

Embryonal Biliary Atresia with Levocardia and Situs Inversus: A Case Report

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Abstract

Background: Biliary atresia (BA) is a rare disease and the end result of a destructive inflammatory process in bile ducts, leading to fibrosis and liver cirrhosis. It has two forms: 1) syndromic or fetal or embryonic (10-35%) with various congenital anomalies, 2) non syndromic (70-90%), in which BA is an isolated anomaly. In this article we report on an infant with the first form of BA in which diagnosis and operation was not based on routine liver biopsy but on associated malformations and clinical features that were highly suggestive of embryonal form of biliary atresia.

Case Presentation: A 70-day old infant with syndromic BA, levocardia, situs inversus and polysplenia. He developed jaundice in 4th day of life, liver was not palpable. Kasai operation was not effective. He developed liver cirrhosis at 3 months of age.

Conclusion: Syndromic type of EHBA is a very rare disease with a worse outcome than non syndromic type of BA. Early diagnosis is important and may be difficult as the liver sometimes could not be palpable because of its malposition.

Key Words: EHBA, Extra hepatic biliary atresia, Malformation, Situs inversus

Introduction

Biliary atresia (BA) is the end result of a destructive, idiopathic, and inflammatory process (viral, immunological, toxic, ischemic, and/or remodeling arrest) that affects intra and extra hepatic bile ducts (table 1) leading to fibrosis and

obliteration of the biliary tract and development of biliary cirrhosis.^[1-5]

Biliary atresia occurs worldwide, affecting an estimated 1 in 8000-12000 live births. Two different forms of BA have been identified^[6]:

1) Syndromic BA or fetal or embryonic form (10-35%) with various congenital anomalies such

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Table 1- Anatomical types of biliary atresia

French classification	Frequency	Description	Upper level of obstruction of the extrahepatic bile ducts	US/UK/Japanese classification
Type 1	~ 3%	Atresia limited to the common bile duct	Common bile duct	Type 1
Type 2	~ 6%	Cyst in the liver hilum communicating with dystrophic intrahepatic bile ducts	Hepatic duct	Type 2
Type 3	19%	Gallbladder, cystic duct and common bile duct patent	Porta hepatis	Type 3
Type 4	72%	Complete extrahepatic BA	Porta hepatis	Type 3

as polysplenia, asplenia, cardiac or intra abdominal defects (situs inversus, pre-duodenal portal vein, absence of retro-hepatic inferior vena cava, intestinal malrotation).

2) Non Syndromic BA or peri or postnatal from (70-90%), in which BA is an isolated anomaly. Several surgical classification of BA have been proposed.^[7,8]

Extra hepatic anomalies reported in BA^[9] are splenic anomalies (polysplenia, double spleen, asplenia), portal vein anomalies (preduodenal, absence, cavernomatous transformation), situs inversus, malrotation, cardiac anomalies, annular pancreas, Kartagener's syndrome, duodenal atresia, esophageal atresia, polycystic kidney, cleft palate, and jejunal atresia.

In this article we report on an infant with the first form of BA in which diagnosis and operation was not based on routine liver biopsy but on associated malformations and clinical features that were highly suggestive of embryonal form of biliary atresia.

Case Presentation

A 70-day old male infant came with prolonged jaundice which had begun from 4th day of life. Jaundice mildly improved after several days but increased again thereafter. Stool was acholic, urine dark yellow. He was product of Caesarean section delivery with a good Apgar score. Birth weight 3750gr. Weight on admission 5200 gr. He

was the third child of related parents; his 2 siblings were normal.

Physical examination revealed jaundice, hydrocele, normal farcies and no organomegaly or stigmata of cirrhosis. Ophthalmologic examination was normal.

In paraclinic evaluation total and direct bilirubin elevated in several measurements (4 to 12mg/dl), direct bilirubin (3.5 to 6.5 mg/dl) was in favor of cholestasis, liver enzymes elevated (3 to 20 times as of normal values). Alkaline phosphatase in several measurements was 1773, 2950, 3088 (normal up to 1200), and Gamma Glutamyltransferase was 795 and 2136 (normal up to 55). Prothrombin time(PT) and Partial Thrombin Time (PTT) prolonged with no normalization after Vitamin K and fresh frozen plasma (FFP). Other laboratory findings (urine and serum chromatography, serum total protein, albumin, globulin, ammonia, lactate, thyroid function test, and α -1-Antitrypsin) were in normal range, but alfa fetoprotein (α FP) was more than 1000 (normal up to 7).

Hepatobiliary iminodiacetic acid (HIDA) scan suggested extra hepatic biliary atresia (EHBA). Abdominal ultrasound showed liver in the left and stomach in the right side of abdomen, polysplenia, malposition of the heart (levocardia, situs inversus), gall bladder less than 1cm in fasting. Triangular cord sign in liver hilum was present. These data was highly suggestive of embryonic or fetal congenital type of BA, so the liver biopsy plan was cancelled, and he was introduced to pediatric surgeon for hepatoporo-enterostomy (Kasai) operation (Fig 1).

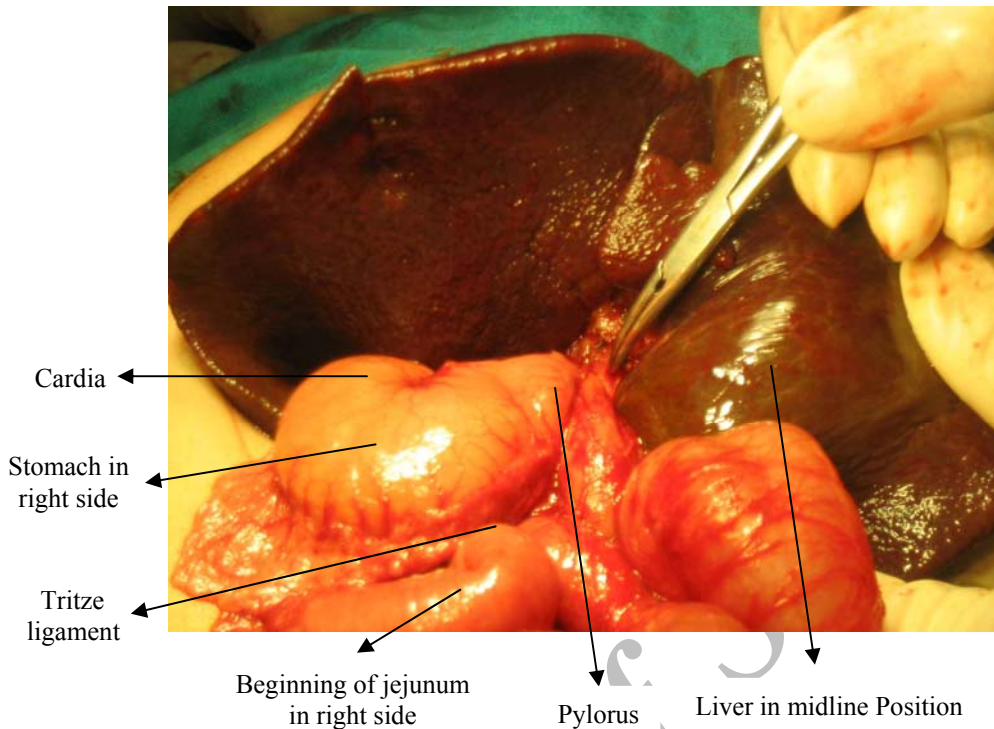


Fig 1- Atretic biliary duct in our patient. Stomach is seen in right side

Report of surgeon: Liver is in the midline mildly shifted to the left, its lobes are enlarged and nodular. Stomach is in the right side. Gallbladder and extrahepatic bile ducts are not developed and fibrotic bundle of them too. So

there was no need for an intra operative cholangiography. Pathology report of open liver biopsy was liver changes compatible with large bile duct obstruction. Hepatitis activity index (HAI) score was stage 6, grade 4, and Scheuer



Fig 2- Dissection of proximal portion of biliary duct. Absence of biliary tract (external)

score was stage 2, grade 4. Hepatoportoenterostomy (HPE) was done (Fig 2).

The patient was discharged after receiving steroid, antibiotics and total parenteral nutrition (TPN). Ursodeoxycolic acid which prescribed at admission was continued and his stool became greenish-yellow.

In monthly follow-up, he developed palmar erythema, spider angioma, firm to hard hepatosplenomegaly, and the serum bilirubin remained high (total 7 and direct: 3.8 mg/dl) due to poor response to Hepatoportoenterostomy (HPE), so he became candidate for liver transplantation when became one year old.

Discussion

This is a rare case of extrahepatic BA with polysplenia, levocardia and situs inversus. EHBA accounts for 30% of cases of cholestasis in young infants. Two forms of disease have been recognized. In the embryonic type, which occurs in 15-30% of cases, EHBA is in association with other congenital anomalies with early presentation of jaundice (in the first week of life).^[10] In the classic non-syndromic perinatal type (70-85%) no other anomalies are present, and the jaundice starts later within the first 2-3 weeks of life.^[10] In another classification, EHBA is divided into syndromic (10%) and non-syndromic (90%) types with the first type being associated with various congenital anomalies^[11]. In a study from Pakistan, the authors reported 2 cases of situs inversus with BA and indicated that this association had not been reported before in that country.^[12]

In one study from South Korea, 45 patients with situs inversus are reported from 1980 to 2004; 58% of them had intra abdominal anomalies such as duodenal atresia, BA, malrotation, and tracheoesophageal fistula.^[13] In another study in a 28-year single center retrospective study 10.2% of cases with BA had BA splenic malformation syndrome and they were more likely to have higher incidence of antenatal pathology like maternal diabetes (our patient did not have such history). In this study

there were no differences in liver histology (e.g. degree of liver fibrosis).^[14] In our patient the liver was cirrhotic at the time of HPE operation. In another study the incidence of syndromic BA was reported 8% and they indicated that this association had worse prognosis and their patients had poor bile secretion after HPE.^[15] One study has reported a unique case of newborn BA associated with esophageal atresia and Tracheo Esophageal Fistula (TEF), anorectal atresia, reovirus type 3 infection and an early switch of fetal into adult hemoglobin^[16]. We have not done such virologic and hematological evaluations in our patient. Another study reported that 25% of BA was associated with other congenital anomalies (BA splenic malformation syndrome), the outcome was worse and total bilirubin in early follow up after Kasai (at first week after operation) was highly predictive of outcome.^[17]

In our patient the bilirubin was high at first weeks after operation too, and he became cirrhotic. In a study from India is indicated that ductal plate malformation was present in all intrahepatic bile duct diseases and in about 26% of EHBA was associated with other anomalies such as congenital hepatic fibrosis, autosomal recessive polycystic kidney disease, Caroli's syndrome and Ivemark's syndrome. Our patient did not have such anomalies.^[18] One important point is that our patient had no organomegaly in physical examination, probably due to the malposition of these organs, although most authors mention hepatosplenomegaly in EHBA as the result of early development of cirrhosis and portal hypertension.^[19,20]

Conclusion

EHBA is a rare disease with complete obstruction of bile flow that develops as a result of sclerosing fibro-obliteration of the extra hepatic bile duct. Syndromic type of the disease is very rare and has worse outcome due to other, associated anomalies. Early diagnosis and appropriate treatment is very important to prevent development of liver cirrhosis.

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