NOTES

Disseminated Intravascular Coagulation Associated with Rotavirus Gastroenteritis: Report of Two Cases

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During one winter season, two children with rotavirus gastroenteritis who developed fulminant disseminated intravascular coagulation were seen at our hospital. Disseminated intravascular coagulation probably resulted from hypovolemic shock and acidosis, although extraintestinal spread of the virus cannot be excluded.

Rotavirus is the most common cause of severe dehydrating diarrhea in children in the United States and around the world. Although disseminated intravascular coagulation (DIC) was listed as a possible complication of rotavirus gastroenteritis in one review article [1], no cases of rotavirus gastroenteritis associated with DIC have been reported in the English-language literature. We report the cases of two infants with rotavirus diarrhea whose course was complicated by DIC.

Case Reports

Case 1. A previously healthy 3-month-old male infant presented to an outside hospital with a 1-day history of tactile fever and profuse, watery diarrhea. He was lethargic and had shallow respirations; his eyes were sunken, his lips were dry, and capillary refill was delayed. His vital signs were as follows: temperature, 41°C; pulse, 240/min; respirations, 80/min; and blood pressure, 78/55 mm Hg. The patient was intubated and resuscitated with normal saline (70 mL/kg). Cultures of blood, urine, CSF, and stool were performed, and therapy with iv ampicillin, cefotaxime, and erythromycin was administered. Laboratory studies revealed the following values in serum: arterial blood gas pH, 7.18; sodium, 148 mmol/L; potassium, 4.7 mmol/L; chloride, 120 mmol/L; bicarbonate, 10 mmol/L; blood urea nitrogen, 6.1 mmol/L; creatinine, 90 µmol/L; glucose, 3.9 mmol/L; hemoglobin, 110 g/L; WBC count, 15 × 10^9/L; and platelet count, 470 × 10^9/L. Laboratory studies revealed the following values in CSF: WBC count, 2 × 10^6/L; glucose, 2.3 mmol/L; and protein, 0.57 g/L. Examination of stool samples with methylene blue did not reveal any WBCs.

After the patient was stabilized, he was transferred to Harbor-UCLA Medical Center (Torrance, CA). Over the next 24 hours, he developed DIC (prothrombin time, 22.1 seconds; activated partial thromboplastin time, 72.1 seconds; fibrinogen level, 1.2 g/L; fibrin split products, >40 mg/L; and platelets, 42 × 10^9/L). Examination of a peripheral blood smear revealed a few schistocytes. Liver enzymes were elevated 24 hours after admission (peak values of aspartate aminotransferase [AST] and alanine aminotransferase [ALT] were 676 U/L and 394 U/L, respectively). The patient received transfusions of platelets and fresh frozen plasma, and his DIC resolved over 3–4 days. He continued to have 20–50 mL/(kg·d) of stool output until hospital day 7. His course was complicated by seizures; findings of a head CT scan were normal. A workup for an inborn error of metabolism was negative.

Bacterial cultures of blood, urine, and CSF were negative. Culture of stool samples yielded a poliovirus, presumably a vaccine strain. Stool cultures were negative for Salmonella species, Shigella species, Campylobacter species, and enterohemorrhagic Escherichia coli. EIA of stool samples was negative for Clostridium difficile toxin, but EIA of stool samples was positive for rotavirus.

Case 2. A 5-month-old female infant with trisomy 21 and atrioventricular canal presented to our emergency department with a 1-day history of fever (temperature to 38.3°C), vomiting, watery diarrhea, and decreased oral intake. She had not been in known contact with anyone who was ill. The infant was in mild respiratory distress; her extremities were cool, and capillary refill was delayed. Her anterior fontanelle was sunken, her lips and mucous membranes were dry, and there was tenting of the skin. Her vital signs were as follows: temperature, 40°C; pulse, 164/min; respirations, 46/min; and blood pressure, 79/46 mm Hg.

Laboratory studies revealed the following values in serum: sodium, 138 mmol/L; potassium, 4.9 mmol/L; chloride, 102 mmol/L; bicarbonate, 13 mmol/L; blood urea nitrogen, 7.5 mmol/L; and protein, 1.3 g/L. Examination of stool samples with methylene blue did not reveal any WBCs.

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mmol/L; creatinine, 60 μmol/L; hemoglobin, 129 g/L; WBC count, 18.3 × 10^9/L (27% polymorphonuclear cells, 30% band forms, 39% lymphocytes, and 4% monocytes); and platelet count, 348 × 10^3/L. Laboratory studies revealed the following values in CSF: WBC count, 0; glucose, 3.7 mmol/L; and protein, 0.27 g/L.

Six hours after several unsuccessful attempts at venous access, a cutdown was performed and maintenance fluids and cefotaxime were administered. Unfortunately, initial fluid resuscitation was not aggressive because of concerns about the patient's cardiac status. Repeated laboratory tests revealed the following levels of electrolytes: sodium, 150 mmol/L; blood urea nitrogen, 27.8 mmol/L; and creatinine, 210 μmol/L. Over the first 12 hours of hospitalization, the patient developed DIC (prothrombin time, 21.2 seconds; activated partial thromboplastin time, >100 seconds; fibrinogen level, 2.5 g/L; fibrin split products, >40 mg/L; and platelet count, 39 × 10^9/L). Examination of a peripheral blood smear revealed occasional schistocytes. The results of liver function tests were obtained 24 hours after admission and revealed an AST level of 885 U/L and an ALT level of 302 U/L; these levels peaked the following day at 2,110 U/L and 605 U/L, respectively.

The patient had frank blood in her stool and urine and bled from her iv catheter sites. She continued to have profuse diarrhea (50 mL/kg·d) during the first 3 days of hospitalization. Her course was complicated by pulmonary edema requiring intubation as well as by seizures; a head CT revealed a left parieto-occipital stroke. She received transfusions of platelets and fresh frozen plasma, and her DIC resolved by hospital day 4. She was discharged from the hospital after 16 days with right hemiplegia. Bacterial cultures of blood, urine, and CSF were negative, and stool cultures were negative for Salmonella species, Shigella species, Campylobacter species, and enterohemorrhagic E. coli. Serologies for hepatitis A, B, and C were nonreactive. EIA of stool samples was positive for rotavirus.

Discussion

DIC describes a constellation of clinical and laboratory abnormalities resulting from a combination of accelerated fibrinogenesis and fibrinolysis. DIC can serve as the final common pathway for a variety of disorders that activate the coagulation system and lead to the systemic circulation of thrombin and plasmin [2]. A cycle of thrombosis and hemorrhage ensues, resulting in compromised organ perfusion and shock. Bleeding manifestations range from petechiae and purpura to life-threatening hemorrhages. Microvascular thrombi can manifest as signs of end-organ dysfunction such as seizures or renal failure. Laboratory findings include thrombocytopenia, prolongation of the prothrombin time and activated partial thromboplastin time, elevated fibrin split products, and reduction in the amount of clotting factors, particularly fibrinogen. The peripheral blood smear may reveal microangiopathic changes in the RBCs such as schistocytes.

Our patients had classic laboratory findings of DIC and clinical evidence of hemorrhage and end-organ dysfunction. Given the proposed pathophysiology of DIC, what in the disease process, specifically rotavirus gastroenteritis, “triggered” DIC?

Shock of any etiology can give rise to DIC. Hypovolemic shock with acidosis, hypernatremia, and multiorgan hypoperfusion is a potential cause of DIC in our patients. The process likely begins either with endothelial damage, which activates the intrinsic coagulation pathway, or with a platelet-release reaction and subsequent activation of the procoagulant system. Further fueling the derangements in coagulation is ischemia-induced liver dysfunction, which leads to impaired synthesis of coagulation-related proteins and to impaired clearance of activated clotting factors and end-products of fibrinogen breakdown.

In children, DIC is most often associated with overwhelming sepsis, particularly with gram-negative bacteria. The proposed mechanism of DIC is endotoxemia, which leads to cytokine-mediated activation of the extrinsic coagulation system, a platelet-release reaction, and endothelial sloughing with subsequent activation of the intrinsic clotting cascade [3]. Could bacterial sepsis have caused DIC in our cases? Damaged colonic mucosa can result in transient bacteremia, which leads to gram-negative sepsis; however, rotavirus infects the small intestinal villus epithelium. Since the small intestine is a relatively sterile environment and our patients had negative blood cultures, gram-negative sepsis is an unlikely cause of DIC in our cases.

Many viruses, such as varicella, cytomegalovirus, and HIV, have been associated with DIC. The inciting mechanisms are unclear, but these viruses may cause endothelial sloughing, lead to formation of antigen-antibody complexes, or stimulate the production of antplatelet antibodies [4]. Many of the viruses linked to DIC cause viremia. Rotavirus antigen has been detected in the sera [5] and in the liver and kidneys [6] of immunodeficient children with chronic rotavirus diarrhea. Rotavirus particles were demonstrated by electron microscopy in the CSF of one child with rotavirus gastroenteritis and encephalopathy [7]. Rotavirus RNA was also detected by PCR in the CSF of another child with rotavirus gastroenteritis and encephalitis [8]. These reports suggest that extraintestinal spread of rotavirus occurs in at least some patients.

We report the cases of two infants with rotavirus gastroenteritis who developed fulminant DIC. Rotavirus infection is very common; thus, when it presents concurrently with another entity, one must be cautious before attributing the association to a cause-and-effect relationship rather than merely a temporal one. Nonetheless, we believe that severe rotavirus gastroenteritis resulted in DIC in our cases. It is likely that DIC was a consequence of hypovolemic shock and its associated metabolic derangements and multiorgan dysfunction, although a direct effect of the virus cannot be excluded. Such devastating complications from a very common illness emphasize the importance of prompt, appropriate hydration therapy and the need for a safe, effective vaccine against rotavirus infection.
References