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CASE REPORT

Congenital choledochal cyst and Noonan syndrome: case report

Marina Julia Luvison[1], Camila Maques de Valois Lanzarin[2], Janaina Cruciani Soldateli[3], Maria Luiza de Andrade Correia[1]

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Abstract

Objective: To report the diagnosis of congenital choledochal cyst, an uncommon condition. During the investigation, Noonan syndrome was also diagnosed, which expanded the research to explore the possible association between Noonan syndrome and congenital choledochal cyst, with few reports of this association described in the literature. **Case report:** A preterm male newborn born to a primigravida mother had a prenatal ultrasound (USG) performed at 22 weeks suggesting the presence of a choledochal cyst. At birth, the baby presented early jaundice and a palpable mass in the upper abdomen, in addition to multiple malformations, including facial dysmorphisms, ocular and breast hypertelorism, cardiac anomalies, and cryptorchidism. Abdominal ultrasound confirmed the presence of an intrahepatic choledochal cyst, while echocardiography showed significant biventricular hypertrophic cardiomyopathy, moderate interventricular communication and wide ductus arteriosus. Laboratory tests showed an increase in direct bilirubin and an increase in Prothrombin Activity Time (PAT). Genetic evaluation raised the suspicion of Noonan syndrome, confirmed by genetic analysis, which revealed a heterozygous pathogenic variant in the PTPN11 gene. Unfortunately, the patient died before surgical intervention to correct the choledochal cyst was possible. **Conclusion:** This report highlights the importance of a multidisciplinary approach involving neonatologists, pediatric gastroenterologists, pediatric cardiologists, geneticists, pediatric ultrasonographers and fetal ultrasonographers in the management of these complex cases. It also highlights the need for greater awareness of this rare association in the medical community.

[1] Universidade Federal de Santa Catarina, Pediatria, residência pediátrica - Florianópolis - Santa Catarina - Brazil.
[2] Universidade Federal de Santa Catarina, Gastroenterologia pediátrica, Pediatria - Florianópolis - Santa Catarina - Brazil.
[3] Universidade Federal de Santa Catarina, Neonatologia, Pediatria - Florianópolis - Santa Catarina - Brazil.

Correspondence to:
Maria Luiza de Andrade Correia.
Universidade Federal de Santa Catarina. Rua Profa. Maria Flora Pausewang, s/n, Trindade, Florianópolis, SC, Brazil. CEP: 88040-900. E-mail: maluandradexx@gmail.com

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INTRODUCTION

Choledochal cysts (CC) are congenital dilatations of the biliary tree, which may be intra- or extrahepatic. CCs are rare and show differing incidence rates among populations: approximately 1:13,000 in Asian populations and 1:100,000 in Western populations, with a higher risk in females compared to males[1].

The classic clinical presentation of CC includes the triad of jaundice, abdominal pain, and a palpable mass in the upper abdominal quadrant, a manifestation more commonly observed in the pediatric population[1,2]. Diagnosis is frequently made by ultrasonography (USG) and may be complemented by other radiological examinations[3]. Definitive treatment consists of surgical removal of the cyst, with the choice of procedure and timing of intervention determined by clinical presentation, cyst classification, and patient age[4].

Noonan syndrome (NS) is a genetic condition with autosomal dominant inheritance, characterized by multisystem involvement with high heterogeneity and variable clinical expression. Its classic triad includes facial abnormalities, hypertrophic cardiomyopathy, and short stature[5]. The estimated incidence of NS is 1:1,000 to 1:2,500 live births[5,6].

The association between CC and NS has been documented only a few times in the literature. One of the earliest reports was published in 1993 by C.D. George, describing a case confirmed by ultrasonography in a patient who, in addition to congenital choledochal cyst, presented with an ectopic kidney and intestinal malformation[7].

Thus, considering the rare clinical presentation of congenital choledochal cysts, this study aims to report a case involving a congenital choledochal cyst, detailing its diagnosis, clinical manifestations, and management in the neonatal period, and to document the association between CC and NS, a relationship with limited published data in the literature.

CASE REPORT

A male preterm newborn (NB), born at a gestational age (GA) of 34 weeks and 3 days, with a birth weight of 2,430 g. He was the son of a healthy 20-year-old primigravida mother. Prenatal care began at 21 weeks of gestation. Maternal rapid tests for syphilis, HIV, and hepatitis B were negative. In the morphological ultrasound (USG) performed at GA 22 weeks and 1 day, an anechoic image in the liver measuring 31 × 27 × 28 mm was identified, suggestive of a choledochal cyst. In addition, right ventricular and pulmonary artery hypoplasia, right-sided clinodactyly, hypoplastic nasal bone, and polyhydramnios were observed.

A repeat USG at GA 33 weeks and 6 days demonstrated multiple dysmorphisms: brachycephaly, low-set ears, cardiac malformation, left pleural effusion, distorted renal architecture, cryptorchidism, and persistence of the anechoic liver image. Fetal karyotyping confirmed 46, XY.

The NB was delivered by cesarean section due to fetal distress, presenting with bradycardia and apnea at birth. Neonatal resuscitation was performed, including orotracheal intubation in the delivery room and left-sided thoracocentesis for decompression. Apgar scores were 2/4/7, and after clinical stabilization, the newborn was transferred to the Neonatal ICU.

On physical examination, the following findings were noted: syndromic facies, ocular and mammary hypertelorism, ectrodactyly, globose abdomen with palpable visceromegaly, a palpable mass 6 cm below the right costal margin, and splenomegaly 3 cm below the left costal margin.

After birth, additional imaging studies were performed. Echocardiography revealed significant biventricular hypertrophic cardiomyopathy, moderate ventricular septal defect, and a large patent ductus arteriosus.

On imaging, the chest radiograph (Figure 1) showed hyperinflated lungs with bilateral pleural effusion, cardiomegaly, and absence of air in the intestinal loops. In the complete abdominal ultrasound (Figure 1b and 1c), dilation of the intrahepatic bile ducts was observed, along with a large anechoic structure with regular contours at the hepatic hilum, occupying the right hemiabdomen and measuring approximately 5.9 × 4.8 cm, suggestive of a choledochal cyst. The liver showed normal topography, morphology, size, texture, and echogenicity, with preserved architecture of the portal system and hepatic veins.



Figure 1. A: Panoramic radiograph showing bilateral pleural effusion, cardiomegaly, and absence of air in the intestinal loops. B: Abdominal ultrasound demonstrating a choledochal cyst. C: Choledochal cyst on the right; normal hepatic parenchyma on the left.

The patient exhibited difficulty tolerating enteral feeding, and extrinsic compression of the digestive tract by the cystic mass could not be ruled out. Meconium elimination was normal.

He was evaluated by the medical genetics team, who raised the hypothesis of Noonan syndrome, and a genetic test was requested for confirmation.

During the clinical course, the patient presented transient elevation of liver enzymes, which stabilized after the fifth day of life, but subsequently developed progressive cholestatic jaundice with increasing direct bilirubin levels, as well as abnormalities in the coagulation profile (Table 1).

Table 1. Laboratory test results.

DV	TGP	TGO	Alb.	BTF	BI	BD	TP	RNI	TTPA	GGT	FA
D1	13	100	-	-	-	-	-	-	-	-	-
D4	9	40	1,9	13,7	12,4	1,3	20,7	1,58	42	-	-
D5	-	-	-	15	12,7	2,3	21,5	1,65	45,8	-	-
D6	32	92	-	13,5	11,7	1,8	-	-	-	1785	108
D8	5	30	2,2	12,7	9,4	3,3	-	-	-	936	130
D9	-	-	2,5	-	-	-	13,5	1,24	35,7	-	-
D11	9	40	2,2	5,7	2,3	3,4	-	-	-	500	137
D13	9	50	-	6,2	2	4,2	-	-	-	552	135

Caption: DV: days of life; ALT: pyruvic transaminase; AST: oxaloacetic transaminase; Alb.: albumin; TBF: total bilirubin and fractions; IB: indirect bilirubin; DB: direct bilirubin; PT: prothrombin time; INR: international normalized ratio; aPTT: activated partial thromboplastin time; GGT: gamma-glutamyl transferase; ALP: alkaline phosphatase.

Due to multiple abnormalities and difficulty achieving initial stabilization, the patient progressed to sepsis of pulmonary origin, refractory septic shock, and death before undergoing the surgical procedure for removal of the choledochal cyst.

The diagnosis of Noonan syndrome was later confirmed by genetic testing, which identified a pathogenic heterozygous variant in the PTPN11 gene.

DISCUSSION

Choledochal cysts (CC) are congenital dilatations of the biliary tree and may be intra- or extrahepatic. These cysts are rare, and their etiology remains unknown, although several theories regarding their development have been proposed. One hypothesis suggests an abnormal junction of the pancreaticobiliary ducts during embryonic development, predisposing to reflux of pancreatic juice into the bile ducts, resulting in chronic inflammation, damage to the duct wall, and cystic changes[8,4]. Other possible causes include fragility of the bile duct wall, distal bile duct obstruction, dysfunction of the sphincter of Oddi, and abnormalities in ganglion cells[9].

The most widely used classification for the different types of CC is the modified Todani classification (Table 2), proposed in 1977, which categorizes cysts into five types (I–V), as described in the literature[10,4].

Table 2. Modified Todani classification.

	TODANI CLASSIFICATION	
Type	**Characteristics**	**Prevalence**
I	Fusiform/cystic dilatations	50%
II	Saccular diverticula of the extrahepatic bile duct	<10%
III	Dilatation of the bile duct within the duodenal wall	<10%
IV	Intra- and extrahepatic cystic dilatations	35%
V	Intrahepatic cysts – Caroli disease	Rare

Source: Prepared by the authors.

Clinically, the classic presentation includes the triad of jaundice, abdominal pain, and a palpable mass in the upper abdominal quadrant, frequently observed in the pediatric population[1,2]. Other manifestations include cholangitis, pancreatitis, portal hypertension, abnormalities in liver function, coagulopathies, and acholic stools[1,2]. In rare cases, biliary rupture with peritonitis may occur, a presentation typically seen in the neonatal period that requires emergency drainage[4,9]. In the reported case, the patient presented the classic triad within the first days of life.

Diagnosis is usually established by ultrasonography (USG) and may be complemented by computed tomography (CT), magnetic resonance imaging (MRI), or magnetic resonance cholangiopancreatography (MRCP), the latter being considered the gold standard for diagnosis and classification[3,11]. In the reported patient, the diagnosis was suggested during the prenatal period, with an anechoic image identified on morphological ultrasound at 22 weeks of gestation, compatible with a choledochal cyst.

Laboratory findings suggestive of CC include elevated levels of direct and indirect bilirubin, AST, ALT, and GGT[12]. In the described case, the patient showed progressive elevation of direct bilirubin and GGT levels even after the first week of life, while transaminases exhibited transient elevations, possibly associated with birth-related trauma.

Treatment of choledochal cysts is surgical, and the optimal timing of intervention remains a matter of debate, particularly in asymptomatic cases. Studies indicate that early diagnosis, especially in the prenatal period, may positively influence the timing of surgery and improve prognosis[12]. The patient in question presented cholestatic symptoms such as jaundice, elevated liver enzymes, and extrinsic compression of the biliary tract by the cyst, indicating the need for surgical intervention.

Noonan syndrome (NS) is an autosomal dominant genetic condition caused by mutations in genes involved in intracellular signaling of the RAS–MAPK pathway[5]. The *PTPN11* gene is the most frequently associated with NS[6] and was

identified in the present case. NS exhibits marked phenotypic variability and multisystem manifestations, including characteristic facial features, hypertrophic cardiomyopathy, pulmonary stenosis, short stature, cryptorchidism, coagulopathies, and renal anomalies[5,6]. Many features may be detected prenatally, such as increased nuchal translucency, cystic hygroma, polyhydramnios, fetal hydrops, and cardiac defects[6].

Although genetic testing is fundamental for diagnosis, up to 10% of cases may yield normal results, making diagnosis reliant on a high degree of clinical suspicion[13]. The reported patient exhibited classic features of NS, including facial dysmorphisms, low-set ears, hypertelorism, hypertrophic cardiomyopathy, and cryptorchidism. The association between NS and choledochal cyst is extremely rare, with few reports in the literature, but is an important consideration due to the potential for malignant degeneration[13].

This report describes the association of two rare conditions—congenital choledochal cyst and Noonan syndrome—highlighting the importance of a multidisciplinary approach in the management of complex cases. The documentation of this association is relevant to increase awareness within the medical community and to reinforce consideration of NS in the diagnostic workup, even in cases in which genetic testing is inconclusive.

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