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CLINICAL CASE

Spontaneous perforation of the bile duct in a neonate: An unexpected finding. Case report

Perforación espontánea de la vía biliar en un neonato: un hallazgo inesperado. Caso Clínico

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Abstract

Introduction: Spontaneous extrahepatic bile duct perforation is rare in newborns. It is a surgical cause of jaundice in this period and the acute presentation is unusual. **Objective:** To report a case of spontaneous bile duct perforation in a newborn due to its serious complications if an early and timely diagnosis is not performed. **Clinical case:** A 10-day-old newborn who developed food rejection, fever and abdominal distension without jaundice, acolia, or coluria two days prior of admission. The laboratory tests showed leukopenia, thrombocytosis, increased C-reactive protein, and normal hepatic function. The abdominal x-ray showed pneumoperitoneum, and the diagnosis of necrotizing enterocolitis was made. Laparotomy was performed; extrahepatic bile duct perforation and biliary peritonitis were noted. Intraoperative cholangiography demonstrated rescatable proximal bile duct and dilated cystic duct. Hepatic-jejunostomy was performed with Roux-en-Y and cholecystectomy. In the postoperative study portal thrombosis was found, so he received anticoagulant treatment. At 8 months of age, the patient had enteral feeding tolerance and adequate weight gain. **Conclusions:** Biliary perforation is a rare entity and more in the neonatal period, a condition that makes it a diagnostic and therapeutic challenge. The prognosis will depend on early intervention and intraoperative findings.

Keywords: Spontaneous perforation of the bile duct, bile peritonitis, newborns

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Introduction

The spontaneous perforation of the extrahepatic bile duct is a very uncommon disease and has an incidence rate of 1.5 cases per 1,000,000 neonates[1]. This disease develops more frequently during the first months of life; nevertheless, it might occur from the prenatal period (25 weeks of gestation) up to 7 years. Its peak incidence is around 6 months[2].

An early diagnosis is essential for an immediate therapeutic intervention; however, its clinical presentation makes it a clinical challenge, due to its low frequency and nonspecific symptoms, which simulate more common diseases during the prenatal period, such as enterocolitis[3]. Its classic presentations on a healthy neonate are abdominal distention, irritability, and fluctuant jaundice. However, jaundice is less common during the acute phase and it simulates an intestinal obstruction[4]. It will begin, less frequently, as a case of acute abdomen[5]. The prognosis depends on an early surgical intervention[6]. In 1932 Dijkstra reported the first spontaneous perforation of the bile duct in pediatrics[7]. The 3-month old patient who died after 5 weeks of jaundice and progressive abdominal distention, the autopsy showed the perforation in the union between the common bile duct and the cystic duct[8]. Since then, less than 150 cases have been reported in the literature[9], from which a very small percentage affected neonates. The spontaneous perforation of the bile duct is an uncommon disease, but it is the third most common cause of surgical jaundice in neonates, the first one is biliary duct atresia and the second one is the choledochal cyst[10]. Its etiology has not been determined yet, however, many consider that the main causes are the deformity of the bile duct walls, congenital weakness and biliary duct ischemia due to microcirculation thrombosis[11]. The congenital wall weakness at the union between the cystic duct and the common biliary duct makes it the most frequent perforation site. In perforation cases, the posterior wall of the bile duct or common hepatic duct, the diagnosis of the exact place is difficult, might be along with gallbladder perforation[12].

Other causes include pancreaticobiliary anomalies, such as the choledochal cyst, and anomalies in the pancreaticobiliary ductal union that cause pancreatitis, the obstruction of the biliary duct is due to stenosis, calculus[13], tuberculosis, viral infections and necrotizing enterocolitis[14], the latter one is an important differential diagnose during the neonatal period.

A case of a 10 days old neonate with a spontaneous perforation of the bile duct was reported, with an acute presentation that was initially treated as necrotizing enterocolitis and its diagnosis was determined during the surgical exploration.

The objective is to present cases of a spontaneous perforation of the bile duct in neonates due to its severe complications if it is not diagnosed early, also to discuss problems with the diagnose and its management in the available literature.

Clinical Trial

A female neonate, daughter of a 19-years-old primiparous mother, who had 4 prenatal controls and 2 prenatal ultrasounds, the first ultrasound during the 29th week and the second one during the 34th week of gestation, which were described as normal. Negative ELISA test for H.I.V. 1 and 2, a non-reactive Serum VDRL test, a negative hepatitis B virus antigen, a negative Toxoplasma gondii IgM/IgG, there was no datum of a neonatal screening test for group B streptococcus.

The birth was normal, at a health-care center during the 38th week of gestation, the weight of neonate was 6.3lb (2,870 grams), height 19.2in (49 cm), and its Apgar score was 8 at the first minute and 10 at 5 minutes. The family history had no relevance. The neonate was fed only with breast milk.

During the 8th day of postnatal life, the mother had to seek for medical advice at the hospital in her city, due to clinical symptoms: unmeasured fever, refusal to breastfeeding, vomiting and abdominal distention. The test showed an abdominal wall erythema and abdominal distention; the laboratory tests showed leukopenia (leukocytes 3,200/uL), thrombocytosis (platelet 510,000/uL), high C-reactive protein (384 mg/L, normal value (NV) < 6 mg/L), hyperglycemia (217 mg/dl). An abdomen X-Ray was performed, which showed a distended loop of bowel A necrotizing enterocolitis was diagnosed and and medical management was started with Ampicillin and Gentamicin. The neonate was referred to more complex hospital.

The patient was admitted to our medical center at her 10th day of life, temperature was 101.12°F (38.4 °C). Clinical features included irritability, abdominal distension, an abdominal wall with erythematous zone in abdominal flanks, abdominal tenderness, signs of umbilical infection, jaundice, acholia nor choluria. The admission medical test showed high numbers of C-reactive protein (269.94 mg/L), leukopenia (total leukocytes: 3,100/uL), normal liver functions (alkaline phosphatase: 47.8 UI/L, aspartate transaminase: 20.8 UI/L, alanine transaminase: 24.8 UI/L), no signs of hyperbilirubinemia (total bilirubin: 1.52 mg/dL, indirect bilirubin: 0.58 mg/dL and direct bilirubin 0.94 mg/dL).

The simple abdomen ultrasound on anteroposterior view showed air in the peritoneal cavity, distributed in the left hypochondrium towards the umbilical region and liquid between loops (figure 1). Advanced

necrotizing enterocolitis was detected, and it was decided to administrate Ampicillin 100 mg/kg every 8 hours, Cefepime 50mg/kg every 12 hours in meningeal doses. Since a lumbar puncture was not performed due to the urgency of the case and the instability of the patient, Metronidazole 7.5 mg/kg per day was added.

The laparotomy showed a spontaneous perforation of the extrahepatic bile duct, with retroperitoneal encapsulation of the bile duct. In addition, 1 cm necrosis from the common bile duct was found, affecting the cystic duct, which did not allow a primary anastomosis. An intraoperative cholangiography was performed, which showed a salvageable proximal bile duct and a dilated cystic duct. Thus, a transmesocolonic Roux-en-Y hepaticojejunostomy was performed, 7.8 in (20 cms) near the Treitz's ligament. In addition, a cholecystectomy and a peritoneal lavage were performed, leaving a drain in the surgical site. The intestinal canal of the patient had no damages.

72 hours later, a second surgical revision was performed. A drainage a big amount of serous fluid from the incision. The Roux-en-Y anastomosis was analyzed, no leakages were found, or bile near the Jackson Pratt's drain in the peritoneal cavity. The previous Penrose's drainage was left, peritoneal lavage and it closed without any difficulties.

Multi-sensitive *Escherichia Coli* bacteremia in the blood culture was found, thus, the Cefepime therapy continued (50 mg/kg every 12 hours, for 14 days). The control blood cultures were negative. The patient required 10 fasting days and 12 days of parenteral nutrition. The enteral nutrition began as a mixture of formula and breast milk, which was adequately tolerated.

The extrahepatic bile duct biopsy showed a severe acute inflammation, liquefaction necrosis and granulation tissue, which was negative in malignancy. The peritoneal liquid culture was negative. Since one of the complications was the portal vein thrombosis, a duplex scanning of the portal blood vessels was performed, an absence of blood flow of the portal vein in the hilium was found, and a predominant arterial intrahepatic flow (figure 2). An abdominal angiotomography was performed, the hilum portal segment from the splenic-mesenteric confluence could not be identified, and instead, a hypodense band that might have been an old zone of a proximal portal thrombosis was found (figure 3). The D-dimer was high (15,850 mcg/L), the lipidic profile was normal (total cholesterol: 155 mg/dL), triglycerides: 198.7 mg/dL). A thrombophilia study was performed, due to that the patient lives in a rural area and to obtain a baseline, the protein S of the coagulation was normal (69%), the protein C of the coagulation was slightly below normal (61%). The patient was evaluated by hematology and based on the paraclinical findings and images, and then the anticoagulation with enoxaparin began (1 mg/kg every 12 hours).

Other follow-up studies of other systems with transfonantelar ultrasounds and echocardiograms were performed, which were normal.

During the follow-up period (2 months), the D-dimer surgery lowered (739 ng/ml) and the hepatobiliary ultrasound showed hepatosplenomegaly, a permeable 4 mm porta hepatis, and in the Doppler test, the portal vein was permeable. The patient received anticoagulation for 3 months.

During the control, at 8-months of life, the patient did tolerate the complementary alimentation without complications; she had an adequate weight increase, and continued with her medical controls.

Discussion

The symptoms of the spontaneous perforation of the bile duct in pediatrics are, usually, sub-acute. 80% of the patients develop with fluctuant jaundice, pale or acholic stools, choluric urine, slowly progressive ascites, abdominal distention and a growth failure. Only 20% of the patients have an acute case of abdominal distention, fever, vomiting, irritability, and signs of severe fulminant peritonitis, which might end up in septic shock and death[2,13,14]. Due to the acute clinical presentation of our patient in the absence of jaundice, initially, it was thought of perforating necrotizing en-

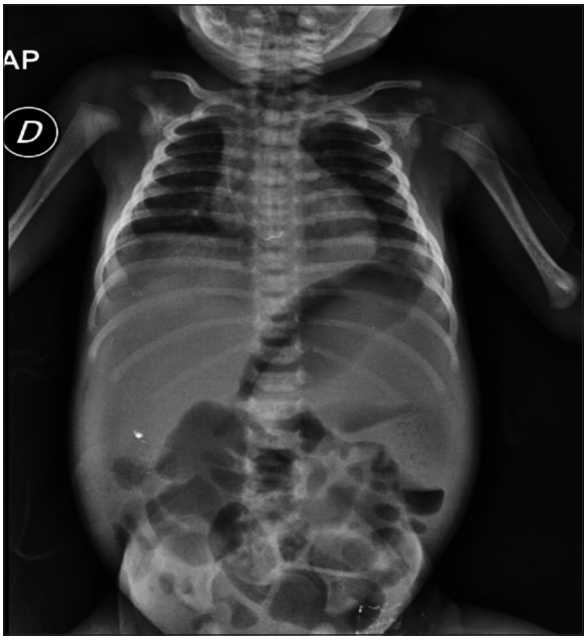

Figure 1. Thoracoabdominal radiography in AP projection: Free air in the peritoneal cavity distributed in the epigastrium, mesogastrium and in the left hypochondrium, associated with distension of small bowel.

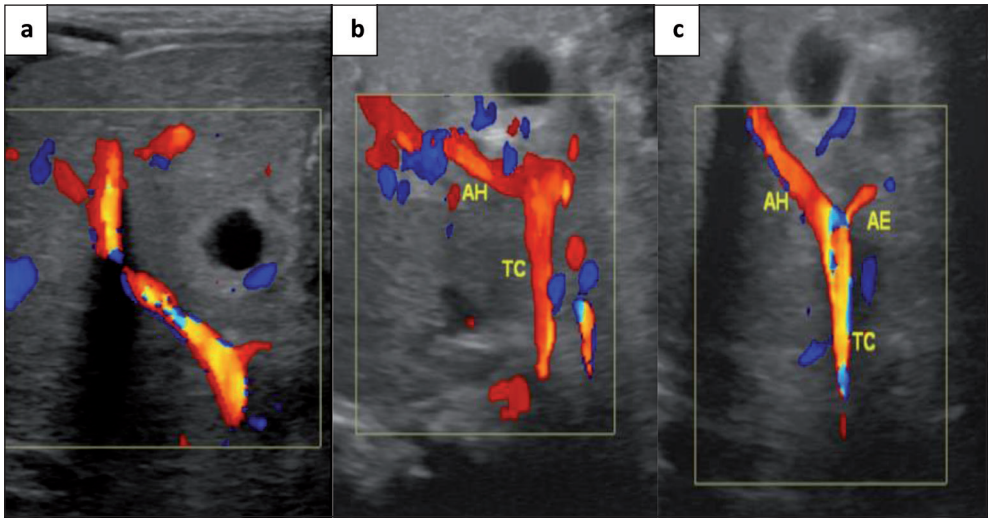

Figure 2. Duplex scanning with assessment of portal blood flow: **a)** Arterial intrahepatic flow is predominant as compared to the absence of portal vein flow at the hilum. **b)** Celiac trunk (CT) and hepatic artery (HA), absence of flow in the portal vein. **c)** Celiac trunk (CT), hepatic artery (HA) and splenic artery (SA), absence of flow in the portal vein.

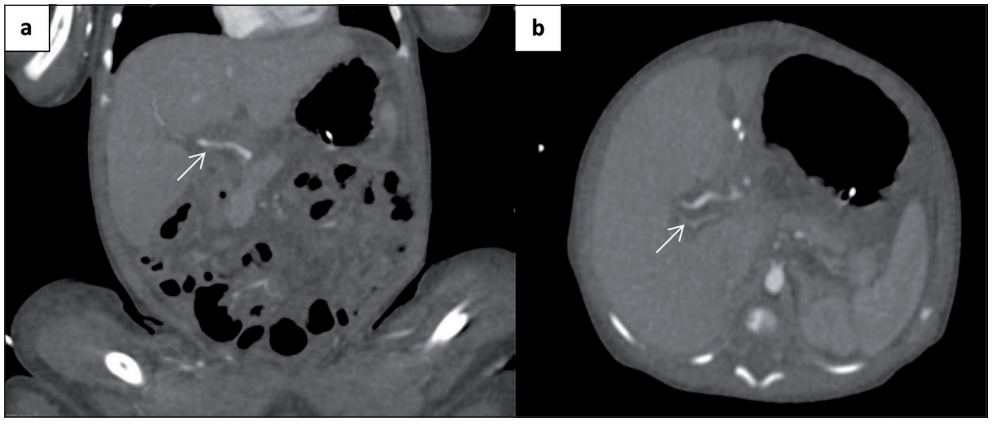

Figure 3. Abdominal angiotomography: **a)** Coronal section: the arrow shows adequate opacification of the hepatic artery in the arterial phase **b)** Transverse section: the image is suggestive of portal vein thrombosis, with a smaller caliber compared to the hepatic artery.

terocolitis, which was why the surgery was performed. The surgical finding of the perforation of the bile duct was the first one in our Intensive care Unit. There is no information of this clinical condition in the reports of pathologies of patients that have required a laparotomy.

The laboratory tests are not pathognomonic, and usually show cholestasis jaundice and an increase of the alkaline phosphatase. Other hepatic function tests are usually normal. The images might be helpful in order to evaluate the state of severity. The abdomen radiography might show pneumoperitoreum or findings that might indicate ascites. The abdomen ultrasound provides additional data such as dilatation of extrahepatic ducts, Intrahepatic ducts are usually normal[4,15]. Other diagnostic methods are the hepatobiliary gammagraphy, which is highly sensitive and specific, and might show that the intraperitoneal liquid originated from the bile duct, and magnetic resonance cholangiopancreatography, which has been used to identify bile duct perforation, as well as to demonstrate anatomical anomalies[17].

Usually, the diagnosis is not suspected until that the paracentesis shows a dark yellow-greenish liquid with higher levels of bilirubin than in the plasma. The pre-operatory diagnose is difficult and, in most of the cases, it is an intra-operatory finding[18,19]. The differential diagnoses include neonatal jaundice, biliary ducts atresia, choledochal cysts, Alagille's syndrome and symptoms that simulate acute abdomen, such as intestinal obstruction and necrotizing enterocolitis[9,19].

An early surgical intervention reduces the mortality and morbidity[20]. The surgical options include simple drainage or without repairing the perforation, cholecystectomy, external biliary derivation or bile duct reconstruction[5]. The treatment must be individualized, however, the biliary-intestinal bypass and the peritoneal drainage with T-tube is a good option for management[21,22]. Ideally, the intra-operatory cholangiography must be performed in every case to detect anomalies

in the biliary duct. If no anomalies are found, another option of management is the external peritoneal drainage; nevertheless, it is important to take into account that the most common complication is the biliary duct stenosis, which might evolve into biliary cirrhosis and portal hypertension[23]. If a patient has a choledochal cyst and biliary peritonitis with posterior perforation, cholecystectomy, and Roux-en-Y reconstructions are recommended[5], in order to prevent biliary cirrhosis, portal hypertension, recurrent pancreatitis, and lastly, biliary carcinoma[24]. A cholechoduodenostomy is not recommended due to the risk of ascending cholangitis[14].

In addition, portal vein thrombosis during the immediate post-operatory period was found. This complication occurs, presumably, because of the chemical irritation or due to the pressure that the local extravasation applies on the bile in the porta hepatis region[25]. The thrombophilia studies of your patient showed a C protein slightly low, which is expected because of the first three weeks after the thrombosis, the C and S protein of the coagulation diminish. The anti-thrombosis treatment began due to the high risk of portal hypertension. Other post-surgical complications include bile leakage, ascendant cholangitis and chylous ascites[1]. A long-term follow-up must guide to ultrasound monitoring to evaluate the sings of portal hypertension, hepatic function tests and multidisciplinary follow-up[12].

Conclusions

The spontaneous perforation of the bile duct is quite uncommon, however, it is an important surgical cause of hyperbilirubinemia in the neonate and it requires a high degree of suspicion. The prognosis will vary on the early intervention and on the intra-operatory findings. It requires a close follow-up, in case of future complications.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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