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A Nine-Month Old Malnourished Baby Girl Presenting with Shigellosis, Pneumonia and Shock

Case 1, 1992

Presentation of the Case

This nine – month old girl was admitted to the Intensive Care Unit (ICU) of the Clinical Research Centre (CRC) of the ICDDR,B on 26 March 1991, with a history of passing stools tinged with mucous and blood, 20 – 25 times/day, occasional vomiting, cough, anorexia, and low grade fever of 4 days duration. She was given oral rehydration salt (ORS) solutions and some unspecified drugs at home without clinical improvement.

The child was born at term and was breastfed; at 4 months of age diluted rice – gruel was added to the diet. The patient was the 3rd child of the parents with poor socio – economic background. She received BCG, two doses of DPT, and polio vaccines. During the preceding 5 months, she had two episodes of diarrhoea and one episode of acute respiratory illness.

On physical examination the infant was found to be severely emaciated weighing only 3.5kg (weight for age, 40% of NCHS median). She looked pale and was lethargic. Her rectal temperature was 38.4 °C, radial pulse was 156/min and weak, respiration 38/min and deep. The child had signs of moderate dehydration. She also had thrush (but no jaundice, oedema, or cyanosis). A few crepitant rales were heard bilaterally at the back. No other clinically abnormal findings were noted. Her blood glucose concentration at admission was determined to be 1.5 mmol/L by a glucocheck machine (Reflolux IIM, Boehringer, Germany). A provisional diagnosis of nutritional marasmus complicated by dysentery, bronchopneumonia, anaemia, oral candidiasis, and hypoglycaemia was made. She had an admission total white blood cell count (TWBC) of 21,300/mm^3 with 47% neutrophil, 52% lymphocyte, 21% haematocrit, serum sodium of 120.4 mmol/L, potassium of 1.84 mmol/L, chloride of 82 mmol/L, total carbon dioxide of 13.2 mmol/L, and creatinine of 253 µmol/L. A rectal swab culture taken on admission subsequently grew *Shigella flexneri*, which was sensitive to nalidixic acid, trimethoprim – sulphamethoxazole, and pivmecillinam. A chest X – ray revealed streaky bilateral infiltrates in all lung zones. An X – Ray of plain abdomen showed distended gut loops with loss of haustration of the colonic mucosal pattern.

Immediately after admission she was given 20 ml of 25% dextrose solution intravenously. Dehydration was corrected with an infusion of a polyelectrolyte solution (sodium 133 mmol/L, potassium 13 mmol/L, chloride 98 mmol/L, and bicarbonate 48 mmol/L in the form of acetate) with 5% dextrose solution. On receiving serum electrolyte results the solution was changed to normal saline (0.9% Nacl) with 5% dextrose and 30 mmol of potassium chloride/L. Because of lack of clinical improvement, even after correction of dehydration and hypoglycaemia, gram – negative septicaemia was suspected. A blood culture was taken and therapy instituted with ampicillin (50mg/kg of body weight every 6 hours) and gentamicin (2mg/kg body weight every 8 hours), both administered intravenously. Additionally, syrup nalidixic acid was administered for suspected shigellosis, and nystatin suspension for oral moniliasis.

Six hours after admission, the child had a seizure. Her blood glucose was 5.5 mmol/L, and she had a body temperature of 38.0 °C. The seizure was controlled with 1.5mg slow intravenous administration of diazepam. The patient subsequently developed gasping respirations. Her abdomen became distended with sluggish bowel sounds. A lumbar tap was performed but CSF studies were normal. The clinical condition of the patient continued to deteriorate and she died in the same evening within 18 hours of admission.

Clinical Discussion

Dr. Syed Samiul Hoque

This patient was admitted to the ICU on 26 March 1991 and died several hours later with a multitude of problems which included severe marasmus, dysentery, lower respiratory tract infection, hyponatraemia and severe hypokalaemia, oral moniliasis, ileus, and suspected, but un – proven, gram – negative septicaemia.

The underlying problem of poor nutritional status compounded the course of her illness and contributed significantly to her death. The causes of

her malnutrition appear to be multiple and may include low birth weight, recurrent infections, and inadequate feeding. She had culture confirmed dysentery due to *Shigella* which is associated with more complications and higher death rates than diarrhoeas due to other agents.

Figure 1. Inflammatory infiltration in the lamina propria of the colonic mucosa with superficial ulceration and presence of mucopurulent exudate on luminal surface, hyperplasia of crypt epithelium and formation of occasional crypt abscess. Submucosa of colon shows pronounced oedema. H & E stain, magnification 33 X.

Figure 2. Ulceration of colonic mucosa, polymorphonuclear infiltration in lamina propria, crypt abscesses, crypt hyperplasia with penetration into submucosa (colitis profunda). H & E stain, magnification 66 X.

The infant had hypoglycaemia on admission perhaps due to malnutrition, or infection, or both. Incidence of hypoglycaemia is common in patients with diarrhoea, especially with shigellosis (6.4%) (1). Pathogenesis of hypoglycaemia is not commonly known, but may be related to multiple factors including anorexia, fever, malnutrition with low glycogen reserve in the liver, and impaired gluconeogenesis. Patients with shigellosis often have sepsis or endotoxaemia which is associated with impaired activity of phosphoenol pyruvate carboxylase enzyme and resulting hypoglycaemia. The case-fatality rate in shigellosis is higher among patients with hypoglycaemia (37%) than among patients without hypoglycaemia (6.6%) (1).

The child also had serum electrolyte imbalance with hyponatraemia and severe hypokalaemia. Hyponatraemia is a major electrolyte abnormality that occurs in shigellosis. Half of the patients admitted with infections due to *Shigella dysenteriae* type 1 in the Clinical Research Centre of ICDDR,B have been shown to have serum sodium concentrations of < 125 mmol/L; the incidence being less (20%) in patients with infections due to other species of *Shigella*. The reasons for severe hypokalaemia in this child include severe malnutrition with marked reduction in muscle mass and increased loss of potassium in the colon. Potassium depletion of this severity is likely to lead to vacuolar changes in the kidneys. This vacuolar nephropathy could cause further loss of potassium in the urine. The cause of lethargy in this patient could be a combination of hypoglycaemia, hyponatraemia and hypokalaemia.

The child developed a seizure after treatment of hypoglycaemia with intravenous glucose. Thus, the seizure was (probably) not related to pre-existing hypoglycaemia. Seizures as a manifestation of encephalopathy is not uncommon in shigellosis especially in association with *S. flexneri* infections (2). This can occur in the absence of fever, usually during the early phase of the illness, and sometimes even before the onset of diarrhoea.

The patient had evidence of impaired renal function. The high serum creatinine was unlikely to be related to moderate dehydration but may be due to metabolic consequences of gram-negative septicaemia or endotoxaemia.

One of the intestinal complications of shigellosis is "toxic megacolon". The incidence observed at this centre is about 3% of all *Shigella*-infected patients; however, the death rate in association with toxic megacolon in shigellosis is very high (33%) compared to patients without this complication (8%) (3). This patient had abdominal distention and radiological features suggesting toxic megacolon. Abdominal distention and sluggish bowel movements were perhaps aggravated by severe hypokalaemia.

This patient presented with signs of moderate dehydration. Compared with other secretory diarrhoeas (e.g. cholera) loss of diarrhoeal fluid is not marked in shigellosis nor is the instance of severe dehydration (4). Association of moderate or severe dehydration in shigellosis, however, is one of the recognised risk-factors for death in shigellosis (5).

This patient also had bronchopneumonia as indicated by auscultatory findings of the lungs and the radiological abnormalities. The pneumonia was probably acquired at home, and the likely organisms could be a virus, especially a respiratory syncytial virus (RSV), or *Streptococcus pneumoniae*, or *H. influenzae*. Tuberculosis is unlikely as the child had

received a BCG vaccination and there is no history of contact with known tuberculosis patient.

Gram – negative septicaemia is a possibility as the patient had developed shock which was refractory to treatment with isotonic fluids. Blood culture failed to grow any organisms. However, the result of only one blood culture done may not be conclusive. The presence of metabolic acidosis in this child favours a diagnosis of gram – negative speticaemia or endotoximia; however, the patient also had renal failure. If indeed that was the case, the most possible source of septicaemia could be an ulcerated colon. *Shigella* bacteraemia has been shown to occur in about 4% of cases of shigellosis, and another 5% to have bacteraemia due to other gram – negative enteropathogens (5).

In summary, the immediate cause of death in this infant was severe hypokalaemia and toxic megacolon as a consequence of shigellosis and gram – negative septicaemia or endotoximia. Severe protein – energy malnutrition was the underlying cause of death.

Pathological discussion

Dr. Moyenul Islam

The autopsy was done a half an hour after the death of this marasmic female infant. The abdominal cavity and peritoneal surfaces appeared unremarkable except that there was slight oedema of the mesentery. Colonic mucosa was oedematous, inflamed, and showed numerous small ulcers up to 1 mm in size, evenly distributed throughout its length. Basal and posterior parts of both lungs showed patches of dark reddish – purple discolouration, but there was no definite consolidation. Other organs appeared grossly unremarkable. Microscopic examination of the colon revealed a layer of mucopurulent exudate on the luminal surface, epithelial damage and formation of multiple small and shallow ulcers, infiltration of leukocytes in the lamina propria, reduction of goblet cells and formation of crypt abscesses. Focal hyperplasia of crypts with penetration into submucosa was seen. There was severe submucosal oedema in the colon and to a lesser degree in the ileum. Renal tubular epithelium showed vacuolar changes suggestive of hypokalaemia. Scattered patches of interstitial pneumonia were seen in the lungs (6).

In summary, this is a case of *Shigella* colitis in a marasmic child who died due to gross electrolyte imbalance.

Dr. AU Ahmed: In the photomicrograph of the lung tissue, there are some broken alveolar septa leading to formation of bullae in some areas of the lung. How do you explain that?

Dr. Moyenul Islam: We have seen this change in cases of interstitial pneumonia who develop respiratory distress; perhaps this occurs following air – trapping due to collection of secretion and exudate in small air passages.

Dr. AU Ahmed: I am curious about the marked submucosal oedema in the colon. Is this generally related to shigellosis and what is the pathogenesis of this oedema?

Dr. Islam: Many patients with acute colitis including shigellosis develop submucosal oedema in the colon and sometimes in the small intestine. However, this is more pronounced in hypoproteinaemic patients and when there is associated segmental necrotizing enterocolitis.

Prof. MS Akbar: Is it possible that the pneumonia could be a terminal event in this case?

Dr. Islam: Yes, I agree with you. But still we should try to understand the pathogenesis of development of pneumonia in these cases, so that one could determine appropriate intervention measures to be taken in future.

Dr. Samiul Hoque: Was the brain examined in this case?

Dr. M Islam: No.

Anatomical diagnosis:

1. Acute *Shigella* colitis.
2. Nutritional marasmus.
3. Focal interstitial pneumonia.
4. Vacuolar changes in renal tubules.

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