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Rainbow of colors: Inspissated bile syndrome secondary to hemolytic disease of the newborn and concomitant serum dynamics

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Abstract

The recent clinical experience with hemolytic disease of the newborn and its post-icteric sequelae is limited among high-income countries because of nearly over four decades of effective prevention care. In this case, we will discuss the sequelae of a baby born with hemolytic disease of the newborn to an Rh negative mother with no prenatal care from remote northern Saskatchewan. Inspissated bile syndrome is a rare but serious complication of hemolytic disease of the newborn. The concentration of hemolytic products parallels with serum color changes.

Keywords

Inspissated bile syndrome, hemolytic disease of the newborn, serum dynamics, biliary sludge

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Introduction

The recent clinical experience with hemolytic disease of the newborn (HDN) and its post-icteric sequelae is limited among high-income countries because of many decades of effective prevention care.[1] HDN may cause diffuse hepatocellular damage and alter bile kinetics. Inspissated bile syndrome (IBS) is a rare but serious complication of HDN with incidence of 1 in 175,000 live births.[2] In this case report, we present a case of IBS in a term infant with HDN and describe parallel serum dynamics.

Case report

The mother of the patient is a 33-year-old O-negative woman. Her past obstetrical history was remarkable for two spontaneous abortions due to alloimmunization and hydrops. Among her seven living children, one required exchange transfusion therapy as a newborn. During the current pregnancy, she had no prenatal care. The first prenatal ultrasound was done on admission to the obstetric ward and showed signs of progressing hydrops (cardiomegaly, pericardial and pleural effusion, ascites), thus, emergency cesarean section was performed. A male infant, approximately 34 weeks of gestation, was delivered with the Apgar's 2, 5, and 6 on 1st, 5th, and 10th minutes, respectively. He was markedly pale and mottled; his cord hemoglobin and bilirubin were 16 g/L and 79 umol/L, respectively. He required double volume exchange transfusion, two doses of IVIG, and intensive phototherapy for ongoing hemolysis and hyperbilirubinemia. In spite of these interventions, the jaundice persisted, and after first week of life, the direct bilirubin surpassed the indirect. An unusual color of serum was noted simultaneously with progression of cholestasis (Figure 1(a)), and these findings correlated with the degree of hemolysis and levels of direct bilirubin (Figure 1(b)).

Final diagnosis

IBS secondary to HDN.

Hospital course

The patient was born to the mother with a history of previous miscarriages due to alloimmunization; thus, he was profoundly anemic at birth. He has a blood group type of

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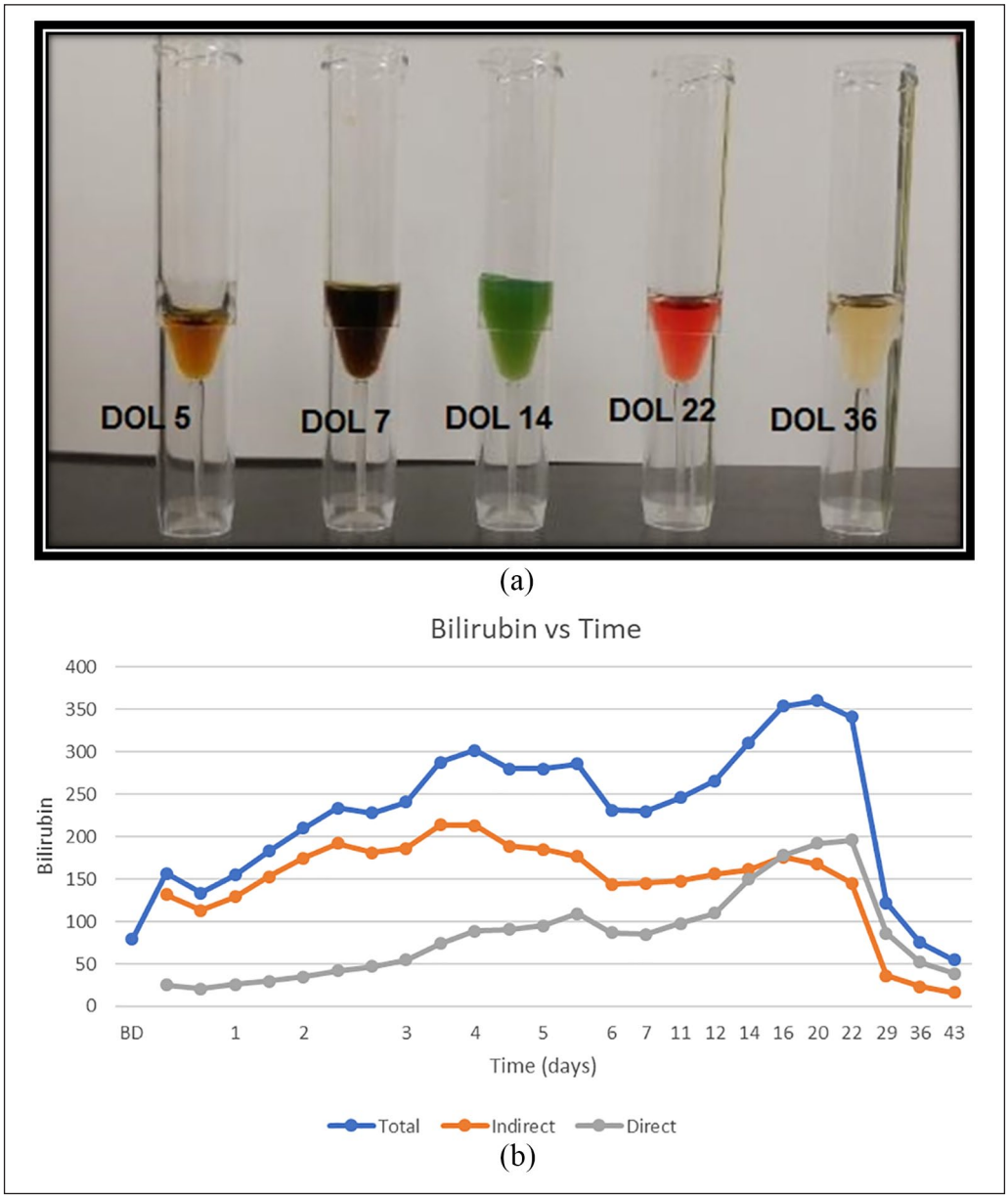

Figure 1. (a) Serum color during clinical course (DOL: day of life). (b) Bilirubin dynamics during clinical course (BD: birth day).

O-positive, and his Direct Antibody Test (DAT) was positive (+++) with high titer of anti-D antibodies (1:32). Maternal obstetrical history, clinical presentation, and laboratory data were suggestive of HDN that was managed with intensive phototherapy, double volume exchange transfusion on day of life (DOL) 1 and repeated infusions of IVIG on DOL 1, 3, and 4. Despite adequate treatment, both the direct and indirect components of bilirubin continued to rise with the direct component surpassing the indirect by DOL 16. An abdominal ultrasound was done at DOL 20 which showed dilated common hepatic and common bile ducts with a fluid-debris level (biliary sludge) suggestive of IBS (Figure 2). After initiation of ursodeoxycholic acid (UCDA), jaundice improved, and total and direct bilirubin levels were normalized.

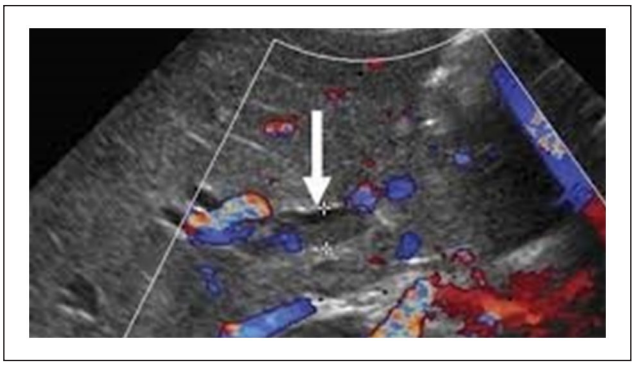

Figure 2. Abdominal ultrasound at day of life 20: biliary sludge in dilated common bile ductus (arrow).

Table 1. Laboratory results during clinical course.

	DOL 2	DOL 5	DOL 7	DOL 14	DOL 22	DOL 36
AST, u/L	344			49		38
ALT, u/L	54			13		16
Haptoglobin, mg/dL			0.3	1.8		14.1
Methhemoglobin, %		0.6		0.8	0.2	

DOL: day of life.

Serum color was changing simultaneously with progression and resolution of hemolysis from dark yellow due to bilirubin staining to black when haptoglobin levels dropped more than 90%, with subsequent color changes to green (haptoglobin decreased less than 50%) and red (normal haptoglobin, porphyrins concentration > 25%). Methhemoglobin levels remained normal during all hospital course (0.2%–0.8%). Normal serum color was noted after normalization of hematological parameters on DOL 36. Liver function tests (alanine aminotransferase and aspartate aminotransferase) were initially elevated with subsequent normalization at third week of life (Table 1). Newborn metabolic screening was reported as normal.

Clinical management was successful, and infant was discharged home in a stable condition on DOL 37.

Discussion

The clinical experience with HDN and its post-icteric sequelae is currently limited among high-income countries because of nearly over four decades of effective prevention care.[1] IBS is a rare but serious complication of HDN.[2] Concentrations of hemolytic products parallel serum color changes. Literature describes dark brown serum in patients with methemoglobinemia or hemolysis.[3,4] Methemoglobinemia in these cases is explained by change of hemoglobin iron from ferrous (Fe2+) into ferric (Fe3+) form. Dukic et al.[5] explained dark serum coloration in patient with intravascular hemolysis by presence of oxidized free heme bound to albumin (methemalbumin). Our patient had normal methhemoglobin levels; methemalbumin measurements were not available in our hospital.

Direct hyperbilirubinemia in the neonate is a well-known phenomenon with a differential diagnosis including biliary atresia, choledochal cysts, Cystic Fibrosis, Alagille syndrome, and various metabolic diseases. IBS is an uncommon cause of direct hyperbilirubinemia and as such, experience is limited in its diagnosis and treatment. It is postulated that predisposing factors for the IBS in neonates usually include prematurity, sepsis, parenteral nutrition, and use of diuretics.[6] In the current case, several predisposing factors (hemolysis, prematurity, suspected sepsis) were present. This case illustrates that exaggerated hemolysis secondary to HDN can also lead to bilirubin overload and trigger cholestasis. The excess of bilirubin densifies as calcium bilirubinate sludge in bile ducts and causes inspissated bile duct syndrome. The diagnosis is made simply by ultrasound of the biliary tract. Classical findings on ultrasound are low level echos at biliary ducts.[7] The pathogenesis of the sludge is similar to gallstones.[8] This case stresses the value of non-invasive abdominal imaging when a cholestatic component compounding hyperbilirubinemia is suspected, because biliary sludge can be identified well in an ultrasound.

In the literature, treatment for IBS ranges from hydration to ultrasound-guided percutaneous cholecystostomy drain catheter placement to physically drain the sludge.[8] With the physiology of IBS in mind, we can understand that the non-invasive treatment options of adequate hydration and UCDA are quite attractive. UCDA protects cholangiocytes against cytotoxicity of hydrophobic bile acids, stimulates hepatobiliary secretion, and protects hepatocytes against bile acid-induced apoptosis. Our case further illustrates that UCDA is an effective treatment consideration for IBS.

Conclusion

IBS secondary to HDN accounts for 8% of all types of surgical jaundice during infancy. In some cases, IBS has been reported to resolve with ursodeoxycholic acid (UDCA) treatment. Concomitant serum changes before and during therapy of IBS could provide additional visual information about intensity of hemolysis.

Declaration of conflicting interests

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Ethical approval

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Informed consent

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