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CASE REPORT / OLGU SUNUMU

Intussusception in a term newborn with duct-dependent congenital heart disease

Duktus bağımlı konjenital kalp hastalığı olan bir term yenidoğanda invajinasyon

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ABSTRACT

Prostaglandin E1 infusion is widely used to maintain patency of ductus arteriosus in newborns with duct-dependent congenital heart disease until surgery. Prostaglandin E1 is a lifesaving drug, but it has many side effects including fever, apnea, bradycardia, hypotension, convulsion, edema, and cortical hyperostosis. The gastrointestinal tract has not been recognized as a major site of serious adverse effects of prostaglandin E1 infusion, although diarrhea is a well-recognized side effect that usually responds to dose reduction. In this report, we present a case of intestinal intussusception presumably induced by prostaglandin therapy in a newborn with duct-dependent congenital heart disease.

Key words: Prostaglandin E1, newborn, gastrointestinal

ÖZET

Prostaglandin E1 infüzyonu, duktus bağımlı konjenital kalp hastalığı olan yenidoğanlarda ameliyat edilinceye kadar duktusu açık tutmak amacıyla yaygın olarak kullanılmaktadır. Prostaglandin E1 yaşam kurtarıcı bir ilactır ancak ateş, apne, bradikardi, hipotansiyon, konvülziyon, ödem ve kortikal hiperostoz gibi birçok yan etkiye de yol açabilir. İlacın doz azaltmasına yanıt veren ishal dışında gastrointestinal sistemle ilgili önemli yan etkisi rapor edilmemektedir. Bu yazıda duktus bağımlı konjenital kalp hastalığı olan ve olasılıkla prostaglandin tedavisi ile tetiklenen intestinal invajinasyon gelişen bir olgu sunuldu.

Anahtar kelimeler: Prostaglandin E1, yenidoğan, gastrointestinal

INTRODUCTION

After Coceani and Olley[1] showed that prostaglandin E1 and E2 were potent dilators of the fetal ductus arteriosus, numerous reports of their efficacy in treating infants with duct-dependent congenital heart defects were released in the literature. Heymann et al.[2] reported that, prostaglandin E1 therapy might be used to maintain ductal patency in newborns who depend on the ductus for oxygenation. An infusion rate of 0.05 μg per kg per min is associated with a high success in maintaining ductal patency and a low risk of complications observed in many systems including respiratory, cardiovascular, and central nervous systems.[3]

The gastrointestinal tract has not been well recognized as a major site of serious adverse effects of prostaglandin E1 infusion.[4] To the best of our knowledge, there are no data about intestinal intussusception induced by prostaglandin E1. In this report, we presented a case of intestinal intussusception presumably induced by prostaglandin therapy in a newborn with duct-dependent congenital heart disease.

CASE

The patient was a full term male baby (weight 3600g) born via vaginal delivery following a normal pregnancy. He did not need resuscitation after birth. However, he was noted to have cyanotic episodes with oxygen saturation of 70% at 2 hours of age despite oxygen therapy. He was intubated and immediately transferred to the neonatal intensive care unit. Echocardiography showed severe pulmonary stenosis, double outlet right ventricle, secundum atrial septal defect, large ventricular septal defect, and situs inversus with duct-dependent circulation.

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At 18 hours of age, an infusion of prostaglandin E1 in a dose of 0.05 µg per kg per min was started to maintain ductal patency until surgical intervention. Following prostaglandin E1 infusion, oxygen saturations of the patient reached to 80%. Inotropic support was used for management of hypotension. Enteral feeding could not be started because of hemodynamic instability.

Abdominal distension was noted at 48th hour of the prostaglandin E1 infusion (cumulative dose of 144 µg per kg). Brown gastric discharge from nasogastric tube and bloody stool were also noted. An abdominal direct X-ray showed no gas shadow except upper part of the abdomen (Figure 1). Arterial blood gas analysis was consistent with mixed acidosis. An upper gastrointestinal contrast study revealed a dilated hypotonic and hypokinetic stomach, duodenum, and jejunum. There was no contrast transition from jejunum to ileum (Figure 2). Doppler ultrasonography excluded malrotation.

On the third day of life, the patient was operated by pediatric surgery team. During operation, a jejunoileal (20 cm in diameter), and an ileoileal (15 cm in diameter) two necrotic intussusception masses were observed. End-to-end anastomoses were performed following extensive jejunoileal and ileal resection (Figure 3).

Figure 1. An abdominal direct X-ray showing no gas shadow except upper part of the abdomen

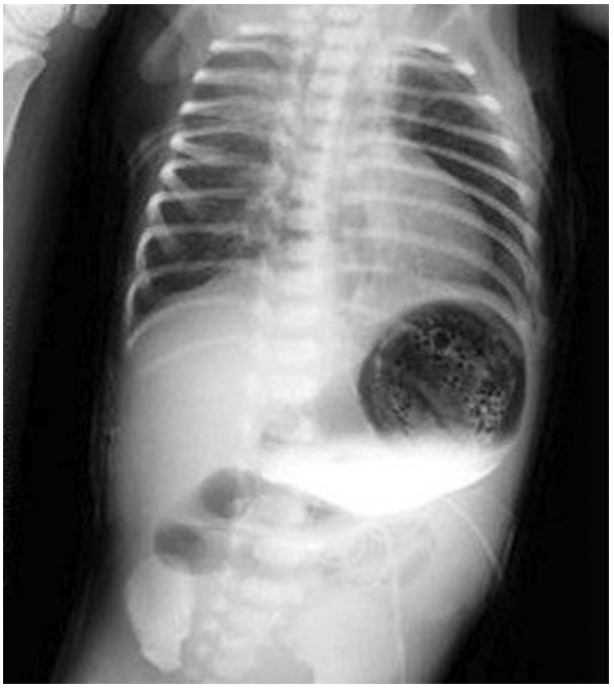

Figure 2. Contrast study showing no contrast transition from jejunum to ileum

Figure 3. Intraoperative photograph of the bowel of the patient. Note a jejunoileal necrotic intussusception mass

Microscopical examinations of the resected masses were consistent with necrosis, perforation, and intussusceptions. Viral studies for adenovirus and rotavirus were also negative.

At postoperative period, serum creatinine value was gradually increased, suggesting acute renal failure. This condition was successfully managed by adequate fluid and electrolyte treatment. Postoperative 7th day, abdominal distention re-developed. A bilious fluid was drained from nasogastric tube. Abdominal ultrasonography revealed dilated stom-

ach with a normal pyloric sphincter. Intussusception was not observed. Abdominal X-ray taken 10 days after the contrast study showed that contrast material did not yet leave the stomach. Abdominal distension and bilious drainage were gradually diminished after the use of procinetic drug (domperidon). Prostaglandin E1 infusion continued during the whole hospitalization period at the same infusion rate with a total dose of 7257 µg.

At the 28th of the hospitalization modified Blalock-Taussig shunt was performed by cardiovascular surgery team. The patient's clinical status was gradually deteriorated. He died of shock and bradycardia after the second day of the cardiac surgery.

DISCUSSION

Prostaglandin E1 is effective in improving pulmonary or systemic blood flow in infants with duct-dependent critical congenital heart defects. However, data on the various side effects are inadequate. The most common side effects are, fever, apnea, tachycardia/bradycardia, hypotension and flushing associated with prostaglandin E1 infusion.[3]

There are rare data on the effects of prostaglandin E1 on gastrointestinal system. Diarrhea is a well-recognized side effect that usually responds to dose reduction. Prostaglandin E2 was suspected of causing necrotizing enterocolitis among infants with symptomatic heart disease, but studies showed this complication was rare.[4] Prostaglandins have complex effects on gastrointestinal tract. They stimulate and inhibit intestinal motility, inhibit gastric acid secretion, and influence glucose and glycogen metabolism in the liver. Their mechanisms of action have not been clearly defined, although it appears certain that their effects are closely involved with the adenylate cyclase-cyclic adenosine monophosphate system.[5]

Prostaglandin E1 may cause gastric antral hyperplasia and pyloric stenosis. In a controlled study performed on adults, oral prostaglandin E1 therapy resulted in mucosal thickening in the stomach that regressed after therapy ended.[6] It can be speculated that sick neonates eliminate prostaglandin more slowly than adults. Therefore, the stimulation of prostaglandin E1 on the gastrointestinal mucosa may be much more intense in newborns. Nissan et al.[7] developed a model for intussusception in mice using intraperitoneal injection of lipopolysaccharide. Their results indicated that the induction of intussusception by lipopolysaccharide proceeds via parallel pathways involving cytokines, prostaglandins, and nitric oxide. Intestinal intussusception developed in our patient during the prostaglandin E1 infusion. To our knowledge, there is no report on this subject in the literature in human studies.

Intussusception is defined as the meshing of two ensuing segments of gastrointestinal tract. It is rare under 3 months of age; the incidence is 0.3% in the neonatal period.[8] Many factors and mechanisms have been proposed as causes for intussusception. Meckel diverticulum, polip, enteric cysts, adenom, hemangiom, hypertrophic ileal tissue, mesenteric lymphoadenopathy, adenoviruses or rotaviruses, cystic fibrosis, abdominal injury, hypoxia, and congenital malformations of the gut may cause intussusception in infancy.[8] We investigated and did not find any possible causes of intussusception except hypoxia due to cyanotic congenital heart disease.

The relation between prostaglandin E1 therapy and intestinal intussusception may reflect the severity of the cardiac lesion and cyanosis rather than a specific effect of prostaglandin E1. Low cardiac output and cyanosis may result in intestinal ischemia. Ulceration and perforation may follow submucosal hemorrhage and edema.[4] In infants, intermittent episodes of ischemia may result in progressive circumferential scarring and formation of strictures that lead to obstruction. The mostly affected areas of the intestine are cecum and terminal ileum, although other zones are also susceptible to ischemic damage. It is not clear whether hypoxia may be implicated alone in the pathogenesis of intussusception as in our case. However, it can be speculated that hypokinetic effect of prostaglandin on intestinal tissue may induce intussusception. Peled et al.[4] showed an association between the duration of prostaglandin E1 infusion and its cumulative dose and the development of antral hyperplasia leading to gastric obstruction in neonates. Kobayashi et al.[9] showed that acute gastric outlet obstruction developed following the administration of prostaglandin E1 (cumulative dose of 2914 µg/kg) in a preterm infant with hypoplastic left heart disease. In this case, cumulative dose of prostaglandin E1 was 144 µg /kg when abdominal distension developed. Subsequently, he was complicated with gastric and

intestinal hypomotility resulting in intussusception. Gastric mucosal hyperplasia or pyloric stenosis was not detected.

In conclusion, prostaglandin E1 may cause intestinal hypomotility resulting in intestinal necrosis, perforation, and intussusception in newborns with duct-dependent critical heart disease even in the first days of the therapy. Therefore, physicians should be aware of all possible side effects of this drug in this population. Prokinetics agents may be useful in prostaglandin induced hypomotility.

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