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Case Report

A 6-DAY-OLD NEWBORN WITH VOMITING AND JAUNDICE

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Abstract: Sixty percent of term neonates and 80% of preterms have jaundice within the first week of life. Jaundice can be pathologic or physiologic, indirect, or direct. Indirect jaundice can be neurotoxic at high levels. In its most severe form, this presents as acute bilirubin encephalopathy or kernicterus. Screening for jaundice using a transcutaneous bilirubin check or serum bilirubin has contributed tremendously to the reduction of kernicterus, which ranges from 0.5-1.3/100,000 births. Often, the etiology is easy to decipher. Otherwise, it may be complicated when there are several factors contributing. We present a case of a 6-day-old with jaundice and vomiting who was suffering from intestinal malrotation and a urinary tract infection.

Keywords: jaundice, hyperbilirubinemia, pediatrics, urinary tract infection, malrotation

INTRODUCTION Sixty percent of term neonates and 80% of preterms have jaundice within the first week of life [1]. Jaundice can be pathologic or physiologic, indirect, or direct. Physiologically, the newborn red blood cells have a lifespan of 90 days compared to 120 days in adults. Bilirubin is produced when red blood cells are degraded. Circulating bilirubin is bound to albumin in its unconjugated form and transported to the liver. In the liver, the enzyme uridine diphosphogluconurate glucuronosyltransferase (UGT1A1) conjugates bilirubin. This system is relatively immature in the newborn, which can lead to jaundice. Due to the paucity of intestinal bacterial flora and increased beta-glucuronidase enzyme activity in the newborn, conjugated bilirubin becomes unconjugated by beta-glucuronidase in the gut mucosa and is reabsorbed. This is known as enterohepatic circulation [2]. Situations that could enhance enterohepatic circulation include impaired intestinal motility, breastfeeding failure, and breastmilk-induced recirculation. Any retained unconjugated bilirubin in the gut is excreted as stercobilin in the stool or urobilinogen in urine.

Jaundice in the physiological sense is not harmful *per se*; however, it can cause neurotoxicity at high levels. This occurs in the form of acute bilirubin encephalopathy or kernicterus. Pathologic jaundice warrants immediate intervention once etiology is detected. Pathologic causes of indirect hyperbilirubinemia include red blood cell enzyme or membrane defects, isoimmune-mediated hemolysis, sequestration of blood within a closed space (cephalohematoma, subdural hematoma, subgaleal hematoma, adrenal hemorrhage), trauma/excessive bruising, genetic syndromes that affect UGT1A1 (Crigler-Najjar, Gilbert), organic anion transporting polypeptides-2 polymorphism, and sepsis. Direct hyperbilirubinemia is always pathologic. Causes include obstructive liver diseases (biliary atresia, choledochal cysts), genetic syndromes (Dubin-Johnson), hypothyroidism, galacto-semia, and panhypopituitarism. Screening for jaundice using a transcutaneous bilirubin check or serum bilirubin has contributed tremendously to reduced incidence of kernicterus, which ranges from 0.5-1.3/100,000 births [3].

We present a case of a 6-day-old newborn with jaundice and vomiting.

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CASE PRESENTATION A 6-day-old late preterm male infant with feeding intolerance, recurrent vomiting, and jaundice since day of life (DOL) 4 was transferred to our hospital from a community hospital.

All infectious screenings in pregnancy were negative. Patient was born at 36 weeks and two days via normal spontaneous vaginal delivery with no complications. Birth weight was appropriate for gestational age at 3130 g. His Apgar scores were 8 and 8 at 1 and 5 minutes, respectively. Blood type for both mother and infant were O+. At DOL 3, when he was discharged home, direct antibodies test was negative. His total bilirubin was 7.2 mg/dL and direct bilirubin was 0 mg/dL. Family history was negative for galactosemia, tyrosinemia, cystic fibrosis, hereditary spherocytosis, glucose-6-phosphate dehydrogenase deficiency, and pyruvate kinase deficiency. The patient was living with his mother and her boyfriend.

On DOL 5, the parents returned to the community hospital and reported that the infant had recurrent vomiting following each feeding. In an effort to ameliorate emesis, the parents switched from a 'soy-based' formula to a 'partially-hydrolyzed protein' formula based on an assumption that his emesis may have been due to milk-protein allergy, but he continued to have recurrent emesis. The vomitus was initially bright yellow and progressed to recurrent episodes of dark green emesis. The patient remained afebrile and active, but irritable. His parents also observed that he had fewer wet diapers than expected and one bowel movement that was described as *hard balls*.

On DOL 5, his total bilirubin was 21.8 mg/dL and his direct bilirubin was 1.9 mg/dL. The patient received phototherapy for about 6 hours. Repeat levels showed his total bilirubin was mildly decreased at 20.3 mg/dL and direct bilirubin was 2.7 mg/dL. Plain abdominal radiographs showed non-specific bowel gas patterns with little gas in the intestine and mild gaseous distention of the stomach with no pneumatosis, portal venous gas, or free air.

On DOL 6 the patient was transferred to our regional center for further management due to persisting emesis and increasing jaundice levels despite phototherapy. On admission, his vital signs were within normal limits, and he was on room air. Physical exam was significant for soft, mildly distended abdomen with hyperactive bowel sounds and no hepatosplenomegaly. Jaundice was noted to the face, chest, and abdomen. He was uncircumcised. He had no rash or dysmorphic features. He was neurologically intact. All other systems were within normal limits.

On admission, he was placed *nil per os* and began on intravenous fluids. He had one more emesis during this time, and we confirmed it was bilious in nature. His white blood cell count was 7.9 $x10^9$/L, reticulocyte count was a 0.02 fraction of red blood cells, and his mean corpuscular volume was slightly elevated at 108 fL. A comprehensive metabolic profile was unremarkable except for metabolic alkalosis with a bicarbonate of 31 mmol/L, total bilirubin of 18.84 mg/dL, direct bilirubin of 1.63 mg/dL, gamma-glutamyl transferase of 200 units/mL, and alkaline phosphatase of 140 units/L. His c-reactive protein level was 1.22 mg/L. Thyroid panel and peripheral blood smear were within normal limits. Urinalysis showed 2+ leukocyte esterase and was negative for nitrites. Urine culture grew a colony count of >100,000 colony forming units/mL *Escherichia coli*. Blood culture remained negative. Due to the persisting bilious emesis, a stat upper gastrointestinal x-ray was performed which showed a markedly distended stomach with high-grade obstruction at the level of the transverse portion of the duodenum. These findings were suggestive of the presence of malrotation with volvulus or partial small bowel atresia.

DIAGNOSES AND DIFFERENTIALS The patient was diagnosed with indirect hyperbilirubinemia secondary to both ongoing urinary tract infection (UTI) and volvulus secondary to malrotation. He was started on cefazolin as pre-operative prophylaxis and had an emergent exploratory laparotomy which showed malrotation with the duodenum on the right. There was no ischemic bowel. He underwent a Ladd's procedure.

Graduated feeding was initiated on DOL 10. He tolerated these feeds with complete resolution of his emesis. Patient received at total of 2 days of double phototherapy with a drop in his total bilirubin to 10.88 mg/dL and direct bilirubin of 0.77 mg/dL. His UTI was sensitive to cefazolin, which was continued for a total of 5 days. He was switched to oral cephalexin with confirmed sensitivities and when oral intake had returned to normal on DOL 12. He was discharged home on DOL 14.

Other differentials which were considered included sepsis, hypothyroidism, other causes of intestinal obstruction

such as intestinal atresia, inborn errors of metabolism (including congenital adrenal hyperplasia), hepatobiliary disorders such as biliary atresia, red blood cell disorders, and alloimmune hemolytic disorders of the newborn.

DISCUSSION According to a recommendation of the American Academy of Pediatrics, investigation of jaundice should include maternal and infant blood grouping, Rhesus typing, direct Coombs testing, and total serum bilirubin level. If the infant has an elevated direct bilirubin, a urinalysis is required to rule out a UTI [4]. On the contrary, a study by Abourazzak *et al*. revealed a predominance of indirect bilirubin in the presence of UTI, suggesting the need for a high index of suspicion for UTI for indirect or direct hyperbilirubinemia cases [5]. The incidence of UTI in prolonged jaundice ranges between 0.2-16% [1,6-8]. The most common pathogens involved in UTI with jaundice are *Klebsiella pneumoniae*, *Enterobacter*, *Escherichia coli*, and *Serratia*. The highest occurrence was in males [1,8-9]. The pathophysiologic relationship between hyperbilirubinemia and UTI is not entirely understood. Özcan *et al*. mentioned the potential for increased hemolysis associated with gram-negative bacteria [8]. Conjugated hyperbilirubinemia with UTI could stem from hepatic microcirculation's immaturity and direct bacterial and endotoxin-mediated products, leading to cholestasis [10].

Bilious emesis in a newborn or infant should warrant an immediate investigation for intestinal obstruction. Any delay in diagnosis increases morbidity and mortality. Intestinal malrotation occurs due to failure of the typical sequence of rotation and fixation of the bowels. The incidence is about 1 in 2,500 live-born infants under 1 year of age [11]. Up to 80% of affected infants present in their first month of life [12]. Cardinal symptoms of intestinal obstruction in infants are bilious emesis, abdominal distension, increased bowel sounds, constipation, or obstipation [13]. Due to an increase in enterohepatic circulation, prolonged jaundice could be an additional finding [14]. Intestinal malrotation is an often-missed diagnosis, with a report by Shalaby *et al*. stating that as many as 72% of infants have symptoms for more than 24 hours, most of which had a prior evaluation in a medical facility. Parents and many health care professionals often do not appreciate the importance of true green emesis [12]. An upper gastrointestinal series with contrast, which has a sensitivity of up to 96% [13] is the best test for diagnosis. Emergent resuscitation, nasogastric tube decompression, and immediate pediatric surgery referral for a Ladd's procedure is the treatment of choice.

Our index case had two etiologies contributing to his jaundice: malrotation, which was life-threatening, and a UTI, which could lead to sepsis and become equally life-threatening. As clinicians, it is easy to identify jaundice in the newborn, and teasing out the underlying etiology may be simple. However, in situations where multiple conditions are present, as in our case, it may be easy to miss an etiology and reduce the recovery chances.

CONCLUSION Jaundice is a common finding in neonates. Most etiologies are easily identified and treatable. However, this case reinforces the reality that finding one etiology should not rule out any additional underlying causes, some of which, unfortunately, could result in poor outcomes.

DISCLOSURES: No animal or human studies were carried out by the authors for this manuscript.

PROTOCOL: IRB approval was not needed for case report per institutional guidelines.

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