

Cholestasis with Congenital Heart Disease in Neonates: A Case Report

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Abstract: ***Introduction:** Cholestasis in neonates is an obstruction to the flow of bile and substances that must be excreted by the liver, which causes an increase in direct bilirubin and a build - up of bile salts. While congenital heart disease (CHD) is an abnormality in the structure and function of the heart that has been present since birth. The association between neonatal cholestasis and CHD, a finding for this diagnosis has not been investigated previously. **Case:** We report a case of cholestasis with congenital heart disease type patent ductus arteriosus and atrial septal defect in neonates. **Conclusion:** Cholestasis in this case was caused by late - onset sepsis and CHD causing systemic disorders, then cholestasis that occurred in the patient was an intrahepatal process. Finally, the theory that liver disease is the result of CHD is more common than heart disease related to liver disease is true.*

Keywords: Neonatal Cholestasis, Congenital Heart Disease

1. Background

Cholestasis in neonates is an obstruction to the flow of bile and substances that must be excreted by the liver, which causes an increase in direct bilirubin and a build - up of bile salts. Disorders can occur from the basolateral membrane of the hepatocyte to the site of entry of the bile duct into the duodenum. While congenital heart disease (CHD) is an abnormality in the structure and function of the heart that has been present since birth. The association between neonatal cholestasis and CHD, a finding for this diagnosis has not been investigated previously. Therefore, the aim of this case report is to find out the correlation existence between.^{1,2}

2. Case Presentation

A 17 - day - old baby boy came to the ER of the Sanjiwani Hospital, Gianyar, complaining of jaundice since 1 day before he was admitted to the hospital. Yellowish appears on the baby's face and the color of the eyeballs is also slightly yellowish. In addition, the color of urine is more yellow than before but still clear. Babies urinate usually about 10 times a day. Likewise, the color of the baby's stool is also paler yellow and the baby is defecating approximately 2 - 3 times a day with a soft consistency.

From the history of previous illness and family, no abnormalities were found. The baby is the first child, born normally, assisted by a gynecologist, at term, and immediately cries. Birth weight 2600 gr, with a body length of 50 cm. Babies get breast milk from birth until now. The economic status of the family is quite sufficient.

On physical examination in the NICU, vital signs were found within normal limits. Icteric sclera was found, heart murmur was found at ICS 2 left mid clavicle line, minimal abdominal distension, liver enlargement 1/3 - 1/3, and visible dilation of veins and skin color greenish yellow. Additional examination of 3 - phase feces found putty - colored stools. Laboratories showed an increase in Leukocyte 20.76 10³/μL, IT - ratio 0.64. Increased liver

function SGOT 588 U/L, SGPT 278 U/L and total bilirubin 9.23 mg/dL, direct 7.22 mg/dL, indirect 2.01 mg/dL. Increased alkaline phosphatase 286.00 U/L. Urine bilirubin positive 3+. The results of echocardiography found small ASD secundum, PDA left to right and ultrasound results showed a contracted gall bladder, no widening of the intrahepatal and extrahepatal bile ducts. There is no triangular cord sign.

First, patient diagnosed cholestasis with CHD (ASD and PDA) and late onset sepsis. The treatments given intra venous access with Tridex 100 support with breastmilk by pacifier, oxygen via canula nasal with 1 liter per minute, Ursodioxolic Acid 15mg every 8 hours, Cholestyramine 0, 8 gr every 5 hours, antibiotic of Cefoperazone Sulbactam 150mg every 12 hours, multivitamin (A, D, and K) drops. The patient eventually referred to SanglahGeneral Hospital for cholestasis tracing and therapy as well as management of pediatric cardiology for the CHD.

3. Discussion

Jaundice, discoloration of the skin, sclera, mucous membranes and body fluids, is a common change found in infants in the first 2 weeks after birth, accounting for 2.4% to 15% of newborns. Jaundice in cholestasis due to biliary atresia ranges from 3 to 12 days while hepatocellular causes are 16 to 24 days. This baby jaundice appears at the age of 16 days after birth. The etiology of cholestasis is hepatocellular; infection, systemic/metabolic disorder, miscellaneous are about 45 to 69%, while obstructive; biliary atresia, choledochal cyst causes are 19 to 55% of all cases. Approximately 20 to 30% of causes of neonatal cholestasis were idiopathic in recent studies.³

Typical findings in infants with cholestasis are prolonged jaundice, scleral icterus, putty - colored stools, dark yellow urine, and hepatomegaly. The accumulation of bile in the blood also makes the baby itch, hypercholesterolemia, SGOT, SGPT, alkaline phosphatase, glutamyltranspeptidase increased.³ - phase stool examination is recommended. The frequency used is 3 phases, is every 8 hours in one day.^{3,4}In

this case, Jaundice is found on the baby's face and eyeballs, the color of the urine that looks more concentrated and the color of the stools is paler. On physical examination, hepatomegaly was also found, the skin color looked yellow, and during observation the yellow color gradually changed to greenish.³ - phase stool examination produces putty stools. Putty - colored stools are caused by obstruction of the biliary tract, causing obstruction to the flow of bile that enters the intestine. Laboratory results showing a drastic increase in liver function levels and hyperbilirubinemia. Suspicion of an increase in bilirubin levels due to cholestasis can also be seen from a direct bilirubin level of more than 1 mg/dL if the total bilirubin is less than 5 mg/dL. Meanwhile, if the total bilirubin is more than 5 mg/dL, the direct bilirubin level is more than 20% of the total bilirubin.⁵ In the case of the total bilirubin level is more than 5 mg/dL which is 9.23 mg/dL and the direct bilirubin level is more than 20% total or more than 1.85 mg/dL.

Abdominal ultrasound is able to describe abnormalities in the biliary tract. In this case, showed a contracted gall bladder, no widening of the intrahepatal and extrahepatal bile ducts, and no triangular cord sign. If there is no contraction of the gallbladder after oral administration, however, it does not exclude the presence of proximal biliary atresia. So it is recommended that ultrasound should be done after 4 hours after fasting. The effect of the contracted gallbladder in the fasting phase is not in accordance with the working mechanism of the gallbladder itself, which is contracting at the time after fasting or after being given a drink.

CHD in infants was diagnosed based on clinical findings of a murmur and echocardiography examination revealed defects in the Atrial Septal Defect (ASD) secundum left - to - right shunt and Persistent Ductus Arteriosus (PDA). In most cases, the cause of CHD is unknown. Several exogenous (drug types, maternal disease, X - ray) and endogenous (Down's syndrome, Turner) factors play a role for the etiology.⁶

Correlation between cholestasis and the incidence of CHD has been reported in 3% - 8% of cases with biliary atresia, but is estimated to occur only in 0.06% - 0.75% of the general population. Few know the relationship between primary liver disease and concomitant CHD defects. However, liver disease resulting from CHD is more common than heart disease associated with liver disease. The mechanisms leading to hepatic dysfunction would be multifactorial, for example, liver dysfunction which is a combination of passive congestion of the liver and hypoxia, which would be accompanied by CHD or pulmonary abnormalities. Excessive or low volume will also lead to congestive hepatopathy and hepatic ischemia. The mechanism of neonates with CHD showing significant results in their bilirubin levels has many contributing factors of congestive hepatopathy and subclinical hepatitis. The increased filling pressure is transmitted to the venous system and causes congestive hepatopathy. Passive congestion can also result in the secretion of bilirubin into the biliary tree by hepatocytes. Increased venous pressure will decrease perfusion pressure resulting in a decrease in oxygen

delivery, more precisely in the centrilobule leading to necrosis.^{7, 8, 9}

Management of cholestasis aims to prevent further liver damage. In infants with pruritus (itching) due to severe cholestasis, this group recommends Ursodioxycolic acid 20 mg/kg/day, Rimfamicin 5 - 10 mg/kg/day and Phenobarbitone 5 - 10 mg/kg/day. Ursodioxycolic acid 15 mg/kg/day maximum dose of 30 mg/kg/day. UDCA is a hydrophilic dihydroxy bile acid, which is reported to be useful for increasing bile flow, preventing hepatocyte apoptosis, altering bile acid components, and having an immunomodulatory effect. Appropriate antibiotics based on the specific site of infection and culture should be administered to patients with sepsis caused by bacteria. Giving Cholestyramine as a treatment for complications such as pruritus and hyperlipidemia can be given 0.25 - 0.5gr/kg/day with a maximum dose of 8gr/day. Cholestyramine is an anion exchange resin that works by binding to bile acids and preventing their reabsorption, anion exchange resins interfere with the absorption of fat - soluble vitamins. Supplementation of vitamins A, D, and K vitamin A 5000 - 25, 000 IU, vitamin D 0.05 - 0.2 ug/kg/day, vitamin E 15 - 25IU/kg/day is recommended.^{1, 10, 11}

Eventually, this patient was referred to a more complete health facility to get a better examination and treatment. The patient was referred to Sanglah General Hospital Denpasar for investigation and treatment of cholestasis as well as management of pediatric cardiology.

A colorectal carcinoma in situ includes an intraepithelial and an intramucosal carcinoma. They are defined as malignant cells that are confined to the basement membrane (intraepithelial carcinoma) and that have invaded into the mucosal lamina propria and have extended into, but not through, the muscularis mucosae (intramucosal carcinoma). A colorectal carcinoma in situ includes an intraepithelial and an intramucosal carcinoma. They are defined as malignant cells that are confined to the basement membrane (intraepithelial carcinoma) and that have invaded into the mucosal lamina propria and have extended into, but not through, the muscularis mucosae (intramucosal carcinoma).

4. Conclusion

We have presented a case of Cholestasis with Congenital Heart Disease (ASD and PDA) in neonates. Cholestasis in this patient is not only caused by accompanying late - onset sepsis, but can also be caused by the patient's CHD causing systemic disorders, so the cholestasis that occurs in the patient is an intrahepatal process. Finally, the theory that liver disease is the result of CHD is more common than heart disease associated with liver disease is true in these patients.

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