INTRODUCTION
Appendicitis is known as inflammation in the appendix of cecum which can be seen frequently in the childhood and very rarely in the neonatal period. Neonatal appendicitis can be associated with inguinal or umbilical hernia, Hirschsprung's disease, meconium plug, cystic fibrosis, group B Streptococcal septicemia and chorioamnionitis. There are reported cases with isolated appendicitis or as a component of Necrotizing Enterocolitis (NEC).1

Although there are NEC cases in newborns with hemolytic jaundice who had received Intravenous Immunoglobulin (IVIg) treatment, to the authors' knowledge this is the first report of neonatal appendicitis in a jaundiced infant with a history of IVIg treatment. Since appendicitis has a higher rate of morbidity and mortality with unspecific clinical presentation in this age group, the potential of severe hemolysis and/or IVIg treatment deserves attention of clinicians as risk factors for this rare disease that needs prompt diagnosis and intervention for favorable outcomes.

CASE REPORT
A term neonate at the 98th hour of life was admitted to the neonatal intensive care unit with jaundice. She was born after an uneventful pregnancy to a 29 years old mother via elective caesarean section with a birth weight of 2500 g. The mother whose blood group was ARh (-) had received Anti-D globulin after her first delivery, but not after her second pregnancy that ended with abortus. Laboratory tests of the infant revealed unconjugated hyperbilirubinemia (19 mg/dl), high lactate dehydrogenase level and mild anemia (hematocrit = 34%). There were signs of hemolysis in the blood smear. The infant had a blood group of ARh (+) and direct Coombs test was strongly positive. There were no other pathological signs or symptoms in her physical examination and laboratory tests. Intensive phototherapy was started according to the clinical practice guidelines of AAP for the management of hyperbilirubinemia in newborns.2 Intravenous Immunoglobulin (IVIg) therapy was given in a dose of 1 g/kg over 6 hours due to rapidly increasing bilirubin levels despite 6 hours of intensive phototherapy. Total bilirubin level decreased to 15.3 mg/dl at the 8th hour of IVIg treatment.

The patient developed abdominal distention, bilious retention and bloody stools 10 hours after IVIg therapy was completed. Repeated blood count and biochemical tests revealed thrombocytopenia (89000/mm³), leukopenia (3500/mm³) and elevated C-reactive protein (3.3 mg/dl, N < 0.8 mg/dl) with no other abnormality. D-dimer level was also normal. Abdominal X-ray showed intestinal dilatation and pediatric surgery was consulted for possible NEC and peritonitis (Figure 1). She was put on antibiotics

ABSTRACT
Neonatal appendicitis is a rare clinical condition that may cause high morbidity and mortality if diagnosis is delayed. There is usually an underlying disease; it can also be a localized form of necrotizing enterocolitis. Here, we present a term neonate who was treated with intravenous immunoglobulin because of severe isoimmune hemolytic jaundice. The patient developed abdominal symptoms within 10 hours of therapy, was diagnosed with acute perforated appendicitis and completely recovered after surgery.

for sepsis as soon as blood and urine cultures were obtained. Yellow-green colored and cloudy peritoneal lavage fluid had a bilirubin of 640 mg/dl (180 mg/dl conjugated), lactate dehydrogenase 1760 U/L, amylase and lipase levels below < 3 U/L. Upon these findings, the patient was operated with the suspicion of bowel perforation. A localized perforation in the appendix of cecum was observed during laparotomy. Other parts of intestines were found healthy.

Histopathological examination showed inflammation and tissue damage in appendix (Figure 2). The patient was completely recovered and was discharged within 4 days after surgery. Differential diagnostic tests to exclude other causes of neonatal appendicitis; such as sepsis, urinary tract infection, congenital cytomegalovirus infection, cystic fibrosis and Hirschsprung’s disease were all negative.

**Figure 2:** Histopathological examination of the appendix. A: Low power view of appendix. A totally necrotic gangrenous mucosa with a few residual glands and prominent flegmonous inflammation throughout the wall. (Haematoxylin-eosin, x40) B: Close up view of mucosa. Polymorphonuclear leucocyte-rich inflammation and residual lymphoid aggregates. (Haematoxylin-eosin, x100) C: Ganglion cells (arrows). (Haematoxylin-eosin, x200) D: Subserosal congested vessels with small fibrin clots in some of them (arrow). (Haematoxylin-eosin, x200).

**DISCUSSION**

Acute appendicitis is an uncommon entity in infants. It is difficult to diagnose, gets easily perforated, and is associated with high morbidity and mortality due to lack of specific clinical signs and symptoms in infancy. A treatment delay less than 48 hours is associated with a 35% incidence of perforation and is greater than 98% after 48 hours in early childhood. Therefore, the incidence of perforated appendicitis is high and ranges from 36.5% to 94% in infancy. Although diagnosed in the first day of admission; the patient also had perforation but recovered shortly after surgery. The thin and inelastic appendiceal wall with its meager blood supply and large amount of lymphoid tissue; small undeveloped omentum and relatively long mesenteries of the hollow viscera are defined as possible causes of high perforation rates in small infants. The relatively small size of the peritoneal cavity allows a more rapid spread of contamination in this population. There is usually an underlying risk factor such as disseminated NEC, Hirschsprung’s disease, cystic fibrosis, inguinal or umbilical hernia, meconium plug or infections like CMV enterocolitis or group-B *Streptococcal* sepsis. Clinical signs and symptoms include irritability, respiratory distress indicating peritoneal inflammation, abdominal distention, vomiting, and inflammation on abdominal wall. Abdominal X-ray may show abnormal gas pattern, free peritoneal fluid and air, thickening on abdominal wall, right scoliosis and obliteration of psoas margin.

In this case, there were no known risk factors or underlying diseases. However, the presence of NEC cases reported after IVIg administration, had brought a possible effect of IVIg for the development of appendicitis to mind. Time range after administration of IVIg seems to be similar to cases reported in literature and it is usually between 2-96 hours. It is known that IVIg therapy reduces the need for exchange transfusion in severe isoimmune hemolytic jaundice. However, important adverse reactions of this treatment are also well described. Hyperviscosity of the IVIg solutions may increase the risk for intestinal thrombosis. Since IVIg is generally administered during the first day of life, its prothrombotic effect may also increase the physiologic hypercoagulability of the fetus and newborn after birth.

The estimated mortality of neonatal appendicitis has remained about 20 - 25% over the past 30 years. It is important to exclude acute appendicitis in newborns with abdominal distention, even if there is another underlying disease. Clinicians should also be aware that IVIg treatment and/or severe hemolysis may increase the risk of compromised intestinal circulation possibly by causing hyperviscosity.

**REFERENCES**


