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CASE REPORT

Biliary atresia in a patient with Cat Eye Syndrome - Case Report

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Abstract

Biliary atresia is a rare condition, of undefined etiology and with a potentially fatal evolution. The cat eye syndrome is a rare chromosomal disease that is associated with several malformations, biliary atresia being among the most rarely described. Male newborn with jaundice onset at 20 days of age, accompanied by fecal hypocholia. Laboratory tests, imaging and liver biopsy were suggestive of biliary atresia. The patient underwent Kasai surgery at 55 days of age. He also had several malformations, and the genetic team diagnosed cat eye syndrome. He presented with a favorable clinical evolution after surgery, maintaining follow-up with several specialties. This genetic syndrome has a variable phenotype and the early identification of associated malformations is essential for proper treatment, which can have a positive impact on both patient survival and quality of life.

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INTRODUCTION

Biliary atresia (BA) is an inflammatory cholangiopathy that causes the obliteration of intrahepatic and extrahepatic bile ducts in neonatal life. Without adequate treatment, BA may lead to liver cirrhosis and death by the age of two years[1]. Its estimated incidence is one in 6,000 to 18,000 live births, with females slightly more affected. Other congenital malformations occur in association with BA in up to 20% of the cases. The disease is the main cause of liver transplantation in pediatric patients[2]. Cat eye syndrome (CES), also known as Schmid-Fraccaro syndrome, is a rare chromosomal disease associated with several malformations, with an estimated incidence of one in 50,000 to 150,000 live births[3]. This article describes the case of an infant referred for evaluation at a tertiary service due to neonatal cholestasis. He underwent extensive investigation and was diagnosed with biliary atresia. The patient improved after he underwent the Kasai procedure. Since he had other malformations, including preauricular pits, imperforate anus and cardiac alterations, genetic tests were ordered and the patient was diagnosed with CES.

CASE REPORT

A full-term male infant aged 38 days, without a history of complications during prenatal care, born with adequate weight for gestational age, was diagnosed with jaundice 20 days after birth and was being followed for acholic stools. On physical examination, he was jaundiced, with a palpable liver 2 cm from the right costal margin. Laboratory workup revealed an increase in total bilirubin with a predominance of direct bilirubin (total bilirubin: 7mg/dl and direct bilirubin: 4.08mg/dl); an increase in transaminases (alanine transaminase: 61 U/L and aspartate transaminase: 184 U/L) and in canalicular enzymes (alkaline phosphatase: 416 U/L, gamma-glutamyl transferase: 397 U/L). The gallbladder was not visualized in abdominal ultrasound examination. Hepatobiliary scintigraphy found bile duct obstruction suggestive of biliary atresia. Liver biopsy findings were also consistent with biliary atresia. The patient underwent an uneventful Roux-en-Y hepatic portoenterostomy (Kasai procedure) 55 days after birth. Biopsies showed intense gallbladder hypoplasia with moderate mixed inflammatory infiltrate and areas of mucosal erosion, an unsuspected lymph node in the cystic duct area, chronic liver disease with biliary obstruction, portal fibrosis with formation of porto-portal septa and intense intracanalicular and ductal cholestasis with associated biliary portal reaction.

The patient presented numerous other changes on physical examination, including pre-auricular pits; long eyelashes; low nasal bridge; plagiocephaly; wide and bulging forehead; retrognathia; hypertelorism; strabismus; single palmar crease; increased internipple distance; and bilateral cryptorchidism. He also had cardiac malformations (interventricular septal defect without hemodynamic repercussions; patent ductus arteriosus; persistent left superior vena cava), imperforate anus (a colostomy was performed when he was one year old) and a rectourethral fistula. Genetic tests supported a diagnosis of cat eye syndrome, with a compatible karyotype: 47XY + mor 29/ 46 XY (21), and a-CGH: Arr (hg 19) 22q 11.1-q11.2. Ophthalmic evaluation showed a trophic iris without coloboma and divergent strabismus.

During clinical follow-up, he had three episodes of urinary tract infection (UTI), without changes in kidney function or formation of kidney scars. He underwent bowel reconstruction surgery and had a rectourethral fistula repaired when he was one year and five months old. He has not had episodes of UTI since. He had chronic constipation requiring multiple enemas and subsequent management with polyethylene glycol. He remained stable during follow-up with the pediatric cardiology team. Two echocardiograms were ordered, with normal results. He was discharged at the age of two years and eight months.

Transaminase and canalicular enzyme levels increased persistently during therapy with ursodeoxycholic acid, and alterations appeared in his ultrasound images (heterogeneous liver, with blunt edges; increased diameter and echogenicity of the portal vein; polysplenia). At two years and 10 months, he developed upper gastrointestinal bleeding secondary to an active gastric ulcer. Upper digestive endoscopy also revealed esophageal and gastric varices. Endoscopic rubber band ligation of varices and a prescription of propranolol and a proton pump inhibitor (omeprazole) improved his overall condition. During follow-up, he also developed portal hypertensive gastropathy. No other episodes of gastric bleeding were recorded. The patient is now four years old. He has been stable, with good weight and height gain (in the 75th percentile of weight and height for his age), adequate global development; total bilirubin: 0.6mg/dL; albumin: 4.2g/dL; INR: 1.26. Figure 1 shows some dysmorphic signs, such as a wide and bulging forehead, long eyelashes, hypertelorism, and divergent strabismus.

DISCUSSION

Biliary atresia (BA) has no defined etiology. Clinical signs and symptoms include cholestatic jaundice starting in neonatal life, possibly associated with other malformations. Incidence varies between countries[4-6]. Useful diagnostic tests include biochemical tests, abdominal ultrasound, hepatobiliary scintigraphy, magnetic resonance cholangiopancreatography and liver biopsy. Histology analysis is more accurate than non-invasive methods, but combined non-invasive tests may be used in the differential diagnosis of neonatal cholestasis[7]. Other markers have been studied, including metalloproteinase-7 (MMP-7), which has shown high sensitivity and specificity for BA[8].



Figure 1. The patient, aged four years, presenting a wide and bulging forehead, long eyelashes, hypertelorism and divergent strabismus.

Early diagnosis is important, since the Kasai procedure, when performed in the first months of life, may help prevent disease progression[9]. A Brazilian multicenter trial found extrahepatic congenital anomalies in 11.8% of the patients with BA; most of these patients were never offered the Kasai procedure or were operated on after 60 days of life[10].

Cat eye syndrome is associated with a partial duplication of chromosome 22, which may present trisomy or partial tetrasomy as a result of a supernumerary marker chromosome idic(22)(q11.2). Some authors have looked into possible relationships between genetic alterations and the clinical signs and symptoms of CES[11]. The syndrome received its name due to the appearance of the vertical iris coloboma found in some patients[12]. Phenotypes, however, vary substantially. The main phenotypical findings include preauricular pits or appendages, anorectal malformations, urogenital malformations, ocular coloboma and congenital heart defects. The association with BA is among rarest findings[13]. Our patient presented several of these characteristics, including preauricular pits, low nasal bridge, hypertelorism, ventricular septal defect, persistent left superior vena cava, imperforate anus and rectal fistula, in addition to BA.

A series of five cases of patients with variable forms of aneuploidy of chromosome 22, including two with the classic form of CES, in which all had significant anomalies of the bile ducts, the main being BA, showed that these changes were significant in the genetic conditions described and might reside among the factors associated with worse outcomes.[14] A Brazilian study with six patients diagnosed with CES described co-occurrence of BA in one case[15].

Despite the comorbid conditions resulting from CES and portal hypertension, early diagnosis and intervention were decisive for the good clinical evolution observed in our patient.

CONCLUSION

Cat eye syndrome is a rare genetic disease that may be associated with biliary atresia, which is an important cause of cholestasis in pediatric patients and the main indication for liver transplantation in this population. Although it is a rare association, early diagnosis of bile duct atresia was decisive for the good clinical evolution of the patient, which demonstrates the importance of testing for BA in patients with cat eye syndrome and jaundice.

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