CASE REPORT

Transient Neonatal Cholestasis Secondary to Coagulase-negative Staphylococci Septicemia: A Case Report

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Abstract

Transient neonatal cholestasis (NC) is characterized by early-onset cholestasis and normalization of clinical and biochemical parameters at follow-up. The causes are multifactorial and include immature bile secretion (as in the case of prematurity) and other perinatal causes. Sepsis is responsible for 20% of cases of NC. It is mandatory to rule out other causes of NC before labeling the neonate as having transient NC. The use of ursodeoxycholic acid in cholestasis has been advocated to bring a faster decline in direct bilirubin levels in neonates. Neonates have to be evaluated early considering associated risk factors so that early intervention could prevent complications and yield better outcomes.

Keywords: Sepsis, Transient neonatal cholestasis, Ursodeoxycholic acid.

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Introduction

Neonatal cholestasis (NC) is defined as conjugated hyperbilirubinemia occurring in the newborn as a consequence of diminished bile flow. Conjugated hyperbilirubinemia is defined as a serum direct/conjugated bilirubin ≥1 mg/dL [when the total serum bilirubin (TSB) is <5.0 mg/dL] or >20% of TSB (when TSB >5.0 mg/dL) detected in a newborn.[1]

In the twenty-first century, NC remains a major clinical challenge for several reasons. Recognition of NC among jaundiced neonates is delayed in a significant number of cases; often due to the lack of awareness among healthcare professionals.[2] The diagnosis of NC is challenging due to the great diversity of underlying entities. Some of them have specific treatment and that must be offered in a timely manner to improve prognosis. Transient NC is associated with several contributing factors and the first priority is to recognize conditions requiring immediate treatment, as the timing of diagnosis is directly related to the outcome.[3-5]

Case Description

A term male neonate was born through vaginal route to a G2P1L1 mother with a birth weight of 2,755 g. There was no ABO/Rh incompatibility (both mother and child O Rh-positive) nor any history of maternal illness. Neonate had respiratory distress which resolved at 5 hours of life. He was started on breast milk feeding.

Day 1

On examination, the baby had a normal cry, tone, and activity. There were no dysmorphic features. Icterus was seen till umbilicus at 15 hours of life. On examination of the abdomen, palpable liver with a span of 7 cm, soft in consistency with smooth surface and regular margins was noticed. The spleen was not palpable. Other systems were normal on examination.

Investigations revealed TSB of 7.8 mg/dL, direct bilirubin of 1.8 mg/dL (23% of TSB), C-reactive protein-3.9 mg/L, direct Coombs test-negative, Hb-12.5 g/dL, total leukocyte count-9,800 cells/mm^3 with 64% neutrophils and 29% lymphocytes, platelet count-1.09 lakhs/µL, and reticulocyte count-8%. Peripheral smear revealed no features suggestive of hemolysis. Blood was drawn for culture and sensitivity and empirical ampicillin was started.

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Day 2 to 6

The baby remained euglycemic throughout, passing normal colored urine and stools. Stool color was monitored daily using a stool card.

Bilirubin levels were monitored daily which revealed a gradual increase in direct bilirubin and GGT levels as shown in Table 1. There was a gradual decrease in Hb levels as shown in Table 2. Thyroid and coagulation profiles were normal. USG abdomen showed hepatic and splenic span at the upper limit, contracted gall-bladder, normal CBD, and portal vein. The α-fetoprotein level was normal (>2,000 ng/mL). Serum ferritin and LDH were elevated (>2,000 ng/mL and 750 U/L, respectively). Urine for reducing substance– negative. The urine sample was sent for IEM workup using GCMS. Ocular examination revealed no abnormalities. Blood culture grew coagulase-negative staphylococci, which was resistant to ampicillin and sensitive to piperacillin/tazobactam. Hence, the antibiotic was changed to piperacillin/tazobactam and continued. CSF analysis was normal. Neonate was started on ursodeoxycholic acid (UDCA) on 6 DOL at a dose of 20 mg/kg/day in divided doses along with fat-soluble vitamins and other nutritional supplementation.[6]

Table 1: Liver function tests (LFT) results

Parameter	*15 hours of life*	*3rd day of life*	*5th day of life*	*10th day of life*	*17th day of life*	*24th day of life*
TSB (mg/dL)	7.8	7.8	7	2.5	1.7	0.8
D.bilirubin (mg/dL)	1.8	2.6	3	1	0.6	0.4
SGOT (U/L)	80	76	47	42	29	36
SGPT (U/L)	26	24	24	30	18	18
T.protein (g/dL)	5.2	5.3	4.8	5.1	5	5.1
S.albumin (g/dL)	3.3	3.4	2.7	3	3	3.4
ALP (U/L)	139	134	132	224	223	315
GGT (U/L)	324	470	508	652	336	140

Table 2: Complete blood picture results

Parameter	*15 hours of life*	*2nd day of life*	*3rd day of life*	*10th day of life*	*11th day of life*	*14th day of life*	*24th day of life*
Hb (g/dL)	12.5	12.5	12	9.2	9.7	10.4	12.5
WBC (cells/mm^3)	9,800	9,000	11,000	14,400	18,700	16,000	14,200
Neutrophil/ lymphocyte	64/29	60/36	50/46	32/57	26/66	26/69	25/67
Hematocrit (%)	35.7	35.6	27.1	28.1	29	31	38
Platelet count (lakhs/µL)	1.09	1.5	1.8	2.9	3.1	4.3	4.45
Reticulocyte count (%)	8	6	5	3	2	2	1

Day 7 to 14

The child continued to thrive well on breastfeeds. Icterus gradually decreased. Hb levels did not drop further. Total and direct bilirubin levels decreased gradually while GGT remained high (Tables 1 and 2). The child received piperacillin/tazobactam for 10 days and stopped. Ursodeoxycholic acid was continued (GGT levels still remained high). The child was discharged on 14 days of life and advised follow-up.

The child was brought for follow-up on day 17 and day 24. The child was accepting breastfeeds, thriving well with decreased GGT levels.

Discussion

Transient NC represents a group of intrahepatic cholestatic disorders in infancy with poorly understood pathogenesis. The onset of abnormalities is early in most cases but usually resolves within 2–3 months after sepsis.[7] It is characterized by the onset of cholestasis in the first week of life along with elevation of biochemical parameters of liver injury.[8] Associated risk factors for transient NC include SGA, IUGR, sepsis, asphyxia, prematurity, prolonged parenteral nutrition, NEC, hypoglycemia, and preeclampsia in mother.[9]

Sepsis is responsible for 20% of cases of NC.[10] Infections cause a systemic and intrahepatic increase in proinflammatory cytokines which result in impaired bile flow.[11] Hepatobiliary dysfunction in the form of cholestatic jaundice or elevated liver enzymes has been reported in more than two-thirds of preterm neonates experiencing neonatal sepsis.[12] The transient nature of the cholestasis in infants with transient NC has been linked to heterozygosity of mutations in genes involved in bile transport (*ATP8B1*, *ABCB11*, and *ABCB4*).[13]

Ursodeoxycholic acid was hypothesized in bringing levels of direct bilirubin, a surrogate marker for hepatic cholestasis. Studies showed UDCA as a better choice of treatment than phenobarbital for NC.[14,15] Ursodeoxycholic acid protects injured cholangiocytes against the toxic effects of bile acids and stimulates bile acid secretion via calcium-dependent mechanisms. Additionally, it directly modulates transcription of transporters and inhibits bile-acid-induced hepatocyte apoptosis.[16]

Conclusion

Sepsis is one of the important causes of transient NC. In our case, the child was diagnosed to have sepsis and treated with culture-sensitive antibiotics and UDCA which showed a response with decreased bilirubin and GGT levels.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity but anonymity cannot be guaranteed.

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