Ro J Pediatr. 2024;73(3)
DOI: 10.37897/RJP.2024.3.5

Biliary atresia and situs inversus in infant: a rare case report

Rendi Aji Prihaningtyas, Seruni, Bagus Setyoboedi, Sjamsul Arief

Department of Child Health, Faculty of Medicine Universitas Airlangga - Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

ABSTRACT

Background. Biliary atresia is the leading cause of liver transplantation in children. It is associated with other congenital anomalies. The presentation of biliary atresia with situs inversus is a rare case.

Case presentation. A 2-month-old female presented with jaundice since 15 days of life, acolic stools, and tea-colored urine. On further evaluation, she was found to have dextrocardia and situs inversus. A liver biopsy was performed and showed hepatic fibrosis due to extrahepatic cholestasis. Abdominal ultrasound and MRCP confirmed a liver in the left hypochondrium and suggested biliary atresia.

Conclusion. Although rare, every patient with biliary atresia should be screened for congenital situs inversus, which has a poor prognosis.

Keywords: cholestasis, biliary atresia, situs inversus, infant

INTRODUCTION

Biliary atresia is a progressive fibrous obstructive cholangiopathy of the biliary system leading to obstruction of bile flow. Biliary atresia is thought to result from defects in the normal remodeling process and a genetic predisposition to biliary atresia has been identified [1]. However, approximately 3% to 20% of biliary atresia cases are associated with related syndromes or other congenital anomalies. The majority of cases of biliary atresia are acquired [2]. Experimental and clinical studies have shown that viral infection triggers the destruction of the biliary epithelium and the release of antigens that stimulate an immune response and cause further damage to the bile ducts. This leads to inflammation and obstructive scarring of the biliary tree [1]. Biliary atresia that is left untreated results in rapidly progressing fibrosis and cirrhosis of the liver. This can lead to death within the first few years of life [2].

There have been reports of an association between biliary atresia and other developmental abnormalities [3,4]. Biliary atresia is thought to result from malformations during embryogenesis leading to other abnormalities. Biliary atresia is associated with other congenital anomalies such as polysplenia, vascular anomalies including preduodenal portal vein, interrupted vena cava, azygous continuation, cardiac anomalies, malrotation, and situs inversus [2]. The diagnosis and surgical management of such rare cases requires careful evaluation. A biliary atresia with situs inversus totalis is reported in this case, which is a rare condition.

CASE DESCRIPTION

A 2-month-old girl was referred to Dr. Soetomo General Academic Hospital, Surabaya with suspicion of biliary atresia. The patient had jaundice, which was followed by pale-colored stools. The mother had been aware of jaundice since 15 days of age but was brought to the pediatrician at 1 month of age and given ursodeoxycholic acid and N-acetylcysteine. The patient was breast-fed but complained of frequent vomiting, and difficulty gaining weight. The abdomen has been enlarged since birth. There were no complaints of other diseases. There was a lump coming out of the navel for the past 1 month, especially when crying. One week before admission,

Corresponding author:
Bagus Setyoboedi
E-mail: bagus.setyoboedi@fk.unair.ac.id

Article History:
Received: 21 June 2024
Accepted: 16 September 2024

the patient had a fever. The icteric sclera appeared darker, accompanied by dark urine that gradually became tea-colored (Figure 1).

The patient was born spontaneously, full term with a birth weight of 3100 grams, cried immediately, and had no history of blue. There is no family history of similar diseases. The patient was immunized with hepatitis B and BCG.

The anthropometric examination revealed a body weight of 4.3 kg, a body length of 57 cm, and an upper arm circumference of 9 cm (Weight-for-Age Z-score < -3 SD; Length-for-Age Z-score -2 to -3 SD, Weight-for-Length Z-score -2 to -3 SD, Arm circumference-for-age <-3 SD) with poor nutritional status and stunted. Physical examination showed stable vital signs. The sclera appeared icteric with jaundice of the skin over the whole body, there was no palmar nevus or spider nevus. There were no rales in the lungs. A heart murmur was present. The abdomen appeared distended with an abdominal circumference of 38 cm. Hepatomegaly 3×2×1cm, splenomegaly S2H1, venous plethora, and umbilical hernia were present. Palpation revealed a liver to the left and a spleen to the right (Figure 1).

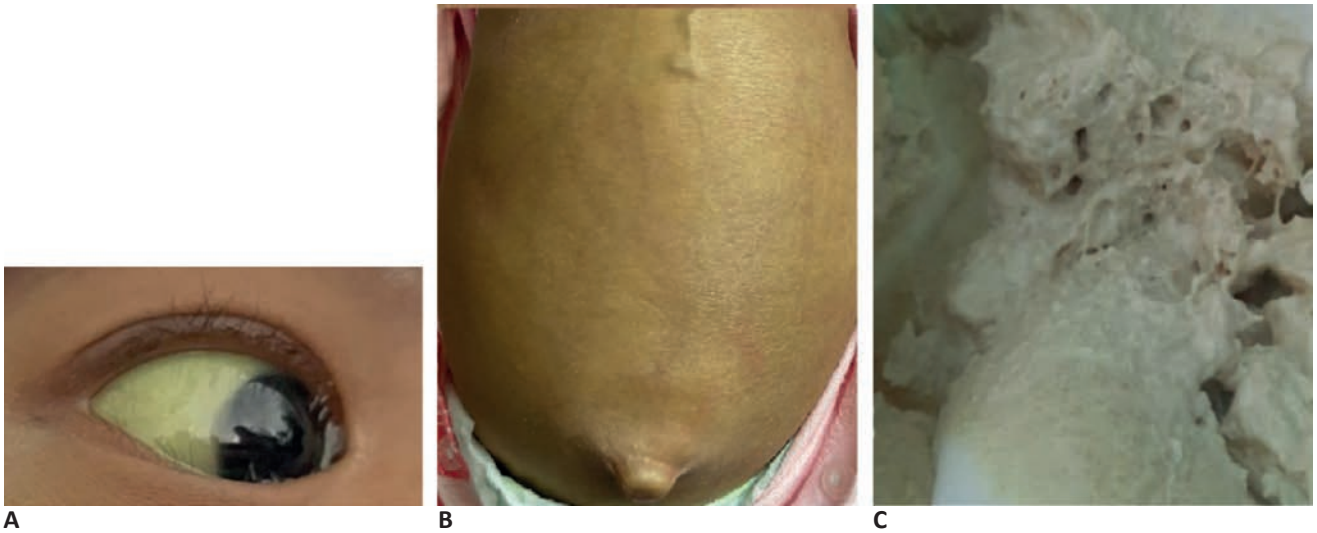
Routine blood examination showed white blood cell 29.7×103/µL (normal range 6.0 to 18×103/µL), hemoglobin 10 g/dL (normal range 10.6 to 16.4 g/dL), platelets 126 (normal range 150 to 450×103/µL). Liver function examination showed cholestasis (total bilirubin 7.7 mg/dL, and direct bilirubin 5.7 mg/dL), Albumin 3.97 g/dL (normal range 3,5 to 5 g/dL), Aspartate aminotransferase (AST) 218 U/L (normal value 0~37 U/L), Alanine aminotransferase (ALT) 285 U/L (normal value 0~55 U/L), Alkaline phosphatase (ALP) 214 U/L (normal value 35~100 U/L) and Gamma-glutamyl transpeptidase (GGT) 3435 U/L (Table 1). Thyroid function test revealed FT4 1,1 ng/dL, TSH 3.48 µUl/mL, serum iron 52 µg/dL, TIBC 303 µg/dL, and transferrin 232.1 mg/dL, Alfa Feto Protein 75.8 ng/mL. The serology for hepatitis A, B, and C were all negative. TORCH serological measurement showed CMV IgG reactive (98.4 AU/mL, CMV IgM non-reactive, Toxoplasma IgG non-reactive, Toxoplasma IgM non-reactive, Rubella IgG reactive (25.8 IU/mL), and Rubella IgM non-reactive. Blood culture examination showed salmonella species with sensitive amoxiclav, ampicillin, ampicillin-sulbactam, aztreonam, cefepime, cefoperazone sulbactam, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, levofloxacin, meropenem, and moxifloxacin.

A two-phase abdominal ultrasound showed an unidentified gallbladder with subcapsular hepatic flow (+) supporting biliary atresia. Percutaneous

TABLE 1. Laboratory parameters of the patient

Laboratory parameter	Value	Laboratory parameter	Value
Hb (g/dL)	10.0	Albumin (g/dL)	3.97
HCT (%)	29.7	AST (U/L)	218
WBC (103/µL)	48930	ALT (U/L)	285
PLT (103/µL)	126000	PPT (s)	26.8
CRP (mg/dL)	1.19	APTT (s)	12.4
Procalcitonine (ng/mL)	1.19	Total bilirubin (mg/dL)	7.70
Natrium (mmol/l)	152	Direct bilirubin (mg/dL)	5.70
Kalium (mmol/l)	3.7	ALP (U/L)	214
Chloride (mmol/l)	126	GGT (U/L)	3435
Calsium	10.0	BUN (mg/dL)	16.7
Phosphate	3.71	Creatinine (mg/dL)	0.4

Hb: Hemoglobin; HCT: Hematocrit; WBC: White Blood Cell; PLT: Platelet; CRP: C-Reactive Protein; UA: Uric Acid; AST: Aspartate Transaminase; AST: Alanine Aminotransferase; PPT: Plasma Prothrombin Time; APTT: Activated Partial Thromboplastin Time; ALP: Alkaline Phosphatase; GGT: Gamma-Glutamyl Transpeptidase; BUN: Blood Urea Nitrogen.



A B C

FIGURE 1. Clinical manifestation (A, B) and acholic stool (C)

liver biopsy revealed the portal tract was found to be proliferated with a small amount of lymphocytic inflammatory cells localized to the portal tract. There was clouding and ballooning of the hepatic lobules composed of degenerated hepatocytes. Dilated canaliculi with bile pigment filling were present. PMNs and mononuclear inflammatory cells were also found among the hepatocytes. Mild fibrosis limited to the portal duct was observed (F1). Percutaneous liver biopsy showed an extrahepatic cholestasis with mild fibrosis (F1). The echocardiogram showed dextrocardia, situs inversus, ejection fraction EF 86%, and small secundum ASD 0.3 cm L to R shunt. CXR showed a normal shape of the heart and a right-sided apex of the heart (Figure 2).

Magnetic Resonance Cholangiography (MRCP) revealed that the Liver was found enlarged on, the left side, v. porta seen on the left side, aorta seen on the right side, no hypo/hyperintense nodules seen, and no gallbladder was identified. MRCP supported biliary atresia and situs inversus features (Figure 3). The patient was hospitalized and received intravenous fluid therapy, antibiotics, ursodeoxycholic

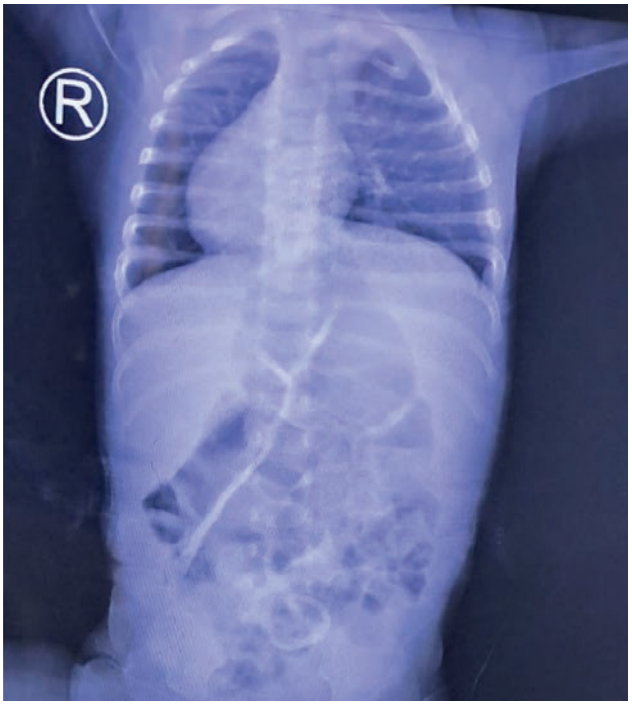


FIGURE 2. Chest X-ray showed the right-sided apex of the heart

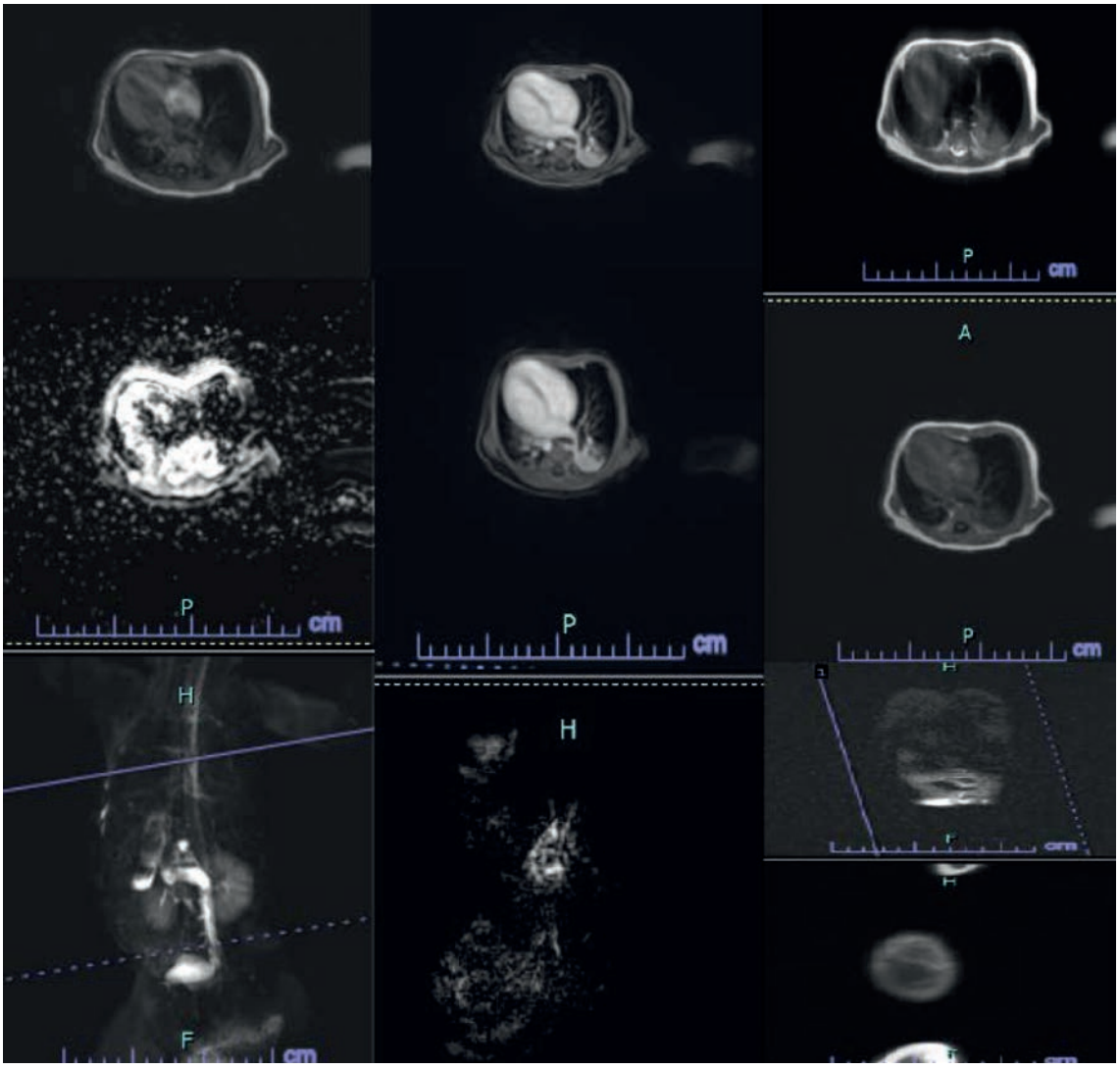


FIGURE 3. MRCP confirmed the features of biliary atresia and situs inversus

acid, fat-soluble vitamin supplementation, nutrition with Medium chain triglycerides (MCT) formula, and Kasai surgery was planned.

DISCUSSION

The incidence of biliary atresia varies from 1/15,000 to 1/19,000 [4]. The incidence of biliary atresia is increasing and varies between countries [5]. In the United States, biliary atresia is 4.47 per 100,000. Biliary atresia is more common in Asian/Pacific Islanders than Caucasians [5].

Biliary atresia has symptoms of persistent jaundice, clay-colored stools, and hepatomegaly. Any infant who has jaundice for more than 14 days is no longer considered physiologic jaundice and should undergo evaluation. Most infants with biliary atresia have initially pigmented stools which later turn acholic as the disease progresses and signs of liver cirrhosis appear [2]. In this case, the infant had jaundice, noticed by the parents at 15 days of age, followed by the stool becoming pale and the urine becoming tea-colored. This was clinically consistent with biliary atresia. The patient had been jaundiced since the age of 2 weeks but was referred at the age of 2 months.

Biliary atresia has also been reported to be associated with small bowel malrotation. The liver, stomach, and spleen were in the abdomen's middle, right, and left sides [6]. There has also been a reported case of biliary atresia with right-sided polysplenia [3]. A rare congenital vascular disorder also found in biliary atresia, the preduodenal portal vein [4]. Situs inversus totalis describes a condition in which organs in the thoracic and abdominal cavities are mirrored, including dextrocardia [7]. Situs inversus totalis is one of the anomalies that occurs in infants with biliary atresia with an incidence of 10 to 20 percent [8].

Modalities in the evaluation of biliary atresia include ultrasonography (USG), Magnetic Resonance Cholangiopancreatography (MRCP), and liver biopsy. Ultrasound is recommended as an initial screening examination and is usually sufficient to help diagnose biliary atresia. An abnormal gallbladder with irregular contours and a triangular cord sign are typical ultrasound findings in biliary atresia [9]. MRCP is a non-invasive method for diagnosing biliary atresia with a sensitivity of 100% and a specificity of 96% [10]. MRCP is also superior in differentiating biliary atresia from cholestasis in preterm versus term infants [11].

Histopathology of biliary atresia includes ductal proliferation, bile plugs in portal bile ducts/ductules, portal stromal edema, giant cell hepatocyte proliferation, and moderate to marked ductal reaction [12]. Among these changes, ductal proliferation is considered highly sensitive and specific for biliary atresia [1], which was present in this case.

Abdominal ultrasound showed gallbladder abnormalities and triangular cord sign. MRCP results showed no visible bile duct and situs inversus. Extrahepatic cholestasis with hepatic fibrosis was found by percutaneous liver biopsy. In this case, the patient had typical biliary findings of biliary atresia. However, the case was further complicated by another congenital abnormality of situs inversus.

Bile flow from the porta hepatis can be restored after resection of the entire fibrotic extrahepatic bile duct, as reported by Professor Kasai. Patients undergoing surgery less than 30 days of age had the best jaundice clearance rate (71.9%) [13]. A higher fibrosis stage and older age at Kasai procedure were associated with a higher risk of transplantation [12]. However, in this case, the presence of congenital anomalies may complicate the case.

CONCLUSION

Patients with biliary atresia should be aggressively evaluated for other structural anomalies, such as situs inversus. Comprehensive management is necessary to improve the outcome and prognosis of infants with biliary atresia.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Vij M, Rela M. Biliary Atresia: pathology, Etiology and Pathogenesis. *Future Sci OA.* 2020;6(5):FSO466. https://doi.org/10.2144/fsoa-2019-0153
2. Siddiqui AI, Ahmad T. Biliary Atresia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 May 20]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK537262/
3. Solanki S, Kanojia R, Reddy M, Ahmad MF, Lal SB, Samujh R. Biliary Atresia Splenic Malformation With Situs Inversus: A Case Report. *Adv Pediatr Surg.* 2022;28(1):17. http://doi.org/10.13029/aps.2022.28.1.17
4. Sabra TA, Abdelmohsen SM, Abdelazeem B. Biliary atresia with rare associations: a case report. *Ann Pediatr Surg.* 2023;19(1):37. http://doi.org/10.1186/s43159-023-00269-5
5. Hopkins PC, Yazigi N, Nylund CM. Incidence of Biliary Atresia and Timing of Hepatoportoenterostomy in the United States. *J Pediatr.* 2017;187:253-7. http://doi.org/10.1016/j.jpeds.2017.05.006
6. Allarakia J, Felemban T, Khayyat W, Alawi A, Mirza A, Alkhazal B, et al. Biliary atresia with an unusual abdominal orientation: A case report. *Int J Surg Case Rep.* 2019;55:152-5. http://doi.org/10.1016/j.ijscr.2019.01.028
7. Eitler K, Bibok A, Telkes G. Situs Inversus Totalis: A Clinical Review. *Int J Gen Med.* 2022;3:15:2437-49. http://doi.org/10.2147/IJGM.S295444
8. Wiederkehr HDA, Carvalho CAD, Ruggeri M, Campos LC, Wiederkehr BDA, Wiederkehr JC. Liver Transplantation in a Patient with "Situs inversus" Associated with Biliary Atresia, Polysplenia and Absence of

Inferior Vena Cava: A Case Report. *Surg Sci.* 2016;07(02):89-95. http://doi.org/10.4236/ss.2016.72012
9. Zhou L, Shan Q, Tian W, Wang Z, Liang J, Xie X. Ultrasound for the Diagnosis of Biliary Atresia: A Meta-Analysis. *Am J Roentgenol.* 2016;206(5):W73-82. http://doi.org/10.2214/AJR.15.15336
10. Kohno M. Diagnostic Modalities for Biliary Atresia. In: Nio M, editor. Introduction to Biliary Atresia [Internet]. Singapore: Springer Singapore; 2021 [cited 2024 May 28]. p. 123-31. Available from: https://link.springer.com/10.1007/978-981-16-2160-4_19
11. Chen WC, Lo HY, Tsai YS, Yang YJ. The accuracy of magnetic resonance cholangiopancreatography in the diagnosis of biliary atresia in preterm infants with cholestasis. *Pediatr Neonatol.* 2023;64(1):12-8. http://doi.org/10.1016/j.pedneo.2022.07.004
12. Russo P, Magee JC, Anders RA, Bove KE, Chung C, Cummings OW, et al. Key Histopathologic Features of Liver Biopsies That Distinguish Biliary Atresia From Other Causes of Infantile Cholestasis and Their Correlation With Outcome: A Multicenter Study. *Am J Surg Pathol.* 2016;40(12):1601-15. http://doi.org/10.1097/PAS.0000000000000755
13. Kitagawa H. Definition and Classifications of Biliary Atresia. In: Nio M, editor. Introduction to Biliary Atresia [Internet]. Singapore: Springer Singapore; 2021 [cited 2024 May 28]. p. 11-7. Available from: https://link.springer.com/10.1007/978-981-16-2160-4_3