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

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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.

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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 × 10^3/uL, a hemoglobin level (Hb) of 8.5 g/dl, and a platelet count of 325 × 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 methyl-prednisolone, 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).

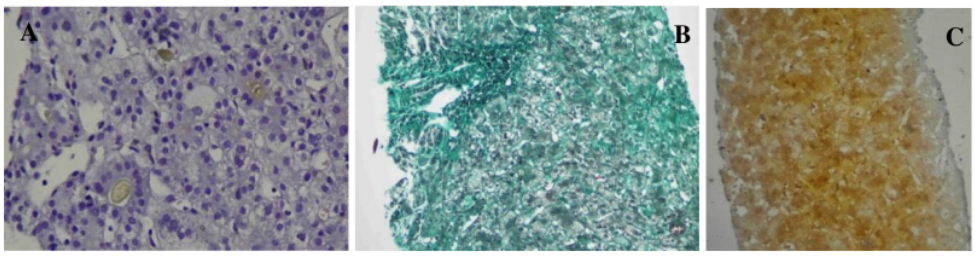

Figure 1. (A) Light microscopic images of the liver biopsy specimen; (B) Mason trichrome staining showed no fibrosis; (C) Reticulin staining showed no fibrosis

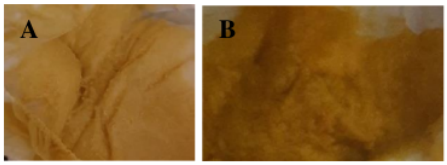

Figure 2. (A) The initial stool looks pale; (B) The stool after 14 days of receiving steroid therapy

Table 1. Time-course of laboratory parameters and therapies performed in the case

Weeks	0	2	4	6
Total bilirubin (mg/dl)	8.04	8.57	6.50	1.56
Direct bilirubin (mg/d)	7.06	7.16	5.20	0.55
AST (U/L)	31	144		78
ALT (U/L)	21	133		86
Therapy	UDCA	UDCA	MP UDCA	MP UDCA

AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; UDCA: Ursodeoxycholic acid, MP: Methylprednisolone

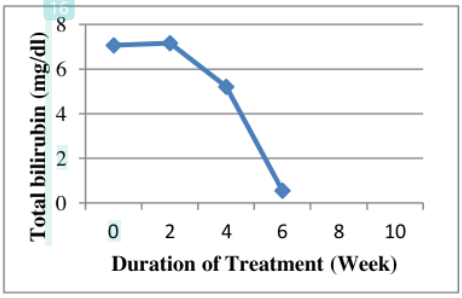

Figure 3. Total bilirubin level during treatment

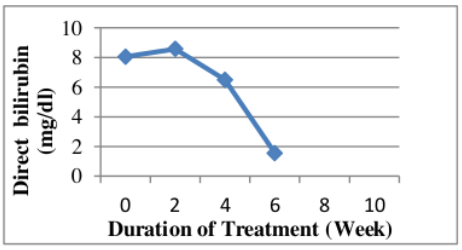

Figure 4. Direct bilirubin level during treatment

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 × 10^3/uL, a hemoglobin level of 12.8 g/dl, and a platelet count of 318 × 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.[3–6] However, this appears to be operator-dependent.[6–9] A percutaneous liver biopsy can help differentiate BA from other etiologies.[10–12] 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 infant who have normal ultrasound. [7,13] As many as 50% to 99% of patients with BA are correctly identified by liver biopsy.[7] Cholestasis and acholic stools, followed by elevated GGT levels, are more specific markers for extrahepatic BA in infants. [11,14,15] 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.[16] 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. [16,17] Immune-related damage to the bile ducts has been suggested to play a role in the development of BA. [18,19] This is consistent with evidence that as many as 50% of BA patients have colored stools early in life and later become acholic. [17,20]

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

Letter of approval for publication was signed by the patient's parent and there is no coercion while signing. Letter of approval attached.

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All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

REFERENCES

1. Di Dato F, Capalbo D, Mirra R, Del Vecchio Blanco F, Salerno M, Iorio R. Case Report: Neonatal Cholestasis as Early Manifestation of Primary Adrenal Insufficiency. Front Pediatr [Internet]. 2021 Nov 11 [cited 2023 Jul 18];9. Available from: /pmc/articles/PMC8632351/
2. Fawaz R, Baumann U, Ekong U, Fischler B, Hadzic N, Mack CL, et al. Guideline for the evaluation of cholestatic jaundice in infants: Joint recommendations of the North American society for pediatric gastroenterology, hepatology, and nutrition and the European society for pediatric gastroenterology, hepatology, and nutrition. J Pediatr Gastroenterol Nutr. 2017;64(1):154–68.
3. Zhou LY, Wang W, Shan QY, Liu BX, Zheng YL, Xu ZF, et al. Optimizing the US Diagnosis of Biliary Atresia with a Modified Triangular Cord Thickness and Gallbladder Classification. Radiology [Internet]. 2015 Oct 1 [cited 2023 Jul 18];277(1):181–91. Available from: https://pubmed.ncbi.nlm.nih.gov/25955579/
4. Ramaswamy PK, Jana M, Sharma R, Kandasamy D, Gupta AK, Bhatnagar V, et al. Novel Scoring Systems and Age-Based Hepatic Shear Wave Stiffness Cut-Offs for Improving Sonographic Diagnosis of Biliary Atresia. Indian J Pediatr [Internet]. 2023 Jun 29 [cited 2023 Jul 18]; Available from: https://pubmed.ncbi.nlm.nih.gov/37380918/
5. Zhou L, Shan Q, Tian W, Wang Z, Liang J, Xie X. Ultrasound for the Diagnosis of Biliary Atresia: A Meta-Analysis. AJR Am J Roentgenol [Internet]. 2016 May 1 [cited 2023 Jul 18];206(5):W73–82. Available from: https://pubmed.ncbi.nlm.nih.gov/27010179/
6. Dong B, Weng Z, Lyu G, Yang X, Wang H. The diagnostic performance of ultrasound elastography for biliary atresia: A meta-analysis. Front Public Health. 2022 Oct 26;10.
7. Moyer V, Freese DK, Whitington PF, Olson AD, Brewer F, Colletti RB, et al. Guideline for the evaluation of cholestatic jaundice in infants: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr [Internet]. 2004 [cited 2023 Jul 18];39(2):925. Available from: https://pubmed.ncbi.nlm.nih.gov/15269615/
8. Lee SM, Cheon JE, Choi YH, Kim WS, Cho HH, Kim IO, et al. Ultrasonographic diagnosis of biliary atresia based on a decision-making tree model. Korean J Radiol. 2015 Nov 1;16(6):1364–72.

9. Yoon H, Lim HJ, Kim J, Lee MJ. [Diagnostic Imaging of Biliary Atresia]. Journal of the Korean Society of Radiology [Internet]. 2022 Sep 1 [cited 2023 Jul 18];83(5):991–1002. Available from: http://www.ncbi.nlm.nih.gov/pubmed/36276203
10. Feldman AG, Sokol RJ. Recent developments in diagnostics and treatment of neonatal cholestasis. Semin Pediatr Surg [Internet]. 2020 Aug 1 [cited 2023 Jul 18];29(4). Available from: https://pubmed.ncbi.nlm.nih.gov/32861449/
11. Feldman AG, Sokol RJ. Neonatal Cholestasis: Updates on Diagnostics, Therapeutics, and Prevention. Neoreviews. 2021 Dec 1;22(12):e819–36.
12. Feldman AG, Sokol RJ. Neonatal cholestasis: emerging molecular diagnostics and potential novel therapeutics. Nat Rev Gastroenterol Hepatol. 2019 Jun 1;16(6):346–60.
13. Hirschfield GM, Beuers U, Corpechot C, Invernizzi P, Jones D, Marzioni M, et al. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol [Internet]. 2017 Jul 1 [cited 2023 Jul 18];67(1):145–72. Available from: https://pubmed.ncbi.nlm.nih.gov/28427765/
14. Urganci N, Çetinkaya F, Kalyoncu D, Çakir EP, Yilmaz B. Infants with cholestasis: Diagnosis, management and outcome. Marmara Medical Journal. 2012;25(2):83–6.
15. Kolestaz İ, Tanı :, Ve Prognoz T. Infants with Cholestasis: Diagnosis, Management and Outcome.
16. Davenport M. Biliary atresia: clinical aspects. Semin Pediatr Surg [Internet]. 2012 Aug [cited 2023 Jul 18];21(3):175–84. Available from: https://pubmed.ncbi.nlm.nih.gov/22800970/
17. Thompson H, Davenport M. Biliary Atresia. Pediatric Surgery: Diagnosis and Management [Internet]. 2023 Jan 8 [cited 2023 Jul 18];1091–9. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537262/
18. Ortiz-Perez A, Donnelly B, Temple H, Tiao G, Bansal R, Mohanty SK. Innate Immunity and Pathogenesis of Biliary Atresia. Vol. 11, Frontiers in Immunology. Frontiers Media S.A.; 2020.
19. Feldman AG, Mack CL. Biliary atresia: Cellular dynamics and immune dysregulation. Semin Pediatr Surg. 2012 Aug;21(3):192–200.
20. Patel KR. Biliary atresia and its mimics. Diagn Histopathol. 2023 Jan 1;29(1):52–66.

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