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Short Communication

A Case of Shigellosis with Intractable Septic Shock and Convulsions

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SUMMARY: Although shigellosis is a potentially fatal disease that may cause a number of extra-intestinal manifestations, intractable septic shock is an unusual complication. Here we describe a 6-month-old infant who developed severe septic shock and convulsions during an episode of dysentery caused by multidrug-resistant *Shigella dysenteriae*. The case presentation demonstrates how shigellosis can lead to rare and potentially misleading complications such as septic shock when not treated adequately and promptly.

Shigellosis occurs worldwide, but it is most common among pediatric age groups in underdeveloped tropical countries. The infection is caused by four species of *Shigella*: *Shigella dysenteriae*, *Shigella flexneri*, *Shigella boydii*, and *Shigella sonnei*. Infection causes a spectrum of clinical features ranging from mild to severe and fatal diseases (1,2). Young and/or malnourished children, particularly those infected with drug-resistant strains and those not treated adequately, are at high risk for severe shigellosis. Different intestinal and extra-intestinal complications may occur with severe *Shigella* infections; however, septic shock is a very rare complication (1,2). The following is a presentation of a case of shigellosis with intractable septic shock and convulsions.

A 6-month-old male infant from a rural district in Northwest Gondar (45 km away from Gondar city) was brought to the University of Gondar hospital with a chief complaint of abnormal body movement for a duration of 4 h. The salient clinical features and laboratory findings of the case are shown in Table 1. The infant had bloody diarrhea associated with severe tenesmus for 5 days. The patient also had high-grade, sustained fever. In addition, he had episodes of vomiting and mild abdominal distension.

The infant had been taken to a nearby clinic at the onset of the illness, where he was given cotrimoxazole and metronidazole syrups, which he took for 3 days without improvement. On the fourth day, he was brought to Gondar University hospital, where intussusception was ruled out by ultrasound examination and the patient was sent home with oral rehydration salt (ORS). Subsequently, the infant was feeding normally and taking ORS. He remained in a similar state as during the previous nights, but his fever had subsided. Four hours prior to admission, the infant began to have a sudden onset of abnormal movements of the body, which persisted until he was seen again at the University of Gondar hospital. On physical examination, his pulse rate was 140 per min and feeble, and his temperature was 35.8°C. Anthropometry was normal. Except for the shock, there was no other sign suggestive of dehydration (neither eye balls nor fontanel were sunken in; buccal mucosa was wet; skin pinch showed rapid return). The patient's abdomen was slightly distended and rectal examination revealed a 2nd-degree rectal prolapse with blood on the examining finger. The Balantyre coma scale rating was one out of five. The patient's neck was arched backwards, he had rigid extremities, and was exhibiting intermittent clonic movement of limbs.

Table 1. Clinical features and laboratory finding of a 6-month-old infant with intractable septic shock due to shigellosis

History/ symptoms	Bloody diarrhea with tenesmus and fever, 5 days
	No response to trimethoprim-sulphamethoxazole, 4 days
	Abnormal body movement, 4 h
Signs	Rapid feeble pulse (shock)
	Coma, generalized tonic-clonic seizure
	No sign of dehydration
	No sign of malnutrition
Laboratory results	Blood film = no blood parasite
	Stool microscopy = pus and red cells (no *E. hystolitica*)
	Stool culture = no *Shigella* or *Salmonella* spp. isolated
	CSF = no cell on microscopy, culture negative
	Blood culture = *Shigella dysenteriae*

CSF, cerebrospinal fluid.

Repeated thick and thin blood films were prepared on a single slide from fresh whole blood and the samples were Giemsa-stained. No hemoparasites were seen after examination of 200 fields, the equivalent of 0.5 μl of a thick blood film (3). Direct stool microscopy using normal saline and Dobell's iodine preparations showed many pus cells and red blood cells. Stool, cerebrospinal fluid (CSF), and blood were cultured and processed following the standard microbiological procedures (3). In brief, stool was inoculated on MacConkey agar (Oxoid, Hampshire, UK) immediately after the sample was taken. No *Shigella* or *Salmonella* spp. were observed on the plate after 24 h of incubation. The CSF was also inoculated on blood agar (Oxoid), chocolate agar, and MacConkey agar plates and was incubated at 35-37°C. The chocolate agar plate was incubated by placement in a candle jar, which provided a 5-10% CO_2 concentration to create microareophilic conditions for fastidious bacteria. After 24 and 48 h of incubation, the plates were examined for the presence of bacterial colonies. However, no bacterial growth was observed after 48 h of incubation. Similarly, the hematological analysis of the CSF was non-revealing. In addition, the blood was inoculated into Tryptone Soya broth (Oxoid) and incubated aerobically. After overnight incubation, samples were sub-cultured on MacConkey, chocolate, and blood agar plates, and the samples were incubated as described above.

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After 72 h of incubation, colony growth was observed. With the help of a series of biochemical tests, which included triple sugar iron agar, indole, Simmon's citrate agar, lysine decarboxylase, urease, and motility tests, *S. dysenteriae* was isolated. A standard method of disc diffusion sensitivity testing developed by Bauer et al. (4) was employed to determine susceptibility patterns of the isolate to the commonly used antibiotics: ampicillin (30 μg), gentamycin (10 μg), penicillin G (10 IU), tetracycline (30 μg), chloramphenicol (30 μg), ciprofloxacin (5 μg), erythromycin (15 μg), and co-trimoxazole (25 μg). Diameters of growth inhibition around the discs were measured and interpreted. The organism was resistant to chloramphenicol, trimethoprim-sulphamethoxazole, ampicillin, and tetracycline, and was sensitive to ciprofloxacin and gentamycin.

With a diagnostic impression of bacillary dysentery with septic shock of gastrointestinal focus, the patient was given intravenous dextrose and a bolus of normal saline (20 ml/kg over 1 h). Intravenous treatment with ceftriaxone was also started. However, despite the measures taken, the patient remained in shock. An additional 10 ml/kg of normal saline was administered twice, but the pulse (including the central pulse) remained persistently feeble. The infant was then given maintenance fluid with normal saline and dextrose solution. The seizure subsided soon after admission, and the patient became conscious some time thereafter, although he remained very weak. The patient then expired 15 h after admission.

Shigellosis may lead to a number of extra-intestinal complications such as dehydration, electrolyte imbalance, hemolytic uremic syndrome, and seizure, which are relatively common in younger people and in cases of *S. dysenteriae* serotype-1 and *S. flexneri* infections (1,2). Septic shock and toxic encephalopathy are uncommon complications of shigellosis. Although bacteremia may be detected in as high as 8% of *Shigella* infections in young malnourished children in developing countries, it very rarely leads to manifestations of severe sepsis (1-3).

The cause of toxic encephalopathy in this case remains unclear, but it is thought to be due to the neurotoxic effects of shigellosis. Toxic encephalopathy presents as a headache and alterations of consciousness, with or without seizure, and may be rapidly fatal (5,6). Shiga toxin is an important toxin produced by *S. dysenteriae* type-1, and has been shown to exert a neurotoxic effect (1). A further characterization of the *S. dysenteriae* isolate in the present report (for type and toxin production) would have been helpful in this respect, but that was not possible given the laboratory setting at that time and place.

The infant discussed was in intractable septic shock, as could be seen from his lack of response to vigorous fluid administration and antibiotic therapy, and based on the isolation of *S. dysenteriae* from a small amount of blood taken for culture. The latter indicated the high level of bacteremia in this infant. The infant was also having repeated convulsions with a loss of consciousness, but later became conscious after the seizures passed. This scenario is more suggestive of post-ictal coma than of toxic encephalopathy.

Bacteremia caused by different species of *Shigella* has been well-described in the medical literature (2,6-8). One study of clinical specimens processed by the bacteriology unit of a referring hospital in Northwest Ethiopia between June 1994 and May 1995 found 5 cases of bacteremia due to *S. dysenteriae* type-1, and all of these cases were in children (9). Additional cases of *Shigella* septicemia (bacteremia accompanied by systemic signs of toxicity) have been reported in various parts of the world (3,9-17). However, progression to severe sepsis is very rare in case of shigellosis (1,3).

A presentation similar to that of our case was described in a report by Beigelman et al. (5) about a 3-year-old child who developed severe septic shock and severe encephalopathy during an episode of dysentery caused by *S. flexineri*. The child was treated in an intensive care unit with mechanical ventilation and intravenous antibiotics, anticonvulsants, inotropics, and fluids until recovery after 4 days. In contrast to our case, *S. flexineri* was cultured from the stool, and other cultures (blood, CSF, and throat) were negative.

The failure to isolate *Shigella* spp. from the stool of the infant in the present report, despite the use of standard laboratory procedures, may have been due to the well-recognized difficulty of isolating *S. dysenteriae* from stool samples. Up to 20% of cases of shigellosis due to *S. dysenteriae* may be culture-negative, and sometimes diagnosis will have to be made based on clinical features and stool microscopy results (18).

Another point to be made in this context is that the organism isolated from the patient's blood was resistant to many commonly used antibiotics, which accounts for the lack of response of the infant to initial empirical treatment. This problem is consistent with the reports of studies conducted in various parts of the country, which have shown a high prevalence of multidrug-resistant *Shigella* strains (19-21). For instance, Mache reported antimicrobial resistance rates of 40, 33, 70, and 64% to chloramphenicol, trimethoprim-sulphamethoxazole, ampicillin, and tetracycline, respectively, among pediatric outpatient *Shigella* isolates in Southwest Ethiopia (21). The physician should be aware of these issues when treating young children with suspected shigellosis, especially if a patient fails to respond to conventional treatment within 48 h. The infant in the present case should have been admitted upon his initial presentation at the University of Gondar hospital, as he had already failed to responded to a 3-day course of antibiotic therapy.

In conclusion, we would like to draw attention to the possibility of encountering an unusual presentation of shigellosis as septic shock, as well as emphasize the possibility of a grave outcome if shigellosis is not treated promptly and appropriately. Such an unusual presentation of shigellosis may have a very rapid course, and physicians need to act quickly with empirical antibiotic therapy based on knowledge of the prevalent antibiotic resistance pattern, since obtaining laboratory culture results typically requires a number of days.

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REFERENCES

1. Niyogi, S.K. (2005): Shigellosis. J. Microbiol., 43, 133-143.
2. Keusch, G. (2001): Shigellosis. p. 975-977. *In* E. Braunwald, K.J. Isselbacher, A. Fauci, et al. (ed.), Harrison's Priniciples of Internal Medicine. McGrawHill, New York.
3. Cheesbrough, M. (1987): Medical Laboratory Manual for Tropical Countries II.
4. Bauer, A.W., Kirby, W.M., Sherirs, J.C., et al. (1996): Antibiotic susceptibility testing by standardized single disk method. Am. J. Clin. Pathol., 45, 433-496.
5. Beigelman, A., Leibovitz, E. and Sofer, S. (2002): Septic shock associated with *Shigella flexneri* dysentery. Scand. J. Infect. Dis., 34, 692-693.
6. Sandyk, R. and Brennan, M.J. (1983): Fulminating encephalopathy

associated with *Shigella flexneri* infection. Arch. Dis. Child, 58, 70-71.
7. eu-Osika, S., Tazarourte-Pinturier, M.F., Dessemme, P., et al. (1996): Fulminant encephalopathy due to *Shigella flexneri*. Arch. Pediatr., 3, 993-996.
8. Greenberg, D., Marcu, S., Melamed, R., et al. (2003): Shigella bacteremia: a retrospective study. Clin. Pediatr., 42, 411-415.
9. Aseffa, A. and Yohannes, G. (1996): Antibiotic sensitivity pattern of prevalent bacterial pathogens in Gondar, Ethiopia. East Afr. Med. J., 73, 67-71.
10. Kim, K.S., Chong, Y., Lee, S.Y., et al. (1981): *Shigella flexneri* bacteremia: a case report. Yonsei Med. J., 22, 21-25.
11. Soumare, M., Diop, B.M., Feller-Dansokho, E., et al. (2000): Shigella bacteraemia: a report of two cases observed in Dakar. Dakar Med., 45,194-195.
12. Saraswathi, K., De, A., Jog, A., et al. (2002): Shigella septicemia. Indian Pediatr., 39, 777-779.
13. Lakshmikanth, C. (1982): Shigellosis with septicemia. J. Assoc. Physicians India, 30, 841.
14. Alkan, M., Salzstein, E. and Simu, A. (1985): Four cases of Shigella septicemia in Israel. Eur. J. Clin. Microbiol., 4, 417-418.
15. Usman, J., Aziz, S., Karamat, K.A., et al. (1997): Shigella septicaemia in an infant. J. Pak. Med. Assoc., 47, 150-151.
16. Yen, J.B., Chang, K.W., Wu, T.L., et al. (2003): *Shigella flexneri* sepsis in an infant. Chang Gung Med. J., 26, 611-614.
17. Kavaliotis, J., Karyda, S., Konstantoula, T., et al. (2000): Shigellosis of childhood in northern Greece: epidemiological, clinical and laboratory data of hospitalized patients during the period 1971-96. Scand. J. Infect. Dis., 32, 207-211.
18. Levine, M.M. (2000): Shigellosis. p. 319-322. *In* Hunter, G.W., (ed.), Hunter's Tropical Medicine and Emerging Infectious Diseases. Saunders, London.
19. Aseffa, A., Gedlu, E. and Asmelash, T. (1997): Antibiotic resistance of prevalent *Salmonella* and *Shigella* strains in northwest Ethiopia. East Afr. Med. J., 74, 708-713.
20. Mache, A., Mengistu, Y. and Cowley, S. (1997): Shigella serogroups identified from adult diarrhoeal out-patients in Addis Ababa, Ethiopia: antibiotic resistance and plasmid profile analysis. East Afr. Med. J., 74, 179-182.
21. Mache, A. (2001): Antibiotic resistance and sero-groups of shigella among paediatric out-patients in southwest Ethiopia. East Afr. Med. J., 78, 296-299.