A Case Report of Kernicterus in a Neonate with Hemolytic Disease of Newborn—Lessons to Learn

Maria F. Saavedra, MD, & Praveen Kumar, MBBS, DCH, MD

KEY WORDS
Bilirubin-induced neurologic dysfunction, hemolytic disease of newborn, kernicterus, neonatal hyperbilirubinemia

INTRODUCTION

Neonatal jaundice is a common but usually benign finding in most newborns. Bilirubin at high levels may lead to bilirubin encephalopathy (BE) and kernicterus (Watchko & Tiribelli, 2013). The term *kernicterus* was initially used to describe a characteristic pattern of central yellow staining in the brain of neonates at autopsy with severe hyperbilirubinemia, defined variably as either 25 mg/dl or greater or 30 mg/dl or greater (American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia, 2004; Johnson & Bhutani, 2011; Wusthoff & Loe, 2015). Kernicterus is the clinical diagnosis for neonates with chronic BE and its sequelae including motor and cognitive delay and auditory and visual abnormalities (Watchko & Tiribelli, 2013).

Kernicterus is preventable and considered a "never event" by the Agency for Healthcare Research and Quality and the Joint Commission but continues to occur in the United States and other developed countries (Bhutani et al., 2013; Wu et al., 2015). Although the true incidence of kernicterus is difficult to establish because of lack of mandatory reporting requirements, it is estimated to range from 0.4 to 2.7 cases per 100,000 live births among term and late preterm neonates in North America and Europe (Bhutani et al., 2013; Greco et al., 2016; Wu et al., 2015). We report a case of a neonate with severe hyperbilirubinemia secondary to hemolytic disease of the newborn (HDN) who developed kernicterus.

CASE PRESENTATION

A female neonate was born at 36 weeks 4 days gestation via cesarean to a 31-year-old Gravida 2, Para 2 Caucasian woman. All prenatal serology results were negative. Birth weight was 3,050 g, and Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The pregnancy was complicated by antigen E alloimmunization. An anti-E antibody titer result at 30 weeks gestational age was 1:8 (should be absent in pregnancies with no antigen E incompatibility) and peaked at 1:16 by 33 weeks. The pregnancy was monitored by weekly ultrasonography from 30 to 34 weeks. Fetal growth was normal with no signs of hydrops, and the middle cerebral artery peak systolic velocities (PSVs) were reported to be normal except at 32 weeks gestation, when multiple of the median was 1.52 (normal

Maria F. Saavedra, Resident, Internal Medicine and Pediatric Residency program, OSF Medical Center, Children's Hospital of Illinois, Peoria, IL.

Praveen Kumar, Visiting Professor of Pediatrics, Associate Head, Department of Pediatrics, OSF Medical Center, Children's Hospital of Illinois, Peoria, IL.

Conflicts of interest: None to report.

Correspondence: Praveen Kumar, MBBS, DCH, MD, Department of Pediatrics, Children's Hospital of Illinois, 530 NE Glen Oak Ave, Peoria, IL 61637; e-mail: Praveen.Kumar@osfhealthcare.org

J Pediatr Health Care. (2018) *32*, 411-415.

0891-5245/$36.00

https://doi.org/10.1016/j.pedhc.2018.03.007

≤ 1.50). PSV in the middle cerebral artery has been used to identify fetuses with moderate to severe anemia. This increase in PSV is related to an increase in cardiac output to meet the oxygen needs of the tissues and decreased blood viscosity as a result of anemia.

The neonate was born at a community hospital near the family's home. She was noted to have jaundice on Day 1 of life, with a peak total serum bilirubin concentration of 12.8 mg/dl. She received phototherapy for about 24 hours. According to the parents, the infant's predischarge total serum bilirubin concentration at 2 days of life was 11.5 mg/dl. The details of workup during this hospitalization were not available. Follow up by the pediatrician on Day 3 of life indicated moderate jaundice. Arrangements were made for follow up in 1 week.

Over the course of the following 2 days, parents noticed her to be lethargic with worsening jaundice and poor oral intake. The neonate was seen in an emergency department and was noted to have a total serum bilirubin concentration of 32.9 mg/dl. She was transferred to a Level IV neonatal intensive care unit at a regional children's hospital for further management and received intensive phototherapy during transport.

The admission examination showed severe jaundice, opisthotonus, high-pitched cry, generalized hypertonia, and periodic breathing with apnea. The infant's admission total and direct serum bilirubin concentrations were 38.5 and 0.8 mg/dl, respectively. Her blood group was AB positive, and a direct Coombs test result was positive for anti-E antibodies, suggesting presence of HDN due to antigen E incompatibility. Basic metabolic panel, serum ammonia, hepatic function panel, and lactic acid results were unremarkable, and her workup for infection was negative.

The infant continued to have apnea after admission, which correlated with seizure activity on video electroencephalogram, which was treated with antiepileptic medications. Her hyperbilirubinemia resolved with intensive phototherapy, intravenous immunoglobulin, and a double volume exchange transfusion. Her total serum bilirubin concentration at the time of discharge was 6.7 mg/dl. A brain magnetic resonance imaging scan on Day 14 of life showed symmetric abnormal hyperintense signal on T1-weighted sequences in the globus pallidus and subthalamic nuclei, two of the primary sites of bilirubin deposition in the brain. These findings were consistent with the diagnosis of kernicterus. She failed a hearing screen bilaterally.

CASE DISCUSSION

About 85% of healthy late preterm and term newborns have elevated unconjugated bilirubin and jaundice during the first week of life (Watchko & Tiribelli, 2013). In most of these neonates, jaundice is physiologic and resolves without any intervention or adverse effects. However, it can progress to severe hyperbilirubinemia (defined variably as either ≥ 25 mg/dl or ≥ 30 mg/dl) and may result in neurotoxicity (American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia, 2004; Johnson & Bhutani, 2011; Wu et al., 2015; Wusthoff & Loe, 2015). Large population-based studies estimate that the incidences of severe hyperbilirubinemia in developed countries such as the United States is 31 to 45 per 100,000 live births. However, the incidences of BE and kernicterus are much lower and are reported to be in the range of 0.6 to 3.7 and 0.4 to 2.7 per 100,000 live births, respectively (American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia, 2004; Bhutani et al., 2013; Greco et al., 2016; Wusthoff & Loe, 2015). Globally, BE is one of the most important preventable causes of neonatal mortality and brain injury (Bhutani et al., 2013; Greco et al., 2016).

In most neonates, jaundice is physiologic and resolves without any intervention or adverse effects.

Early stages of acute BE (ABE) are characterized by nonspecific symptoms such as lethargy, decreased activity, and poor feeding (Johnson & Bhutani, 2011; Perlman & Volpe, 2018). Prompt interventions at this stage may result in full recovery. If serum bilirubin levels continue to rise, the neonate develops hypertonia, retrocollis, opisthotonus, shrill cry, and apnea. Onset of clinical findings of late stages of ABE suggest a high probability of sequelae, even with intensive treatment (Johnson & Bhutani, 2011; Perlman & Volpe, 2018). Although death and kernicterus are the two most serious adverse outcomes of hyperbilirubinemia, it is suggested that less severe hyperbilirubinemia can result in milder degrees of brain injury that usually go unnoticed and unreported (Perlman & Volpe, 2018).

The characteristic sequelae in a patient with kernicterus include dystonia, athetoid cerebral palsy, sensorineural hearing impairment, upward gaze paralysis, and abnormal teeth enamel. Athetoid cerebral palsy, also referred to as dyskinetic cerebral palsy, is characterized by inability to control muscle tone and maintain symmetric posture. Affected patients have involuntary writhing movements of either a part of the body or the entire body and usually appear at 18 to 24 months of age but manifest later in childhood. Hearing impairment is one of the most common findings in these children, and it is due to the injury to cochlear nuclei and auditory pathways. Hearing loss is usually most prominent in high frequencies and can range from mild to severe. Although upward gaze paralysis is the most common visual abnormality in these neonates, other gaze abnormalities and ocular palsies leading to strabismus can also be seen. Hypoplasia of