Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Biliary atresia with rare associations: a case report and literature review

Basel A. Zaben, MD[a,*], Ahmad M. Abualrub, MD[a], Waleed M. Malhes, MD[a], Anas M. Barabrah, MD[a], Anas R. Tuqan, MD[a], Ibrahem A. Tahhan, MD[a], Wael Amro, MD[b]

Introduction and importance: Biliary atresia is a rare, progressive cholangiopathy that affects newborns, causing jaundice and other manifestations of hyperbilirubinemia. The incidence is higher in Asia than in Europe. The only available treatment is a surgical operation called Kasai portoenterostomy. In this case, the authors highlighted rare congenital anomalies that came with biliary atresia.
Case presentation: A 10-day-old male infant was admitted to the hospital due to recurrent vomiting, yellowish skin, and scleral icterus. Laboratory investigations revealed elevated total serum and direct bilirubin levels. An atrophic gallbladder was observed on ultrasound. Intrahepatic cholangiography confirmed the diagnosis of biliary atresia, leading to the performance of a Kasai procedure. Additionally, the patient had intestinal malrotation and volvulus, which were managed with a Ladd's procedure. Following surgery, there was notable improvement in liver enzymes and bilirubin levels, and the patient was discharged after 7 days. The infant has been initiated on oral vitamins, ursodeoxycholic acid, and antibiotics.
Clinical discussion: Biliary atresia is a challenging condition characterized by progressive narrowing and fibrosis of the biliary tree. It is rarely associated with rare congenital anomalies like situs inversus totalis, intestinal malrotation, and volvulus. Diagnosis involves abdominal ultrasound and MRCG. The biliary atresia was managed by the Kasai procedure and the intestinal malrotation, and volvulus were managed by Ladd's procedure.
Conclusion: This case report highlights the importance of considering rare associations such as situs inversus, intestinal malrotation and volvulus in the diagnosis of biliary atresia in newborn. Early diagnosis and prompt intervention are crucial for optimal outcomes.

Keywords: biliary atresia, case report, intestinal malrotation, Kasai procedure, situs inverses

Introduction

Biliary atresia is one of the rare, progressive cholangiopathies in which the neonate sustains jaundice by the age of 2–6 weeks, in addition to other manifestations of hyperbilirubinemia including pale stools, dark urine, and scleral icterus. The occurrence of biliary atresia can be influenced by maternal risk factors, both prior to pregnancy, such as having type 2 diabetes mellitus, and during pregnancy, including the use of vitamins or nutritional supplements, infections, and exposure to alcohol or toxins[1,2]. Comparing Asia to Europe, the incidence is higher in Asia where ~100–500/100 000 live births in Taiwan and Japan are affected[3], as opposed to Europe where 5–25/100 000 live births are affected[4].

HIGHLIGHTS

- Biliary atresia, a condition of unknown origin, may be linked to other anomalies, warranting consideration.
- Diagnosing biliary atresia involves multiple modalities, beginning with ultrasound and HIDA scan, with intraoperative cholangiogram providing definitive confirmation.
- Prompt surgical intervention for biliary atresia is essential to prevent potential complications such as liver fibrosis and cirrhosis.

The consequences of untreated biliary atresia are devastating, as it may lead to cirrhosis, portal hypertension, and end-stage liver disease. The only available treatment at this time is a surgical operation known as a Kasai portoenterostomy (KPE), which has a success rate of about 60% of cases when done in expert centers[5]. However, failure to resolve intrahepatic cholangiopathy can occur in ~50% of the patients[6]. Consequently, liver transplantation is usually required in those patients, accounting for ~80% of all pediatric liver transplantations[7].

This case has been reported in line with SCARE criteria[8].

Case presentation

A 10-day-old male infant was admitted to our hospital presenting with recurrent vomiting of normal gastric content, non-billious in nature, and yellowish skin discoloration persisting for one day.

[a]Faculty of Medicine, Al-Quds University, Jerusalem and [b]Department of Pediatric Surgery, Palestine Medical Complex (PMC), Ramallah, Palestine

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Al-Quds University-School of Medicine, Abu-Dis, East Jerusalem. Tel: +970 259 206 6102. E-mail: basel.253.111@gmail.com (B. A. Zaben).

Annals of Medicine & Surgery (2024) 86:6713–6716

Received 23 February 2024; Accepted 5 May 2024

Published online 8 August 2024

http://dx.doi.org/10.1097/MS9.0000000000002173

The mother reported no changes in bowel habits but noted light-colored stools. The patient, born full term with a birth weight of 3500 g in another institute, had an uncomplicated prenatal course with the mother adhering to multivitamins. Postnatally, the infant was admitted to the neonatal intensive care unit (NICU) for transient tachypnea of the newborn (TTN), managed with 2 l/min of O_2 via head box. TTN was resolved after 3 days of birth and the patient was discharged on the fourth day. The patient has a medical history significant for dextrocardia and situs inversus, diagnosed incidentally at another institute by echocardiography and abdominal ultrasound, respectively. There is no consanguinity between the parents and no family history of genetic diseases.

On physical examination, the infant appeared well, with yellowish scleral and skin discoloration but no signs of dehydration. Vital signs were within normal limits, with a temperature of 36.5° C, oxygen saturation of 97%, heart rate of 142 beats per min, and blood pressure of 63/31 mmHg. Anthropometric measurements indicated appropriate growth parameters. Cardiorespiratory examination was unremarkable except for an apex heartbeat on the right side. Abdominal examination revealed a soft, lax abdomen without palpable masses.

Diagnostic workup included a negative direct Coombs test ruling out hemolysis and a full septic workup with negative cultures. Elevated levels of total serum bilirubin (TSB: 11.16 U/l) and direct bilirubin (4 U/l) were noted, along with elevated liver enzymes including gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Abdominal ultrasound revealed an atretic gallbladder and triangular cord sign, with the liver situated on the left side without intrahepatic biliary dilation, and a normal-sized spleen on the right side.

The pediatric surgeon devised a plan to conduct Intrahepatic cholangiography and perform the Kasai and ladd's procedures. An incision was made transversely in the upper abdomen, allowing for extracorporealization of the liver and identification of the atrophic gallbladder. Intraoperative cholangiogram was performed, which confirmed the presence of biliary atresia. During abdominal exploration, the patient was found to have intestinal malrotation and volvulus. Subsequently, the gallbladder and cystic duct were excised, and ligation of the right hepatic artery was carried out. Further dissection of the liver pedicle was performed, followed by the implementation of Portojejunostomy and jejuno-jejunostomy procedures (Fig. 1). As part of the Ladd's procedure, the surgeon skillfully resolved the torsion caused by malrotation by untwisting the intestines. Subsequently, the surgeon identified and severed the bands that were responsible for the volvulus, thereby restoring the correct anatomical alignment. As a precautionary measure against potential confusion between appendicitis and recurrent volvulus, an appendectomy was performed. Liver biopsy showed variable ductular and cellular cholestasis, mixed portal inflammation, and bridging fibrosis.

Postoperatively, the patient remained nothing by mouth (NPO) for 3 days, followed by gradual oral feeding. Liver enzymes initially elevated, and improved by postoperative day 3, while TSB decreased with persistently high direct bilirubin levels. Physical examination revealed a soft abdomen, normal respiratory status, and renal function. The patient was discharged after seven days with cephalexin, ursodeoxycholic acid, oral vitamins D and E, and vitamin K supplementation.

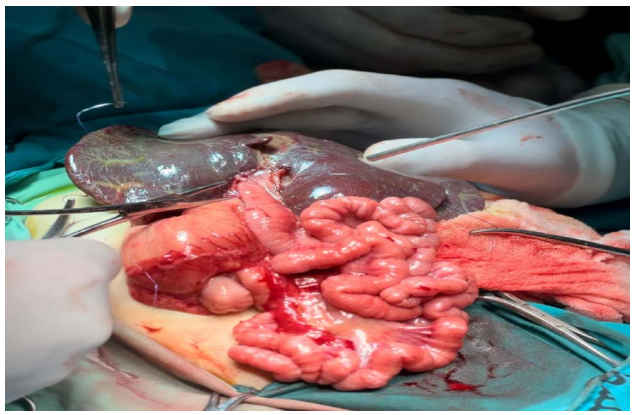

Figure 1. This image illustrates a surgical intervention conducted on our patient, wherein a hepatoportojejunostomy procedure was performed.

Discussion

Biliary atresia is a progressive fibrosis and obliteration of the biliary tree whose etiology is still unknown[9]. However, some identified risk factors were found, including type 2 diabetes mellitus, non-dependent drug abuse[1], anxiety or stress during pregnancy, lower birth weight, fathers from ethnic minorities of China, older age of fathers, lower income of parents, and exposure to infection[2]. It is one of the most common neonatal cholestatic diseases, with incidence rates of 100–500 per 100 000 live births in Asia and 5–25 per 100 000 live births in Europe[6]. It is known that biliary atresia can coexist with different anatomical variations, such as midgut malrotation, situs inversus totalis, cardiovascular deformities, polysplenia syndrome, or preduodenal portal vein[10]. These represent 10% of cases, the remaining 90% present as an isolated biliary atresia[10]. Patients typically present at the neonatal age with scleral icterus, acholic stool, and Jaundice due to progressive conjugated hyperbilirubinemia[11].

One notable structural variation linked to biliary atresia is situs inversus totalis, an exceedingly rare congenital malformation affecting 1 in every 10 000 individuals[10]. This condition mirrors internal thoracic and abdominal organ placement, often accompanied by dextrocardia, posing unique challenges for surgeons[12].

Another associated anomaly is intestinal malrotation, a spectrum of developmental anomalies altering the positioning of the small and large intestines and their mesenteric attachments[9]. Notably, the combination of situs inversus and intestinal malrotation in biliary atresia patients has been reported only four times in the literature for this specific association[9]. (Table 1) presents documented cases of biliary atresia alongside their associated conditions as reported in the literature.

For the diagnosis of biliary atresia, multiple modalities can be used. Abdominal ultrasound is one of the first tests to be considered when investigating biliary atresia, as it can detect some clues that help in the diagnosis (absent common bile duct, absent gallbladder)[12]. Non-invasive method, such as magnetic resonance cholangiography (MRCG), with HIDA scan are two known modalities, with sensitivity of 100% and a specificity of 96% for MRCG, and a sensitivity of 98.7, and specificity of 70.4% for HIDA scan[19,20]. Biliary epithelial injury markers,

Table 1

Studies reporting biliary atresia with rare associations

Reference	Age (day), sex	Presentation	Associated anomalies
Baglaj *et al.*[13]	1, F	Bilious vomiting and upper abdominal distension	Preduodenal portal vein, jejunal atresia, malrotation, and complex cardiac anomaly
Gunawardena *et al.*[14]	60, F	Cholestatic jaundice	Dextrocardia, azygos continuation of the inferior vena cava, multiple spleens, central liver, right sided stomach and preduodenal portal vein.
Allarakia *et al.*[9]	45, F	Fever	Malrotation and situs ambiguous
Xiang *et al.*[15]	34, F	Yellowish skin	Preduodenal portal vein
Sabra *et al.*[10]	60, F	Severe jaundice and poor feeding	Situs inversus totalis, midgut malrotation, and a preduodenal portal vein
Elebute *et al.*[16]	60, F	Prolonged jaundice, pale-colored stools and dark yellow urine	Polysplenia and intestinal malrotation
Rashid *et al.*[17]	60, M	Prolonged history of jaundice, pruritus, yellow-colored urine, and pale stools	Ventricular septal defect
Zaben *et al.*[18]	10, M	Recurrent non-bilious vomiting and jaundice	Intestinal malrotation and volvulus

F, female; M, male.

such as gamma glutamyl transferase and matrix metalloproteinase-7, play a role in the diagnosis[12]. Liver biopsy is another modality but considered as an invasive technique, it may reveal fibrosis, and portal inflammation, which is consistent with the diagnosis, but it may also suggest a diagnosis of neonatal hepatitis[9]. To confirm the diagnosis, Intravenous cholangiogram during surgery is used[3]. In our case, abdominal ultrasound was done, it showed atretic gallbladder, during the surgery intravenous cholangiogram was done and confirmed the diagnosis of biliary atresia, intestinal malrotation and volvulus were found on abdominal exploration.

Kasai procedure or portoenterostomy, is the treatment of choice before 2 months of age, as there is less inflammation and fibrosis[21,22]. However, after 2 months and during the first year of life, liver transplantation is highly recommended[21,22]. However, favorable results can be achieved with an isolated liver transplant, even in the absence of a prior Kasai procedure[12]. Moreover, when biliary atresia is a part of other syndromes, many studies reports that Kasai procedure is less effective and has poor rates of success, so infant liver transplantation is considered[23,24]. After Kasai procedure (KPE), medical management involves addressing complications like cholangitis, optimizing nutrition[12]. In our case, Kasai and Ladds procedures were done for BS and SI.

If biliary atresia patients were undetected till 2 months of age or left untreated, they will develop fibrosis and cirrhosis, resulting in portal hypertension, and hepatic failure[9]. On the other hand, complications with Kasai procedure can occur, especially if it was associated with other factors[25]. Early complications include cholangitis, anastomosis leak, ileus, intestinal obstruction, and bleeding, while late complications such as, recurrent cholangitis, portal hypertension, bile flow cessation, ascites, hepato-pulmonary syndrome, and cirrhosis can also occur[20].

Many prognostic factors play a crucial role in treatment success, including severity of the existing liver damage prior to transplantation, operator experience, colangitis frequency, and age at operation[20]. Surgery after the age of 2 months is considered a poor prognostic factor. On the other hand, studies report that good outcomes are most likely associated with doing the procedure before the age of 2 months[26]. Furthermore, the evaluation of the results after performing the Kasai can be approached through assessing jaundice clearance and percentages of native liver survival[20]. Ten-year survival has been documented to range from 27 to 53%[20].

Our case reports a unique association of biliary atresia, which can result in serious complications. Therefore, early diagnosis and management is required to avoid undesirable outcomes. The limitation in our case arises from the limited data in the literature, as prognosis is yet to be known. However, some studies have reported no difference in the overall survival[27].

Conclusion

The presence of biliary atresia combined with anatomical variations like situs inversus and intestinal malrotation is a rare association that can have severe consequences if not addressed promptly. The potential outcomes include cirrhosis and end-stage liver disease, which present unique challenges in terms of surgical management. Early detection through the use of MRCG and Intravenous cholangiogram during surgery is crucial for confirming the diagnosis. The most favorable outcomes are observed when the Kasai portoenterostomy procedure is performed before the age of 2 months. However, in cases where treatment fails or when biliary atresia is associated with other syndromes, liver transplantation is typically necessary.

Ethical approval

This study is exempt from ethical approval at our hospital.

Consent

Written informed consent was obtained from the patient's parent for reporting this case. The consent is available for review on request.

Source of funding

Not applicable.

Author contribution

Data collection: B.A.Z., A.R.T., A.M.A., W.A. Writing the manuscript: B.A.Z., A.M.A., W.M.M., A.M.B., A.R.T., I.A.T., W.A. Study concept or design: B.A.Z., A.R.T., W.A. Review and editing the manuscript: B.A Z., A.R.T.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Dr Wael Amro.

Data availability statement

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Chang C-M, Kuo K-C, Chen W-H, *et al*. Maternal risk factors associated with offspring biliary atresia: population-based study. Pediatr Res 2023; 93:1064–71.
[2] Jiang J, Wan R, He S, *et al*. Epidemiological characteristics and risk factors of biliary atresia: a case-control study. BMJ Open 2021;11: e049354.
[3] Tiao M-M, Tsai S-S, Kuo H-W, *et al*. Epidemiological features of biliary atresia in Taiwan, a national study 1996-2003. J Gastroenterol Hepatol 2008;23:62–6.
[4] Davenport M, De Ville De Goyet J, Stringer MD, *et al*. Seamless management of biliary atresia in England and Wales (1999-2002). Lancet 2004;363:1354–7.
[5] Altman RP, Buchmiller TL. The Jaundiced Infant: Biliary Atresia. Pediatric Surgery. Elsevier; 2006. 1603–1619.
[6] Lendahl U, Lui VCH, Chung PHY, *et al*. Biliary atresia—emerging diagnostic and therapy opportunities. EBioMedicine 2021;74:103689.
[7] Spada M, Riva S, Maggiore G, *et al*. Pediatric liver transplantation. World J Gastroenterol 2009;15:648.
[8] Agha RA, Franchi T, Sohrabi C, *et al*. The SCARE 2020 Guideline: Updating Consensus Surgical CAse REport (SCARE) Guidelines. Int J Surg 2020;84:226–30.
[9] Allarakia J, Felemban T, Khayyat W, *et al*. Biliary atresia with an unusual abdominal orientation: a case report. Int J Surg Case Rep 2019; 55:152–5.
[10] Sabra TA, Abdelmohsen SM, Abdelazeem B. Biliary atresia with rare associations: a case report. Ann Pediatr Surg 2023;19:37.
[11] Antala S, Taylor SA. Biliary atresia in children: update on disease mechanism, therapies, and patient outcomes. Clin Liver Dis 2022;26: 341–54.
[12] Eitler K, Bibok A, Telkes G. Situs inversus totalis: a clinical review. Int J Gen Med 2022;15:2437–49.
[13] Baglaj M, Gerus S. Preduodenal portal vein, malrotation, and high jejunal atresia: a case report. J Pediatr Surg 2012;47:e27–30.
[14] Gunawardena R, Weerawardhana P, Lamahewage A. Biliary atresia with rare collection of congenital anomalies. J Case Rep 2019;9:117–9
[15] Xiang X-L, Cai P, Zhao J-G, *et al*. Neonatal biliary atresia combined with preduodenal portal vein: a case report. World J Clin Cases 2021;9: 7542–50.
[16] Elebute OA, Timo MT, Alakaloko FM, *et al*. Biliary atresia splenic malformation: a case report from a tertiary centre in west africa and the lessons learnt. J West Afr Coll Surg 2023;13:106–10.
[17] Rashid S, Zahier NA, Haidari F, *et al*. A case report on congenital biliary atresia with ventricular septal defect. Integr J Med Sci 2023;10: 715–7.
[18] Zaben BA, Abualrub AM, Malhes WM, *et al*. Biliary atresia associated with polysplenia syndrome, situs inversus abdominus, and reverse rotation of intestine. Ann Med Surg 2024;3. doi: 10.1097/MS9.0000 000000002173
[19] Mirza B, Iqbal S, Sheikh A. Biliary atresia associated with polysplenia syndrome, situs inversus abdominus, and reverse rotation of intestine. APSP J Case Rep 2012;3:14.
[20] Sinha CK, Davenport M. Biliary atresia. J Indian Assoc Pediatr Surg 2008;13:49–56.
[21] Wada H, Muraji T, Yokoi A, *et al*. Insignificant seasonal and geographical variation in incidence of biliary atresia in Japan: a regional survey of over 20 years. J Pediatr Surg 2007;42:2090–2.
[22] AsensioLlorente M, Ja LE, OrtegaLópez J, *et al*. First orthotopic liver transplantation in patient with biliary atresia and situs inversus in spain. Cir Pediatr 2003;16:44–7.
[23] di Francesco F, Caruso S, Bonsignore P, *et al*. Preduodenal portal vein reconstruction at liver transplantation: the challenges and a solution. Liver Transplantation 2019;25:1841–4.
[24] Falchetti D, Brant de Carvalho F, Clapuyt P, *et al*. Liver transplantation in children with biliary atresia and polysplenia syndrome. J Pediatr Surg 1991;26:528–31.
[25] Davenport M, Sinha C. Biliary atresia. J Indian Assoc Pediatr Surg 2008; 13:49.
[26] Bijl EJ, Bharwani KD, Houwen RHJ, *et al*. The long-term outcome of the Kasai operation in patients with biliary atresia: a systematic review. Neth J Med 2013;71:170–3.
[27] Guttman OR, Roberts EA, Schreiber RA, *et al*. Biliary atresia with associated structural malformations in Canadian infants. Liver Int 2011; 31:1485–93.