THE SUCCESSFUL ADMINISTRATION OF STEROID IN EXTRAHEPATIC CHOLESTASIS: A CASE REPORT

Anindya Kusuma Winahyu, Rendi Aji Prihaningtyas, Bagus Setyoboedi, Sjamsul Arief

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

ABSTRACT

Biliary atresia is the most common cause of liver transplantation in children. Kasai surgery is still a bridging therapy for biliary atresia, but patients are often late for treatment. Based on the currently proposed theory, biliary atresia results from a progressive inflammatory process and progresses to fibrosis of the bile ducts. A case of a 1.5-month-old boy with prolonged jaundice followed by acholic stools and dark urine was presented. He had cholestasis, elevated GGT levels, and a liver biopsy suggesting extrahepatic cholestasis. He was treated with methylprednisolone, ursodeoxycholic acid, and vitamin supplementation was started orally. After steroid therapy, direct bilirubin levels decreased rapidly to 0.55 mg/dl on day 14. Jaundice, acholic stools, cholestasis, and liver function tests were improved. Therapeutic opportunities based on the pathogenesis of inflammation in biliary atresia using steroids may provide new opportunities for non-surgical management of biliary atresia in the early phase of the disease.

INTRODUCTION

Cholestasis in infants with jaundice is abnormal. The most common cause of cholestasis in infants is biliary atresia (BA). Inflammation is the pathogenesis of biliary atresia, which is currently being developed. The opportunity for drug therapy to suppress the inflammatory process is not widely known for its benefits in biliary atresia.1,2

We reported the presentation of extrahepatic cholestasis jaundice in infants. This case provided an overview of the clinical and diagnostic examination of infants with extrahepatic cholestasis and the opportunity to provide adjuvant therapy.

CASE REPORT

A boy weighing 2500 g, 37 weeks of gestation was born by cesarean section due to pre-eclampsia. Two weeks after birth, the infant had jaundice, acholic stools, and abdominal distension. He was taken to a pediatrician and was given therapy, but the jaundice did not improve. At 1.5 months old, he was referred to a hepatology outpatient clinic due to cholestasis. There was no fever, no
vomiting, the weight gain was poor, and there were no bleeding manifestations. He received exclusive breast milk. Hepatomegaly was observed. Anthropometry measurements showed a body weight of 2.6 kg, length of 51 cm, and head circumference of 33 cm.

Initial laboratory examination showed a white blood cell count (WBC) of $7.3 \times 10^3$/uL, a hemoglobin level (Hb) of 8.5 g/dl, and a platelet count of $325 \times 10^3$/uL. C-reactive protein (CRP) was 0.4 mg/dl. He received a PRC transfusion. The hepatic function test results were normal, with an aspartate aminotransferase (AST) level of 31 IU/L, and alanine amino-transferase (ALT) level of 21 IU/L, the coagulation parameters were normal (Plasma Prothrombin Time (PPT) of 10.9 s (9-12 s), Activated Partial Thromboplastin Time (APTT) of 30.2 s (23-33 s)), albumin of 3.56 mg/dl, total bilirubin (TB) level of 8.04 mg/dl, direct bilirubin (DB) level of 7.06 mg/dl, and Gamma Glutamyl Transferase (GGT) of 478 U/L. IgM and IgG Rubella were non-reactive, IgM anti-Cytomegalovirus (CMV) and Toxoplasma were non-reactive, but IgG anti-CMV and Toxoplasma were reactive, and HbsAg was non-reactive. Thyroid function was normal. Other causes of neonatal cholestasis, such as galactosemia and α1 antitrypsin deficiency, were not evaluated due to limited facilities.

The gallbladder was determined to be in normal size, and ultrasonography failed to detect a triangular cord sign that might indicate biliary atresia. Liver pathology tests showed extrahepatic cholestasis with a few bile pigments and within the bile. Hepatocytes were found with some dilated canaliculi containing bile pigment, and some multinucleated giant cell hepatocytes. There were foci of inflammatory infiltration of lymphocytes and neutrophils between the liver lobules. Hepatic extra nodular foci were also found. No fibrosis was found (Figure 1).

He was treated with methylprednisolone, ursodeoxycholic acid, and vitamin supplementation was started orally. After steroid therapy, direct bilirubin levels decreased rapidly to 0.55 mg/dl on day 14. His cholestasis and acholic stools improved gradually (Figure 2).

![Figure 1](image1.jpg)

Figure 1. (A) Light microscopic images of the liver biopsy specimen; (B) Mason trichrome staining showed no fibrosis; (C) Reticulin staining showed no fibrosis
Successful Administration on Steroid in Extrahepatic Cholestasis

Table 1 shows the time course of the laboratory parameters during the entire observation period and the therapies performed. Evaluation of laboratory results showed a white blood cell count of $6.5 \times 10^3$/uL, a hemoglobin level of 12.8 g/dl, and a platelet count of $318 \times 10^3$/uL. Evaluation of anthropometry measurements showed a body weight of 3.7 kg, a length of 51 cm, and a head circumference of 34 cm. There was a clinical improvement and laboratory value for cholestasis after steroid administration (Figures 3 and 4).

**DISCUSSION**

A case of an infant who experienced prolonged jaundice at the age of more than two weeks, followed by acholic stools and dark urine, was presented. There was no history of significant previous illnesses. The infant was born prematurely. Physical examination revealed jaundice and hepatomegaly. Based on laboratory examination, cholestasis was found, an increase in direct bilirubin levels > 20% of total bilirubin. An abdominal ultrasound examination and liver biopsy were also performed to establish the etiology of cholestasis. In this case, the abdominal ultrasound results showed normal, but the liver biopsy showed extrahepatic cholestasis with no fibrosis.

The sensitivity and specificity of the triangular cord sign in diagnosing biliary atresia were 74% and 97%, respectively. However, this appears to be operator-dependent. A percutaneous liver biopsy can help differentiate BA from other etiologies. Liver biopsy can predict BA with an accuracy of 85-95%, sensitivity (99%), and specificity (92%), which is a valuable tool in the diagnosis of
BA in infants who have normal ultrasound. 

As many as 50% to 99% of patients with BA are correctly identified by liver biopsy. Cholestasis and acholic stools, followed by elevated GGT levels, are more specific markers for extrahepatic BA in infants. In this case, an infant with prolonged jaundice, cholestasis, acholic stools, elevated GGT levels, and liver biopsy results suggested extrahepatic cholestasis. These conditions lead to BA.

The etiology of BA is unknown. However, the theory suggests that BA occurs due to genetic and acquired factors. Currently, the pathogenesis of BA has been widely studied due to the inflammatory process that occurs in the biliary tract, which can be triggered by a virus. Rotavirus, CMV, and reovirus type 3 have been extensively studied as perinatal animal models that produce biliary atresia. Inflammatory and infectious processes are thought to play a role in the pathogenesis of the disease. Immune-related damage to the bile ducts has been suggested to play a role in the development of BA. This is consistent with evidence that as many as 50% of BA patients have colored stools early in life and later become acholic.

In this case, an infant with prolonged jaundice, cholestasis, acholic stools, elevated GGT levels, and liver biopsy results suggest extrahepatic cholestasis. These conditions lead to BA. The patient received steroids based on the pathogenesis of BA due to inflammation. The steroid given was methylprednisolone at 2 mg/kg/day and the dose was tapered-off every week. Therapeutic evaluations, such as clinical and laboratory tests, were performed every two weeks. In addition to steroids, the patient also received ursodeoxycholic acid and vitamins according to the standard therapy. There was improvement in clinical and laboratory results for cholestasis after therapy. New therapeutic options with steroids may provide new hope for preventing fibrosis in BA. Further study is needed to prove the benefit of steroids early in preventing cholestasis progression to BA.

**CONCLUSION**

This case report highlights the potential for steroid therapy in infants with extrahepatic cholestasis and acholic stools who are at risk of developing biliary atresia.

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**CONFLICT OF INTEREST**

All Authors certify that have no involvement in any organization or entity with any financial interest such as educational grants, participation in speakers bureaus membership, employment, consultancies, expert testimony or patent-licensing arrangements or non-financial interest (such as personal or personal or professional relationships, affiliations, knowledge or beliefs in the subject matter discussed in this manuscript).

**PATIENT CONSENT FOR PUBLICATION**

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REFERENCES


15. Kolestaz İ, Tanı :., Ve Prognoz T. Infants with Cholestasis: Diagnosis, Management and Outcome.


