Severe Upper Gastrointestinal Hemorrhage in the Newborn†

LUMDUAN WONGSAWASDI, M.D.*,
NUTHAPONG UKARAPOL, M.D.*,
SOMPORN CHOTINARUEMOL, M.D.*

Abstract

Three infants with severe upper gastrointestinal hemorrhage with esophagogastroduodenoscopic (EGD) findings were reported. The underlying conditions of these infants included Down's syndrome, hypoplastic left heart, and diaphragmatic hernia. The precipitating factors were identified in all cases, including prenatal stress, hypoxemia, prolonged ventilatory support, and gastroesophageal reflux. The EGD findings were composed of multiple gastric ulcers and a duodenal ulcer in the first 2 cases, whereas esophagitis and gastritis were noted in the last case. These ulcers were classified as secondary peptic ulcers. All cases responded well to medical treatment, including ranitidine, sucralfate, omeprazole, cisapride, and octreotide.

Key word : Gastrointestinal Hemorrhage, Newborn, Esophagogastroduodenoscopy

**WONGSAWASDI L,
UKARAPOL N, CHOTINARUEMOL S
J Med Assoc Thai 2002; 85: 114-119**

Severe upper gastrointestinal bleeding in the neonate is an uncommon condition which has been sporadically reported. The underlying pathology includes esophagitis, gastritis, or peptic ulcers. It is usually classified as secondary stress ulcers(1) and associated with other serious conditions, such as intracranial bleeding, increased intracranial pressure, congenital heart disease, asphyxia, respiratory failure, hypoglycemia, and the prolonged use of drugs, e.g. dexamethasone(2), indomethacin(3), tolazoline(4),

* Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

† Presented at the 14th Annual Meeting of the Gastroenterological Association of Thailand, Kanchanaburi, 13-15 December 2000.

sulindac[5] and ketorlac[6]. The ulcer, usually solitary, occurred more commonly at the duodenum and appeared to be acute without a marked surrounding inflammatory cell infiltration noted histologically. Primary peptic ulcer has been occasionally reported in healthy full term neonates who did not have any perinatal complications and presented with massive upper gastrointestinal hemorrhage bleeding in the first week of life[7-9]. In these infants, diffuse hemorrhagic gastritis with multiple gastric erosions accounted for the bleeding. However, there was a report of esophagitis and gastritis, presented with bloody amniotic fluid and dilated intestinal loop, which were diagnosed by endoscopy at birth[10]. Therefore, prenatal stress is responsible for another precipitating factor[11]. Recently, Benhamas et al reported risk factors for severe esophageal and gastric lesions in term neonates by a case control study, in which the use of antacid by mothers during the last month of pregnancy and breast feeding might play an offensive and protective role against severe lesions in neonates, respectively[12].

The report aimed to study the underlying pathology in three newborns with severe upper gastrointestinal hemorrhage which was defined as bleeding requiring blood transfusion and significant vital sign change. We also demonstrated the benefit of fiberoptic upper gastrointestinal endoscopy in the newborn.

Case 1

A 2,400-gram, female, full term baby was born by vacuum extraction due to an ineffective voluntary expulsive force (IVEF) to a 38-year-old primigravida mother. The mother felt less fetal movement about 10 days before delivery. The Apgar score was 9 and 10 at 1 and 5 minutes, respectively. While she was being formula fed, she was unable to suck properly and cyanosis was noticed on the first day of feeding. At 24 hours of age, she vomited fresh blood and nasogastric tube lavage revealed coffee ground contents. She also passed melena. Her vital signs were temperature 36°C, RR 70/minute, HR 135/minute, BP 60/mmHg. The oxygen saturation was 80-85 per cent. The physical examination was unremarkable except for clinical Down's syndrome. The hemoglobin was 17 g/dl, WBC 22,000/mm^3, and platelets count 235,00/mm^3. The blood taken for PT and PTT was clotted. Four hours later, her hematocrit dropped to 48 per cent. The packed red cell was transfused and gastroscopy was carried out. Esophagitis, gastritis with multiple small gastric ulcers and a 1-cm duodenal ulcer were noted. Intravenous ranitidine at 1.5 mg/kg/dose every 6 hours and sucrafate suspension at 250 mg every 6 hours were given. Ampicillin and gentamicin were also prescribed for sepsis. She did well later with no further bleeding and could be formula fed on day 8 after the bleeding. Ranitidine and sucralfate were continued for 1 and 2 weeks, respectively. She was followed-up for 6 months without any bleeding being observed.

Case 2

A 2,500-gram, full term boy was born with an uneventful delivery to a 32 year-old primigravida. The Apgar score was 9 and 10 at 1 and 5 minutes, respectively. He was initially breast fed and passed normal meconium on the first day of life. At 2 days of age, a progressive lethargy, regurgitation, and blood stained stools were noted. The initial investigation showed hematocrit 41 per cent, WBC 30,600/mm^3, PMN 93 per cent, and the platelet count 65,000/mm^3. PT and PTT were 32.4 and 86.3 minutes, respectively. The plain abdomen revealed a fixed bowel loop dilatation. He was incubated and treated with cefotaxime and amikacin. Then, the patient was referred to our hospital with a diagnosis of sepsis and suspected gut obstruction.

After admission, he was afebrile. Reintubation was performed and a blood clot was seen at the end of the endotracheal tube. He subsequently became active and alert with a heart rate of 160/min and blood pressure of 61/40 mm Hg. The physical examination was unremarkable. The antibiotic was changed to ceftazidime because of suspected *Pseudomonas* infection at our hospital. After supportive treatments, the patient could be extubated the following day. Twelve hours after extubation, fresh blood was noted on the nasogastric tube with bleeding per rectum. The blood pressure decreased to 45/30 mmHg. The hematocrit dropped from 53 to 38 per cent. PT and PTT were14 and 40.3 seconds, respectively. He was transfused with packed red cells at 10 ml/kg 5 times, and fresh frozen plasma was also given at 10 ml/kg. Dopamine at a rate of 10 micrograms/kg/min was also administered. Gastroscopy was performed the next day, which revealed generalized hyperemia of gastric mucosa and multiple gastric ulcers with a diameter of 0.3-0.5 cm at the lower gastric body and antrum. No active bleeding was noted during the procedure. The duodenum

could not be identified, due to a lot of blood content. Because of the severe hemorrage, octreotide at 1 microgram/kg was started, followed by a continuous drip at a rate of 1 microgram/kg/hour. Omeprozole at 1 mg/kg/day was also given intravenously for 4 days with sucralfate at 70 mg/kg/day. The initial treatment was then replaced by ranitidine at 1.5 mg/kg/dose every 8 hours after the bleeding was controlled. The patient gradually recovered from the upper gastrointestinal bleeding, but later developed dyspnea and was found to have a hypoplastic left heart syndrome.

Case 3

A 3,100-gram, full term male was delivered vaginally without complications with a gestational age of 42 weeks. The Apgar score was 8 to 9 at 1 and 5 minutes, respectively. Immediately after birth, he was intubated and put on a ventilator because of respiratory distress. He was found to have left a diaphragmatic hernia and referred to Chiang Mai University Hospital. The patient was operated on to close the hernia with a prosthetic graft patch on the 4th day of life. During post-operative care, he needed ventilatory and parenteral nutrition support. During the second week of life, he was noted to have intermittent abdominal distention and intolerance to feeding. Fifteen milliliters of coffee ground content was noted from the nasogastric tube. The hematocrit dropped from 47 to 34 per cent. Packed red cell at 10 ml/kg was transfused. Gastroscopy demonstrated erythema of the esophagus, gastric body, and antrum with some blood clots. The duodenum was normal. An esophageal biopsy revealed evidence of intraepithelial infiltration of the neutrophils up to the surface. Ranitidine at 1.5 mg/kg/dose was administered intravenously with sucralfate suspension at 100 mg given orally every 6 hours. Cisapride was added at a dose of 0.2 mg/kg/dose for treating gastroesophageal reflux, demonstrated by esophagitis. The patient improved very well, with no coffee ground contents and he seemed to tolerate feeding adequately with weight gain. Ranitidine and sucralfate were given for 2 and 4 weeks, respectively. Twenty-four hour pH monitoring confirmed the diagnosis of gastroesophageal reflux with a reflux index of 27 per cent.

DISCUSSION

Acute peptic ulcer in newborns is a rare entity and has been sporadically reported in the literature. The patients could present with upper gastrointestinal bleeding, perforation, and recurrent vomiting[7,13]. Vomiting might result from pylorospasm, associated with pyloric channel ulcer[7]. This was similar to pyloric syndrome in adults. Most of these lesions were described as secondary peptic ulcers and were associated with stressful events, for instance sepsis and asphyxia. Similar to adults, children are also at risk of developing stress ulcers [14]. An imbalance between defensive (mucosal layer, motility) and aggressive (gastric acid, bile salts, enzymes) factors is principally responsible for the pathogenesis of the stress ulcer. The basic pathophysiology may be similar in children and adults, but there might be differences in the time of developing ulceration, ulcer location, and the number of ulcers. Other causes of upper gastrointestinal bleeding consist of the adverse effects of many drugs, such as corticosteroids and indomethacin, hemorragic disease of the newborn, and isolated cavernous hemangioma of the stomach[15].

Initially, it is essential to exclude maternal blood using the Apt-Downey test, particularly in a neonate presenting with upper gastrointestinal hemorrhage on the first day of life. A contrast radiographic study appears to be a useful and well tolerated procedure for diagnosing ulcers. Thomson et al reported using barium contrast radiography and fluoroscopy to demonstrate ulcers in 81 per cent of young infants with upper gastrointestinal hemorrhage[7]. Not only could it demonstrate the location of the ulcers, but also pylorospasm and gastric outlet obstruction. With the advent of fiberoptic gastrointestinal endoscopy, this excellent technique is ideal for making a specific diagnosis, such as stress ulcer, gastritis, esophagitis, esophageal varices, and any abnormal mucosal lesions. It is well tolerated without any significant complications. All three cases in this study reported lesions by endoscopy. Multiple gastric lesions with esophagitis and gastritis were classified as secondary peptic or stress ulcers. The precipitating factors included hypoxia in the second case, and the prolonged use of a ventilator with gastroesophageal reflux in the third case. However, in the first case, there was no known precipitating factor, except that her mother had an ineffective voluntary expulsion force requiring a vacuum extraction delivery. This probably resulted in prenatal stress to the baby. Interestingly, there was also a report that social stress can cause gastrointestinal hemorrhage[10].

Early report of peptic ulcer disease in infancy revealed a high mortality rate and among the affected individuals, surgery was the only hope for survival[13]. With the improvement of conservative medical management and adequate blood transfusion, most of the patients recovered successfully. Thomson et al reported the successful medical treatment of severe upper gastrointestinal hemorrhage infants and only one patient in this report required atropinization for persistent pylorospasm[7].

Although severe gastrointestinal bleeding can be managed conservatively, the role of antacids, H_2 antagonists, and proton pump inhibitors is difficult to determine. Antacids have been used for a long time. Nontheless, there was a report of antacid bezoars in a premature infant, which contained a high concentration of magnesium[16]. H_2 blockers have been used for prophylaxis as well as treatment of stress induced gastric lesions. Among these, cimetidine has been reported in the treatment of gastrointestinal bleeding in neonates. However, there was evidence that it might partially abolish the effect of tolazoline in the treatment of persistent pulmonary hypertension and cause further episodes of hypoxemia[17]. Moreover, it was not proven that cimetidine prevents gastrointestinal bleeding during steroid therapy[18]. In contrast to cimetidine, ranitidine has been considered safe for the treatment of critically ill neonates[19]. It was shown to keep the intraluminal gastric pH over 4 with a dose of 1.5 mg/kg, three times a day for term infants, and at 0.5 mg/kg, twice a day for pretmature infants[20]. Omeprazole, a potent inhibitor of gastric acid secretion, is usually reserved as a second line treatment for patients unresponsive to the H_2 recepter antagonists. However, there has been no report of omeprazole being used in gastrointestinal bleeding in the neonate. The effective dose in children is 0.3-0.7 mg/kg/day. The octreotide, a somatostatin analogue, has been reported safe and effective in controlling nonarterial severe gastrointestinal bleeding in children[21]. It has been also used in a newborn with persistent hyperinsulinemic hypoglycemia of infancy. However, tachyphylaxis resulting from continuous use, limited its effect[22]. Our report showed successful medical treatment in neonates with severe upper gastrointestinal hemorrhage. Ranitidine and sucralfate are still the effective drugs for treating stress ulcer in neonates without any complications. However, omeprazole and octreotide were given with a promising result in the second patient of this report because of massive bleeding. This report also showed that fiberoptic upper endoscopy is helpful to establish the correct diagnosis and provide the appropriate treatment, particularly in a case with unknown precipitating factors, such as esophagitis secondary to gastroesophageal reflux as in the last patient.

ACKNOWLEDGEMENT

The authors wish to thank Dr. Torpong Sanguansermsri, Head of the Pediatric Department, for supporting and allowing us to publish this report.

(Received for publication on June 14, 2001)

REFERENCES

1. Nord KS. Peptic ulcer disease in the pediatric population. Pediatr Clin North Am 1988; 35: 117-40.
2. Wolf YW, Reyna T, Schrapp KP, et al. Steroid therapy and duodenal ulcer in infants. J Pediatr Gastroenterol Nutr 1991; 12: 269-71.
3. Soll AH, Kurata J, Mc Guigan JE. Ulcers, nonsteroidal anti-inflammatory drugs and related matters. Gastroenterogy 1989; 96: 561-8.
4. Butt W, Auldist A, Mc Dougall P, et al. Duodenal ulceration: A complication of tolazoline therapy. Aust Paediatr J 1986; 22: 221-3.
5. Ng PC, So KW, Fok TF, et al. Fatal haemorrhagic gastritis associated with oral sulindac treatment for patent ductus arteriosus. Acta Paediatr 1996; 85: 884-6.
6. Alcaraz A, Lopez- Herce J, Serinal G, et al. Gastrointestinal bleeding following ketolac administration in a pediatric patient. J Pediatr Gastroenterol Nutr 1996; 2: 479-81.
7. Johnson DL. Heureux P, Thompson T. Peptic ulcer disease in early infancy: Clinical presentation and roentgenographic features. Acta Paediatr Scand 1980; 69: 753-60.
8. Goyal A, Treem W, Hyams JS. Severe upper gastrointestinal bleeding in healthy full-term neonates. Am J Gastroenterol 1994; 89: 613-6.
9. Liebman WM, Thaler MM, Buvanover Y. Endoscopic evaluation of upper gastrointestinal bleeding in the newborn. Am J Gastroenterol 1978; 69: 607-8.
10. Bedu A, Faure C, Sibony O, et al. Prenatal gastrointestinal bleeding cause by esophagitis and gastritis. J Pediatr 1994; 125: 465-7.
11. Pugh RJ, Newton RW, Piercy DM. Fatal bleeding from gastric ulceration during first day of life-possible association with social stress. Arch Dis Child 1979; 54: 146-8.
12. Benhamou PH, Francoual C, Glangeaud MC, et al. Risk factors for severe esophageal and gastric lesions in term neonates a case-control study. J Pediatr Gastroenterol Nutr 2000; 31: 377-80.
13. Bird CE, Limper MA, Mayer JM. Surgery in peptic ulceration of stomach and duodenum in infants and children. Ann Surg1941; 114: 526-42.
14. Crill CM, Hak EB. Upper gastrointestinal tract bleeding in critically ill pediatric patients. Pharmacotherapy 1999; 19; 162-80.
15. Nagaya M, Kato J, Niimi N, et al. Isoated cavenous hemangioma of the stomach in a neonate. J Pediatr Surg 1998; 33: 653-4.
16. Kaaplan M, Ozeri Y, Agranat A, et al. Antacid bezoar in a premature infant. Am J Perinatol 1995; 12: 98-9.
17. Kuint J, Linder N, Reichman B. Hypoxemia associated with cimetidine therapy in a newborn infant. Am J Perinatol 1996; 13: 301-3.
18. McDonnell M, Evans N. Upper and lower gastrointestinal complications with dexamethasone despite H2 antagonist. J Paediatr Child Health 1995; 31: 152-4.
19. Fontana M, Tornaghi R, Pertrillo M, et al. Ranitidine treatment in newborn infants: Effects on gastric acidity and serum prolactin levels. J Pediatr Gastroenterol Nutr 1993; 16: 406-11.
20. Kuusela Al. Long term gastric pH monitoring for determining optimal dose of ranitidine for critically ill preterm and term neonates. Arch Dis Child Fetal Neonatal Ed 1998; 78: F151-5.
21. Siafakas C, Fox Vl, Nurko S. Use of octreotide for the treatment of severe gastrointestinal bleeding in children. J Pedatr Gastroenterol Nutr 1998; 26: 356-9.
22. Anit Apak R, Yurdakok M, Oran O, et al. Preoperative use of octerotide in a newborn with persistent hyperinsulinemia of infancy. J Pediatr Endocrinol Metab 1998; 11: 143-5.

เลือดออกในทางเดินอาหารส่วนต้นอย่างรุนแรงในทารก†

ลำดวน วงศ์สวัสดิ์, พ.บ.,*
ณัฐพงษ์ อัครผล, พ.บ., สมพร โชตินฤมล, พ.บ.**

รายงานภาวะเลือดออกจากทางเดินอาหารส่วนบนอย่างรุนแรงในเด็กทารก 3 ราย พร้อมผลการตรวจทางเดินอาหารส่วนบนด้วยกล้องส่องกระเพาะ ผู้ป่วยทั้ง 3 รายต่างมีโรคพื้นฐานอยู่ก่อนได้แก่ Down's syndrome, hypoplasic left heart และ diaphragmatic hernia โดยมีปัจจัยที่ทำให้เกิดเลือดออกจากทางเดินอาหาร คือ prenatal stress, hypoxemia, prolonged ventilatory support และ gastroesophageal reflux ผลการตรวจกระเพาะอาหารด้วยการส่องกล้องพบเป็น multiple gastric ulcers และ duodenal ulcer ในผู้ป่วยรายที่ 1 และ 2 ส่วนในผู้ป่วยรายที่ 3 พบว่ามี gastritis และ esophagitis พยาธิสภาพที่พบเป็นแผลทุติยภูมิที่มีปัจจัยการเกิดต่างกัน ผู้ป่วยทั้ง 3 รายได้ผลดีต่อการรักษาโดยการให้ยาคือ ranitidine, sucralfate, omeprazole, cisapride, และ octreotide

คำสำคัญ : เลือดออกทางเดินอาหารส่วนต้น, ทารก, การตรวจด้วยกล้องส่องกระเพาะ

ลำดวน วงศ์สวัสดิ์, ณัฐพงษ์ อัครผล, สมพร โชตินฤมล
จดหมายเหตุทางแพทย์ ฯ 2545; 85: 114–119

* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่, เชียงใหม่ 50200

† เสนอรายงานในการประชุมประจำปีของสมาคมโรคทางเดินอาหาร ครั้งที่ 41 ณ โรงแรมพาวิลเลี่ยน กาญจนบุรี วันที่ 13–15 ธันวาคม 2543