Neonatal Shigellosis

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Neonatal shigellosis is a very rare condition. However, the complication rates (such as sepsis and colonic perforation) and mortality rates of this disease are much higher than in older infants. The clinical picture often mimics that of other more frequent and severe conditions such as necrotizing enterocolitis, mid-gut volvulus, and intussusception. In the nursery, it may spread to other neonates or to members of the hospital staff. An aggressive approach to diagnosis and therapy is essential in order to achieve full recovery. Previous reports have referred to individual cases and small series, mostly from countries with poor sanitary conditions [1]. We review the current data on this severe infection in the light of our own experience of two recent cases of neonatal shigellosis.

Patient Descriptions

Case 1

A male term infant presented with watery, mucoid-bloody stools on day 3 of life, but with no change in his otherwise good general condition. He was fed on a milk-based infant formula. His mother and brother had diarrhea 2 weeks before the delivery, but no stool cultures were obtained at that time.

Abdominal X-rays were normal. Following stool culture and a full septic work-up, treatment with intravenous cefotaxime 150 mg/kg/day was begun. After 3 days, stool culture yielded *Shigella sonnei*, but blood cerebrospinal fluid and urine cultures were negative. Treatment was continued for 5 days and the infant made an uneventful recovery. Repeat cultures of family members were negative.

Case 2

An 8 day old term female infant presented with fever, apathy and refusal to eat, but no diarrhea. She had been fed on a milk-based infant formula. Her family was healthy. Her abdomen was distended but not tender, and abdominal X-ray showed non-specific bowel dilatation. Following a sepsis work-up she was started on intravenous ampicillin and gentamicin. Only on the second day of admission did she pass several bloody diarrheal stools. Stool cultures after 4 days of incubation grew *S. flexneri*, which was resistant to ampicillin and sensitive to cefotaxime. Blood, CSF and urine cultures were negative. Treatment was changed to intravenous cefotaxime 150 mg/kg/day, and she made a full recovery after 7 days. Stool cultures that were obtained from the parents, three other children and nursery staff were all negative.

Comment

To the best of our knowledge these are the first reported cases of neonatal shigellosis in Israel. In a recent study conducted in northern Israel, the median age for hospitalized children with shigellosis was 3 years and no neonates with the infection were found. *S. sonnei* and *S. flexneri* type 1 were cultured from 74% and 21% of the patients respectively [2]. The highest incidence of shigellosis occurs in children 1–4 years of age, while the incidence of neonatal shigellosis is 0.6% of all cases in children up to 10 years of age, and only 1.6% of all infants exposed to the infection become ill [2]. The incidence during the first 6 months of age is 60-fold lower than among older children. The infection in neonates is rare, although maternal feces routinely contaminate the newborn during labor, even in developed countries. The reason for this is not clear, since several factors may contribute to increased susceptibility of neonates to enteric infections. These include: underdevelopment of local and systemic immune response; lack of fully developed aerobic and anaerobic enteric flora, which protect the gastrointestinal of older infants and children; a less gastric bactericidal barrier; less intestinal mucus; and less motility. Also, the older infant may have been fed powdered formula that could have been mixed with contaminated water.

Neonates with shigellosis may have a mild diarrheal syndrome or severe colitis. However, compared to older infants, neonates are more prone to have severe disease associated with dehydration, meningitis, sepsis, colonic perforation, toxic megacolon, and death. Infants are twice as likely to die as older children. In Halatin's [3] series of 16 new and 8 previously reported cases of neonatal shigellosis, there were 2 deaths from peritonitis following intestinal perforation. The neonates did not undergo surgery due to delayed diagnosis, which was attributed to the rarity of the infection in this age group. It was postulated that colonic mucosal ulceration and necrosis allow ready access of *Shigella* and other enteric pathogens to the bloodstream. The different clinical features observed in infants and older children are not well understood and cannot be attributed to differences in the proportions of *Shigella* species in the two groups. In a multiple, logistic regression analysis [4], independent predictors of death in infants were gram-negative bacteremia, ileus, decreased bowel sounds, hyponatremia, hypoproteinemia, and a lower number of erythrocytes detected on microscopic examination of stool specimens.

Previous studies have found that approximately 20% of all deaths caused by *Shigella* occur in infants 3 months of age or younger. The mortality rate of neonatal shigellosis is less than 1% in industrialized societies, but may reach 30–40% in less developed countries. The difference in the mortality rates is related to nutrition and the availability of medical care, antibiotic resistance of many *Shigella* strains, the frequency of sepsis, and the higher frequency of *Shigella dysenteriae* serotype 1 in less developed countries [4].

Neonatal shigellosis is a mimic, and should be included in the differential diagnosis of newborns presenting with shock and abdominal symptoms along with necrotizing enterocolitis, mid-gut volvulus, intussusception and sepsis. Diarrhea management algorithms that rely only on clinical findings of dysentery to diagnose and treat shigellosis are likely to be unreliable in this high risk age group.

The geographic variation in species causing the infection is not well understood. In the USA and in Israel, most *Shigella* infections are due to *S. sonnei* or, less commonly, to *S. flexneri*. In developing countries the relative importance of these species is reversed and other *Shigella* types, especially *S. dysenteriae* type 1, are identified more frequently. However, in these countries there is a significant difference in epidemiology between neonates and older infants. Neonatal *Shigella* infections caused by *S. boydii* and *S. sonnei* are more common, while *S. dysenteriae* type 1 infections are less common in neonates than in older children; the proportion of *S. flexneri* infections is equivalent in the two groups [3].

The incubation period of shigellosis is usually between 12 and 48 hours. Only a few bacteria need to be ingested in order to cause disease. Half of the described neonatal shigellosis cases occurred within 3 days of birth, consistent with vertical fecal-oral transmission during labor from symptomatic or carrier mothers. In Halatin's [3] series of 16 cases of neonatal shigellosis, 3 of the mothers or other family members tested positive for *Shigella*, and 11 patients had family members with diarrhea at the time of presentation. Given the ease of transmission, the explanation for the low

CSF = cerebrospinal fluid

frequency of neonatal *Shigella* infection is not well understood. The protective effect of breast-feeding has been confirmed in surveys of sporadic gastroenteritis, in community epidemics, and in outbreaks in newborn nurseries; however this alone does not explain the resistance of infants to shigellosis since many infants are bottle-fed, as were our patients.

Neonates with shigellosis can be a source of infection to their surroundings. In the nursery the bacteria may spread to other infants as well as to hospital staff. Awareness of the infection, an aggressive approach to diagnosis, emphasis on hand-washing and the use of gloves continue to be critical components of infection control policy. Nonetheless, in at least one study it has been shown that enteric isolation techniques failed to halt the spread of shigellosis once established [5]. Antimicrobial treatment of all infected and uninfected patients was required for control of the outbreak. The other simple measure to decrease the risk of neonatal shigellosis spread is to support breast-feeding.

Treatment of neonatal shigellosis consists of prompt supportive therapy such as hydration, correcting electrolyte imbalance, and good nutrition. It has been shown that proper antibiotic therapy shortens the duration of the disease and may halt the spread of the bacteria. More important is that such therapy may decrease the rates of complications and mortality. The empiric choice of antibiotics is dictated by susceptibility data on the strains circulating at the time patient infection occurs. Currently in Israel, most *Shigella* strains are resistant to ampicillin and trimethoprim-sulfamethoxazole and therefore a third-generation cephalosporin should be administered in every neonate suspected of suffering from shigellosis.

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