ORIGINAL RESEARCH PAPER

Medical Science

LETHAL TOXIC ENCEPHALOPATHY DUE TO SHIGELLA SONNEI INFECTION IN TWO OMANI CHILDREN

KEY WORDS: Shigella, Toxic Encephalopathy, Children, Brain Oedema

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ABSTRACT

Ekiri syndrome is lethal toxic encephalopathy that is associated with shigella infection. We report two children with Ekiri syndrome secondary to shigella sonnei infection. However, it may develop in the absence of severe intestinal or metabolic derangement. The exact pathogenesis of this syndrome remains unknown, and despite intensive treatment, the outcome is often associated with high mortality rate.

Introduction

Shigellosis is a common infection especially in underdeveloped countries. Almost two-thirds of shigellosis cases occur in children, and 99% in developing countries. (1)

The most common extra intestinal complications of shigellosis are neurological, particularly seizures occurring in 12-45% in children (2) followed by encephalopathy and hallucinations (2,3). Adult patients may have peripheral neuropathy (4). Mortality is mainly due to extraintestinal complications, mainly lethal toxic encephalopathy or Eriki syndrome (ES). ES is a serious neurologic complication, which often manifest as altered consciousness, seizures, and coma. (5,6). It is considered to be a severe, toxic and lethal form of encephalopathy which is associated with shigella infection and may arise in the absence of severe intestinal manifestations (7). This syndrome was first described in Japanese patients during the first half of twentieth century and named the Ekiri syndrome (8,9). However, it is rarely seen and its exact pathogenesis remains obscure. Despite intensive and prompt treatment, the outcome is often associated with high fatality rate even in developed countries (2).

In this report, we discuss two cases of Ekiri syndrome secondary to shigella sonnei presenting with catastrophic encephalopathy and rapidly deteriorating to death despite aggressive management.

Case report 1:

A 3 year old previously healthy boy with no significant past medical history, presented with one day history of vomiting, bloody diarrhea, fever and tonic-clonic seizure. At presentation, the child was unconscious, , His vital signs were as follows: temperature of 38C, heart rate was 119 beats per minute, blood pressure of 113/43, respiratory rate of 34/min, with oxygen saturation of 93% in room air. Glasgow Coma Scale was seven (out of 13). The child was not dehydrated . The rest of examinations were unremarkable.

Initial investigations showed×10 high white cell count (WBC) (21.5 3/uL-

range 6-18) with×10neutrophilia (18 3 /uL), hyponatremia (129mmol/l-

range 135-145), hypokalemia (3.1mmol/l -range 3.5-5), hyperglycemia (9.11mmol/l- range 3.8-7.8), arterial blood gas showed compensated metabolic acidosis . Liver function test, serum urea, serum creatinine, bone profile, and coagulation profile were normal.

Brain computerized tomography (CT) scan has been done at the same day of admission and showed brain oedema. as shown in figure 1 (A&B).

Despite aggressive measures of management consisting of intubation, ventilation and antibiotic and antiviral therapy with ceftriaxone and acyclovir respectively, the child continued to deteriorate. Within two hours of admission he developed, bradycardia, desaturation and had fixed dilated pupils. Repeated brain CT scan on the following day showed worsening brain edema. Stool culture indicated growth of shigella sonnei (sensitive to ceftriaxone, chloramphenicol and ampicillin; and resistant to ciprofloxacin and co-trimaxazole). Blood and urine cultures were negative. The child continued to be comatose on ventilatory support and supportive management. Apnea test confirmed brain death, and he passed away one month later.

His six-year old sister presented on the same day of her sibling's admission with diarrhea and low grade fever. Her stools grew the same organism. She had mild course, requiring antibiotics and hydration and was discharged home three days later.

Case report 2:

A one-year old girl presented with four days history of fever, vomiting and diarrhea. She was admitted to local hospital with impression of acute gastroenteritis. Four days later, the child started to be drowsy, developed partial seizures and was transferred to a secondary health care hospital. Upon arrival, the child was unwell and drowsy. Not dehydrated. She deteriorated rapidly and developed cardiopulmonary arrest. Cardiopulmonary resuscitation was carried out and she was revived. On examination after resuscitation, the patient was unconscious, afebrile, tachypnic, blood pressure of 90/50mmhg and pupils were sluggishly reacting

bilaterally. Blood×10	workup showed leukocytosis (47.7	^{3}/uL - range 6-18)
with neutrophilia×10	(40.6	^{3}/uL), hyponatremia (125.6mmol/L - range 135-

145), potassium of 3.5mmol/L (range 3.5-5), glucose of 8.4mmol/L (range 3.8-7.8). Brain CT scan without contrast was normal as shown in figure 2 (A&B).

In the intensive care unit, she was managed with ceftriaxone, vancomycin and acyclovir. Unfortunately the child arrested five times on the next day. Cardiopulmonary resuscitation in the fifth time failed to revive the patient. Stool culture reported as mixed growth of shigella sonnei and salmonella.

Shigella sonnei sensitive to ciprofloxacin and chloramphenicol, and resistant to ceftiaxone, ampicillin and co-trimaxazole.

Discussion:

The two reported children presented with gastrointestinal symptoms, followed by rapid deterioration of clinical status resulting in seizures, coma and ultimately death. This drastic presentation fits into the clinical picture of Ekiri syndrome (ES) that is known to be associated with shigellosis. The estimated annual number of Shigella episodes throughout the world is 164.7 million, of which 163.2 million occurring in developing countries, with 1.1 million deaths (3)- 61 percent of all shigellosis-related deaths are seen in children younger than 5 years of age. The exact magnitude and etiology of the diarrheal illness in Oman is unknown. One study from a single region in the country estimated that among 856 children admitted with diarrhea, bacterial

etiology was found in 15.2%; of which 10.6% is due to Shigella infection. Shigella Sonnei was the commonest isolated Shigella serogroup (10). Beside febrile convulsions, other neurological manifestation of childhood shigellosis may include severe headache, lethargy, meningismus, delirium, and coma. Also, presence of headache is a prominent feature may precede ES (4).Cerebral edema is a common finding reported in most patients with shigella-associated encephalopathy, either by brain CT scan or at autopsy (11). However, the symptoms of ES may present in the absence of brain edema and death may occur within 6-48 hours especially with *shigella dysenteriae*. Both of our presented children had history of mild vomiting and non bloody diarrhea with low grade fever. However, they both rapidly deteriorated and became comatose in a very short time and only one had cerebral edema demonstrated in CT scan.

The presence of features known to cause altered consciousness such as fever, severe dehydration, hypoglycemia, hyponatremia, or meningitis were assessed in both patients. This presentation is highly suggestive of shigella toxic encephalopathy and should be managed aggressively even prior to obtaining brain imaging. The prompt management of brain edema may prevent progression and ultimately death.

The pathogenesis of neurologic manifestations during shigellosis is still unclear. Earlier hypothesis suggested that shiga toxin may be play a role in the pathogenesis of this syndrome but this was not supported by the fact this

complication was seen with all shigella species. Previous clinical data support the occurrence of cerebral edema in most cases of ES (2,5, 6, 9,12,).

Complementary studies in a murine model documented the early development of brain edema and the major pathogenesis role of host response factors, such as tumor necrosis factor alpha, IL-1_, and nitric oxide production.(13,14)

Our first case supports the notion that host factors plays a major role in the pathogenesis as the patient's sister had the infection at the same time but she only manifested with mild gastroenteritis without developing the syndrome.

Ekiri syndrome is associated with high fatality rate reaching up to 100%, regardless of the prompt initiation of aggressive treatment measures, and even in most developed countries (15,16).

Conclusion:

Ekiri syndrome remains a challenging manifestation of a common infection. The early recognition of shigella encephalopathy and rapid intervention to prevent evolution syndrome may improve the outcome and mortality rate (17). Further studies are needed in order to elucidate the exact pathogenesis and predict risk factors for developing the syndrome.

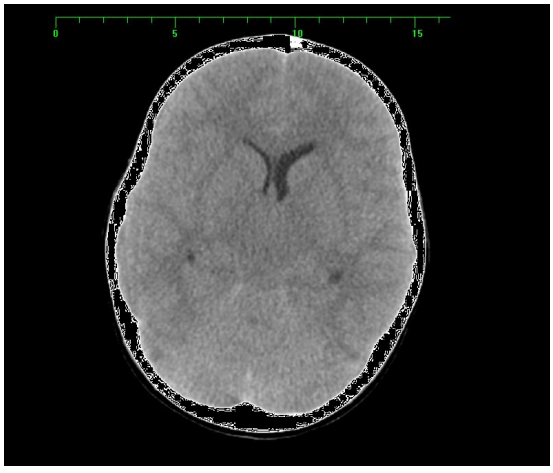

Fig. 1 (A)

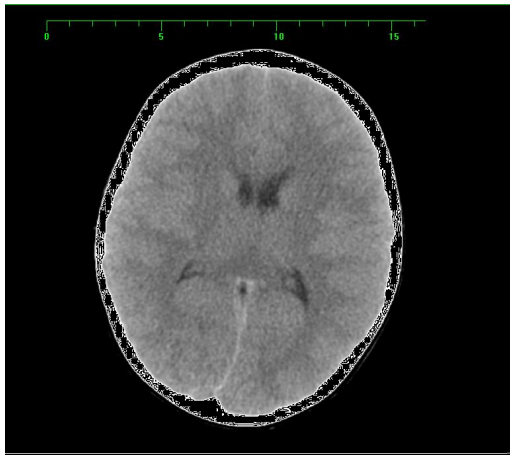

Fig. 1 (B)

Figure 1 (A&B): two cross-sectional images of CT brain showed diffuse brain oedema.

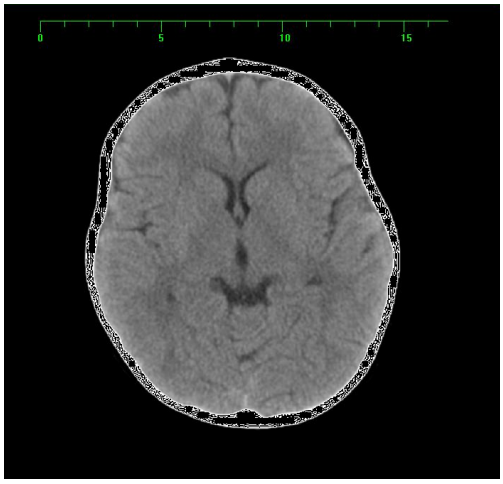

Fig. 2 (A)

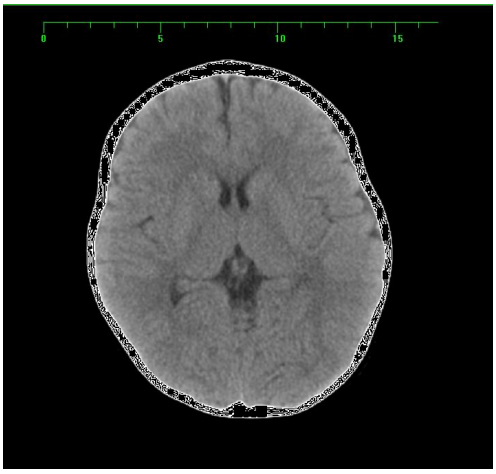

Fig. 2 (B)

Figure 2 (A&B): two cross-sectional images of CT brain with preserved brain parenchyma and no evidence of brain oedema.

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