stool cultures are recommended in those patients with or without intestinal symptoms.

Early recognition and prompt and intensive measures to prevent or treat brain edema may improve the outcome.

ACKNOWLEDGEMENT

Our thanks are due to Dr. Essam A Ismail, Consultant Pediatrician, Farwaniya Hospital for revising the manuscript and to Dr. A K Lahiri, Consultant Radiologist, Farwania Hospital for revising the illustration captions.

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