Complications of Biliary Atresia in a 27-Year-Old Male Patient

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ABSTRACT

Biliary atresia (BA) is a disease of the extrahepatic biliary tree that presents with biliary obstruction in the neonatal period, which is caused by fibro-obliterative process. Kasai procedure, a hepatoportoenterostomy (HPE) as an attempt to restore bile flow from the liver to the proximal small bowel, has been shown to improve survival in BA patients. Many BA survivals who had undergone Kasai HPE will have slowly progressive liver disease and the majority of patients will ultimately require liver transplantation. In spite of many experimental treatments, cirrhosis still occurs in BA patients survival.

This case report presents a male patient with biliary atresia that has survived for 27 years after Kasai procedure. He had been repeatedly admitted to hospital with complications caused by cirrhosis, such as repeated variceal and hemorrhoid bleeding and also refractory ascites. These complications are indications for liver transplantation. Although Kasai HPE procedure improves survival in BA patients in Indonesia, long-term complications of cirrhosis makes the patient awaits for liver transplantation.

Keywords: *biliary atresia, Kasai procedure, hepatoportoenterostomy, cirrhosis, liver transplantation*

ABSTRAK

Atresia bilier (AB) adalah penyakit pada saluran bilier ekstrahepatik yang menimbulkan sumbatan bilier pada periode neonatal disebabkan proses fibro-obliterasi. Prosedur Kasai merupakan suatu hepatoportoenterostomi (HPE) adalah tindakan untuk mengalihkan aliran empedu dari hati ke usus kecil, telah meningkatkan kesintasan pasien AB. Kebanyakan pasien AB yang selamat setelah menjalani Kasai HPE akan menderita penyakit hati yang progresif dan akhirnya mayoritas pasien akan membutuhkan transplantasi hati. Walaupun terdapat banyak terapi yang telah dicoba diberikan, sirosis tetap terjadi pada pasien AB yang selamat.

Kasus ini melaporkan pasien laki-laki dengan atresia bilier yang dapat bertahan sampai 27 tahun setelah menjalani prosedur Kasai dan mendapat perawatan berulang kali karena komplikasi sirosis seperti perdarahan varises dan hemoroid serta refraksi asites. Komplikasi yang terjadi merupakan indikasi dari transplantasi hati. Walaupun prosedur Kasai HPE dapat meningkatkan kesintasan pasien AB di Indonesia, komplikasi jangka panjang seperti sirosis masih memerlukan penatalaksanaan lanjutan yaitu transplantasi hati.

Kata kunci: *atresia bilier, prosedur Kasai, hepatoportoenterostomi, sirosis, transplantasi hati*

INTRODUCTION

Biliary atresia (BA) is a progressive, idiopathic, fibro-obliterative disease of the extrahepatic biliary tree that presents with biliary obstruction exclusively in the neonatal period. The overall incidence of BA is low, i.e. about one in 10,000 to 20,000 live births. The incidence of BA varies from 5/100,000 live births in The Netherlands, 6/100,000 in the British Isles,

6.5/100,000 in Texas, 7.4/100,000 in Atlanta USA and in Japan, 10.6/100,000 in Hawaii, up to 32/100,000 in French Polynesia. Incidence of BA reaches the highest in Asia and the Pacific region.[1]

After diagnosis of BA is confirmed by cholangiogram, a Kasai procedure which is a hepatoportoenterostomy (HPE) should be performed promptly. The procedure is an attempt to restore bile flow from liver to proximal small bowel. Despite the bile flow is established after Kasai procedure and cholestasis is improved, many patients will have slowly progressive liver disease and the majority of patients will ultimately require liver transplantation.[2,3] Although the performance of Kasai HPE clearly improves survival overall, but the long-term prognosis is difficult to predict. Half of the 20-year survivors had cirrhosis and 20% underwent liver transplant or experienced death within a few years of period.

Improvements in medical therapy after Kasai HPE, such as prophylaxis against cholangitis, improvements in nutrition, bile flow, and experimental therapy such as anti-fibrotic or anti-inflammatory agents may increase survival of BA patients in the future. This case report will discuss a male patient with biliary atresia that has survived for 27 years after Kasai procedure. He has been repeatedly admitted to hospital with complications caused by cirrhosis. These complications need immediate management, including liver transplant. In spite of improving survival rate of BA patients in Kasai procedure, further evaluation and management must be performed to minimize complications.

CASE ILLUSTRATION

A 27-year-old male patient was admitted to emergency room of Cipto Mangunkusumo Hospital with a chief complaint of altered consciousness one day before admission. Two weeks prior to the admission, he experienced bloody stool and underwent colonoscopy revealing internal and external hemorrhoid, which was treated further with sclerotherapy and he also had complaints of vomiting and abdominal pain since 3 days before the admission. He had brown-colored stool with no blood nor acholic, urine was dark colored. He has never experienced fever, cough, dyspnea or palpitation.

When patient was two months old, he was diagnosed with biliary atresia and underwent Kasai procedure for repair of cholestasis in Harapan Kita Women and Children Hospital. After a successful Kasai procedure, the dark-colored urine and acholic stool were improved. He had routine visits to Harapan Kita Women and Children Hospital and finally had no more complaints until he was 17-years old. At 17 years of age, his complaints of dark-colored urine and acholic stool recurred and he was diagnosed with biliary cirrhosis. The complaints of coffee-ground stool and vomiting appeared for first time when he was 21-years old and since then, patient had undergone esophagogastroduodenoscopy and ligation for grade III esophageal varices for 4 times. Patient was admitted to hospital for 11 days and was discharged home on treatment of omeprazole, sucralfate,curcumin and spironolactone.

The physical examination revealed normal vital signs. The patient was awake and fully-alert. The conjunctivas of his eyes were anemic and the sclera was jaundiced. His liver was enlarged in the size of 4 fingers below the costal arch with blunt edge. Spelneomegaly was found (Schuffner II), but no shifting dullness was found and clubbing fingers were noticed, which are illustrated in Figure 1.

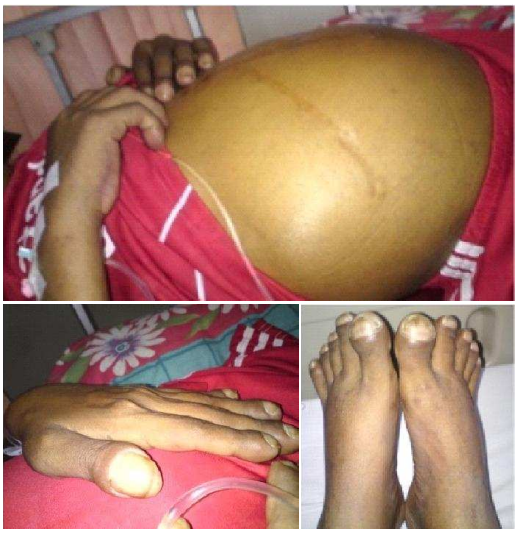

Figure 1. Physical findings showed ascites and clubbing fingers

Ultrasound (US) examination, which was performed on January 1st, 2012, showed decreased in the size of the left hepatic lobe with irregular border, widened portal vein, increased echogenicity of intra and extrahepatic biliary tract as well as lienalis artery. It was difficult to evaluate the common bile duct. (Figure 2).

Two weeks later, the patient underwent esophagoduodenoscopy which revealed grade III esophageal varices and severe portal hypertensive gastropathy. Afterward, in one month, the results of colonoscopy examination showed small external hemorrhoid, large grade II internal hemorrhoid,

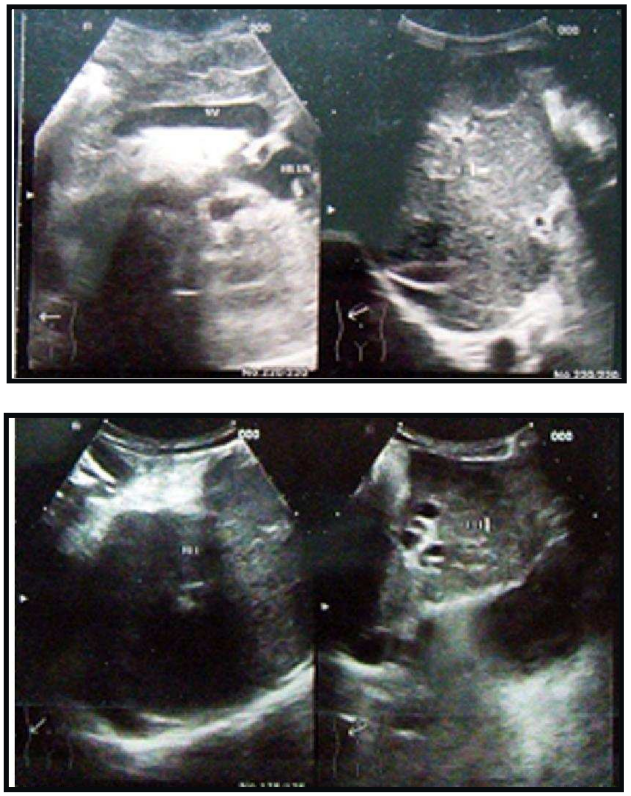

Figure 2. Abdominal ultrasonography of the patient showed decrease in the size of the left hepatic lobe with irregular border, widened portal vein, increased echogenicity of intra and extrahepatic biliary tract as well as lienalis artery. It was difficult to evaluate the common bile duct

colonopathy, enteropathy, and no active bleeding (Figure 3.). Further laboratory evaluation revealed hemoglobin level of 10.3 g/dL, leukocytes count of 8,370/µL and platelet count of 58,800/µL. His prolonged activated partial thromboplastin time (APTT) was 52.7 seconds (normal limit of 32.6 seconds), and the prothombin time (PT) was 17.4 s (normal limit of 11.8 s). The aspartate transaminase (AST) and alanine aminotransferase (ALT) level were increased to 353 IU/L and 101 IU/L. The patient had hypoalbuminemia with albumin level of 2.4 g/dL and the bilirubin levels were increased too with total, direct, and indirect were 38.77 mg/dL, 25.18 mg/dL, 13.59 mg/dL, respectively.

The patient's problems were biliary cirrhosis with history of hepatic encephalopathy, thrombocytopenia and coagulopathy, grade III esophageal varices, internal and external hemorrhoid, biliary atresia with history of Kasai Procedure in infancy period. Patient was treated with L-ornithin L-aspartate, propranolol, furosemide and spironolactone, vitamin K, ceftazidime and levofloxacine during hospitalization. Patient received fresh frozen plasma transfusion for the correction of coagulopathy. After having a ligation procedure of esophageal varices, the patient was discharged home.

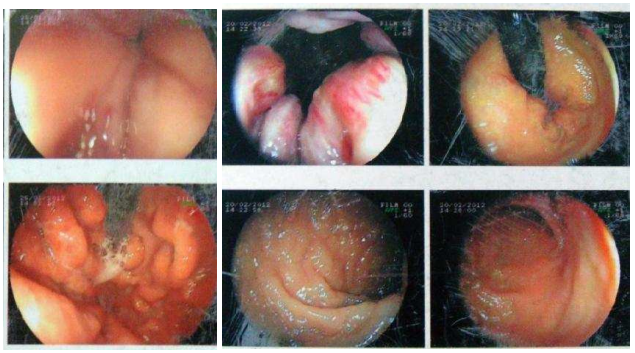

Figure 3. Esophagoscopy and colonoscopy showed small external hemorrhoid, large grade II internal hemorrhoid, colonopathy, enteropathy, and no active bleeding

DISCUSSION

Biliary atresia (BA) is a progressive, idiopathic, fibro-obliterative disease of the extrahepatic biliary tree that presents with biliary obstruction and occurs exclusively in the neonatal period. BA is the most common cause of neonatal jaundice for which surgery is indicated and also as indication for liver transplantation in children.[1]

Infants with BA can be categorized into three groups: (1) BA without any other anomalies or malformations. This pattern is sometimes known as perinatal BA that occurs in approximately 70% of infants with BA. Typically, these children are born jaundice-free, within the first two months of life, jaundice develops and stools become progressively acholic; (2) BA in association with laterality malformations, which is also known as biliary atresia splenic malformation (BASM) or embryonic biliary atresia. It occurs in 10 to 15% of infants with BA; (3) BA in association with other congenital malformations that occurs in the remaining 10-15% of BA cases. It is associated with congenital malformations including choledochal cyst, kidney anomalies, and/or heart malformations.[2-5] Regardless of the type of BA, the histology and cholangiogram are similar. Histologic findings typically show inflammation, portal tract fibrosis, cholestasis, and bile duct proliferation; while the cholangiogram indicates loss of patency of the bile ducts.

The cause of BA is unknown, although several mechanisms have been implicated. In some patients, several of these mechanisms may contribute to the development of BA. In others, BA may be the common phenotype that can be caused by a variety of injuries to the biliary system occurring in the perinatal period. Studies suggest a possible viral etiology, also with the possibility of a toxin-mediated inflammatory response. Until today, neither specific virus nor toxin has been implicated in the development of BA in both animals and human subjects. Genetic factors may play a causative

role in the small subgroup of patients with BASM malformations, such mutations in the CFC1 gene.[2-4]

The evaluation process involves a series of serologic, laboratory, urine, and imaging tests. If BA is confirmed by cholangiogram, a Kasai procedure of hepatoporto-enterostomy (HPE) should be performed. If successful, the remaining small patent bile ducts will drain into the roux limb and jaundice will start to resolve in the weeks following surgery. If unsuccessful, bile drainage will not be achieved, and the child remains jaundiced. If there is persistent jaundice three months after the Kasai, the patient should be referred for liver transplant evaluation. Revision of a non-functioning HPE is not recommended except in rare circumstances.[1-3]

Even if bile flow is established and cholestasis improves, many patients will have slowly progressive liver disease despite undergoing the Kasai procedure, and the majority of patients with BA will ultimately require liver transplantation. At least 50% of patients who undergo HPE will require liver transplantation by two years of age as a result of primary failure of the Kasai HPE and/or growth failure. The patient's age at the time of HPE can predict native liver survival at later time points. For patients who undergo HPE $\leq$ 30 days of life, the chance of native liver survival at four years of age is nearly 50%; while among those who undergo HPE between 31 and 90 days of life, the chance of native liver survival at four years of age is 36%.[6-8]

The Kasai HPE obviates the need for liver transplantation in a substantial minority and significantly delays the liver transplantation for many others. If bile drainage is achieved, it is likely that transplantation will not be needed for years or decades. Historical series before the Kasai procedure was introduced in 1968 report a 10% survival rate at three years of age, as compared with the 35 to 50% survival rates with native liver at four years of age. Medical care following Kasai HPE consists of the following interventions, i.e. the choleretics and possible use of anti-inflammatory medications, nutritional rehabilitation, fat-soluble vitamin supplementation, prevention of cholangitis, and management of portal hypertension and its sequelae.[9,10]

Cholangitis is a common complication in patients with BA who have undergone a Kasai HPE ranging between 40 and 90%, with the majority of patients experiencing at least one episode prior to two years of age. The chronic hepatobiliary inflammation characteristic of BA leads to progressive biliary cirrhosis.[9-11]

The majority of individuals with BA eventually require liver transplantation, where BA is the most common indication for liver transplantation in infants and children. In the current era, at least 60 to 80% of patients with BA will require liver transplantation, even with optimal management. The indications for liver transplantation in patients with BA include primary failure of the Kasai HPE or lack of bile drainage, refractory growth failure in spite of adequate supplemental nasogastric tube feeding, complications of portal hypertension, repeated variceal bleeding, refractory ascites that compromises respiratory function, hepatopulmonary syndrome, portopulmonary hypertension, progressive liver dysfunction, progressive cholestasis, and refractory coagulopathy.

For those children who require liver transplantation, the prognosis is generally good. In international series, long-term survival rates are approximately 70 to 80% at both 5 and 10 years and these rates continue to improve as demonstrated in more recent case series. The liver transplant surgery in BA patients is complicated by the presence of intra-abdominal adhesions attributed to previous HPE.

Long term prognosis for BA patients is still variable, but complementary approaches of HPE and liver transplantation improve long-term survival with up to 90% of BA patients survived into adulthood. Overall survival rate with native liver ranges from 30-55% at 5 years and 30-40% at 10 years.[9] One study with long-term follow-up included 271 patients who underwent the procedure between 1968 and 1983 found that 63 patients (23%) were alive with native liver for at least 20 years after surgery. The majority of survivors (61 patients) had evidence of chronic liver disease or cirrhosis. Most required lifelong care for management of hepatobiliary complications.[10] Latest series reported 5-, 10-, and 20-year survival rates with native livers of 63%, 54%, and 44%, respectively. Half of the 20-year survivors had cirrhosis, and 20 % went on to liver transplant or death within a few years.[11] Experimental therapy such as anti-fibrotic or anti-inflammatory agents may improve outcomes in the future. Because biliary atresia is not restricted to the extrahepatic bile duct, patients with successful HPE display abnormalities of the intrahepatic biliary tree, including stenosis, dilatation, and sometimes pseudocyst formation. Intrahepatic change could lead to hepatic cirrhosis and affect portal hypertension.[11,12]

This case reported a 27-year-old male patient is an example of successful Kasai HPE, which had been performed to BA patient in the neonatal period. It

also shows the predicted outcome of that successful procedure, i.e. the biliary cirrhosis along with its complications due to portal hypertension. Furthermore, the case also reminds us about the need of liver transplantations in BA patients after Kasai HPE, which should be taken into consideration in the follow up of BA survivals.

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