HEMOLYTIC UREMIC SYNDROME ASSOCIATED WITH SHIGELLOSIS: REPORT OF TWO CASES

CHERDCHAI RONGNOPARAT and RATANA PANPANIT

Udornthani Hospital, Udornthani 41000, Thailand.

INTRODUCTION

Hemolytic uremic syndrome was described by Gasser *et al.*, (1955) as the association of hemolytic anemia, thrombocytopenia and acute renal failure. Hemolytic uremic syndrome occurs mainly in infants and children under 4 years old and had no prediliction for any sex or race (Drummond, 1983). In the majority of cases no causative agents have been found, however it has also been reported from different parts of the world, in association with a variety of bacterial and viral illnesses. In reports from Bangladesh (Koster *et al.*, 1978) and India (Raghupathy *et al.*, 1978) hemolytic uremic syndrome has been observed to develop in a large proportion of patients suffering from bacillary dysentery. Hemolytic uremic syndrome following shigellosis has many features, both clinical and histopathological which resemble the idiopathic hemolytic uremic syndrome. It is postulated that endotoxemia in shigellosis patients play an important role in the pathogenesis of hemolytic uremic syndrome. In Thailand, there have been reports of cases of hemolytic uremic syndrome (Tunpijitr, 1978), idiopathic hemolytic uremic syndrome from Nakhonratchasima Hospital (Pongritsuda *et al.*, 1984) and recently, Thisyakorn (1986) reported a case of hemolytic uremic syndrome associated with shigellemia. This report describes two cases of hemolytic uremic syndrome associated with *Shigella* infection who were admitted to Udornthani Hospital, Northeast Thailand.

REPORT OF CASES

Case I : An 11-month-old boy was admitted to Udornthani Hospital, in December 1985 with a three day history of high fever, bloody diarrhoea and tenesmus. Physical examination revealed temperature 39.5°C, pulse rate 130/min, respiration 36/min, blood pressure 100/70 mm Hg and body weight of 8.8 kg. The patient was mildly dehydrated. Complete blood count showed hematocrit 32%, white blood count of 9,100 cells/c.mm with 12% neutrophils, 83% lymphocytes and 5% monocytes, platelet count was 400,000 cells/c. mm. Stool examination showed numerous red blood cells and moderate white blood cells. Initially he was treated with intravenous fluid and oral co-trimoxazole. During the next three days, he passed 15-20 mucus bloody stools per day. On the fourth hospital day his temperature was 40.5°C. The patient was lethargic, irritable and developed vomiting which precluded the oral intake. His stool culture yielded *Shigella dysenteriae* which was sensitive to ampicillin, amikacin, cefotaxime, ceftazidime, gentamicin and kanamycin. It was resistant to co-trimoxazole and chloramphenicol. The oral co-trimoxazole was changed to intravenous ampicillin. On the ninth hospital day he developed anuria. The physical examination disclosed puffy eyelids with pallor. The lungs were clear. A Grade 2 systolic murmur was heard along the left sternal border. The abdomen was soft with tenderness. The liver was 2 cm below right costal margin. Mild pitting edema were noted at extremities. Blood electrolytes showed sodium 118 mEq/l, potassium 7.48 mEq/l, chloride 83 mEq/l, bicarbonate 20.5 mEq/l, BUN 54.5 mg/dl and creatinine 4.5 mg/dl. Complete blood count showed a hematocrit of 16%, a white blood cell count of 26,800

celis/c.mm with 81% neutrophils, 4% band forms, 11% lymphocytes, 1% monocyte and 3% metamyelocytes. The platelet count was 45,000 cells/c.mm. Peripheral blood smear revealed frequent schistocytes and many Burr cells. Coagulogram revealed prothrombin time 14 seconds (control 10-15 seconds), partial thromboplastin time 21 seconds (control 35-50 seconds) and thrombin time 15 seconds (control 13 seconds). A catheter was inserted into the bladder and yielded 5 ml urine which showed trace protein and occult blood, the sediment count was 10 red cells per high power field. Abdominal X-rays showed nonspecific ileus. An ECG disclosed widening of the P wave and ventricular complex, prolonged P-R interval, with a rate of 120 per minute. Glucose, calcium gluconate and furosemide were administered. Peritoneal dialysis was initiated with a 1.5% dialysis solution. After 48 hours of dialysis, his urination was re-established and he was alert without abdominal discomfort. The peritoneal dialysis catheter was then removed. Packed red blood cells transfusion was also given. Twenty days post dialysis, he was completely normal on physical examination with good renal function.

Case II : A 32 - month-old Thai boy was admitted in May 1986 with a ten day history of high fever, bloody diarrhoea and tenesmus. Five days before admission the fever subsided, but he developed vomiting. One day before entry he was admitted to a private hospital and was treated for dehydration with intravenous fluid. Ampicillin was also given but occasional generalized seizure was noted, so he was transfered to Udornthani Hospital. Physical examination revealed temperature 37.5°C, pulse rate 130/min, respiration 34/min, blood pressure 90/60mmHg and body weight of 9 kg. The patient was a thin pale child, moderately dehydrated and lethargic. Complete blood count showed hematocrit 16%, white blood count of 50,600 cells/c.mm with 67% neutrophiis, 6% metamyelocytes and 26% lymphocytes. Peripheral blood smear revealed many schistocytes and Burr cells, platelets were rarely seen. Urinalysis showed moderate proteinuria and red blood cells. Stool examination disclosed numerous red blood cells and moderate white blood cells. Blood electrolyte showed sodium 105 mEq/l, potassium 3.68 mEq/l, chloride 74 mEq/l, bicabonate 20 mEq/l, BUN 88.2/dl and creatinine 5.0 mg/dl. The patient was treated with ceftriaxone, partial parenteral hyperalimentation and blood transfusion. The stool culture grew *Shigella flexneri* which was sensitive to ampicillin, amikacin, cefotaxime, gentamicin and kanamycin. It was resistant to co-trimoxazole and chloramphenicol. Blood culture showed no growth. The patient improved steadily with normal renal function 2 weeks after admission.

DISCUSSION

These two reported cases had clinical features of hemolytic uremic syndrome. Shigellosis was the preceding illness in both patients. Shigellosis has been well documented to be associated with the hemolytic uremic syndrome. It was suggested that severe colitis in shigellosis is associated with circulating endotoxin from the colon which damaged vascular endothelium and leading to coagulopathy, renal angiopathy and hemolytic anemia. Endotoxemia preceded the onset of hemolysis defined by the limulus test occurred more frequently in patients with the hemolytic uremic syndrome than in patients wih uncomplicated shigellosis (Koster *et al.*, 1978). Recently, Butler *et al.*, (1985) demonstrated that the lipopolysaccharides of *Shigella* species produce leucocyte-mediated renal cortical necrosis in an animal model resembles histopathologically the renal lesion in the hemolytic uremic during shigellosis in human. This finding supported the proposed mechanism that endotoxemia developed in

some patients with acute shigellosis, and play an important role in the pathogenesis of hemolytic uremic syndrome. Further evidence on the role of leucocytes in causing the hemolytic uremic syndrome is the observed association between the leukemoid reaction and hemolytic uremic syndrome in shigellosis (Butler *et al.*, 1984). Thus it is plausible that invasive intestinal shigellosis with resultant endotoxemia, stimulates the bone marrow to produce and release additional leucocyte into the blood (Butler *et al.*, 1985). The increased numbers of leucocytes may be further activated by the endotoxin to generate procoagulant activity thus triggering the deposition of fibrin in renal glomeruli resulting in the hemolytic uremic syndrome.

Both cases reported here had severe colitis and developed renal failure thereafter. The peritoneal dialysis was done in the first case and symptomatic treatment in the second case. Both showed complete recovery. It was suggested that when hemolytic uremic syndrome is preceded by a prodomal phase with digestive disturbance the prognosis is better than when there is no such phase. (Trompeter *et al.*, 1983). As in the idiopathic hemolytic uremic syndrome, reversibility of renal failure determine prognosis. The goal of therapy is to provide adequate time for spontaneous recovery of renal function and resolution of the microangiopathy. Early and repeated peritoneal dialysis in severe cases has reduced mortality.

SUMMARY

Two patients with hemolytic uremic syndrome admitted to Udornthani Hospital, Thailand, were reported. The preceding illness was shigellosis. The stool culture was positive for *Shigella dysenteriae* in one patient and *Shigella flexneri* in another. The management was successful with peritoneal dialysis in one and symptomatic treatment in another. Both patients had complete recovery.

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