MR Findings in Kernicterus

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Summary: We describe the MR appearance of kernicterus (bilirubin encephalopathy). T2-weighted images show high signal bilaterally in the globus pallidus, a known area of cerebral deposition of bilirubin.

Index terms: Brain, diseases; Brain, metabolism; Infants, diseases

Kernicterus is a neurologic condition in the neonate characterized by cerebral deposition of unconjugated bilirubin (1). Also known as bilirubin encephalopathy, it is a rare complication of infantile hyperbilirubinemia resulting from preferential deposition of bilirubin in the globus pallidus, subthalamic nuclei, hippocampus, putamen, thalamus, and cranial nerve nuclei (especially III, IV, and VI) (2). We report the magnetic resonance (MR) findings in a neonate with clinical and laboratory evidence of bilirubin encephalopathy.

Case Report

A term neonate (uncomplicated spontaneous vaginal delivery, Apgar score of 9 at 1 and 5 minutes) was seen at 8 days of age with irritability, severe jaundice, and opisthotonus. Total bilirubin level was 49.4 mg/dL. Two immediate exchange transfusions reduced the total bilirubin to 26 mg/dL. By 13 days old, the bilirubin level had dropped to 6.3 mg/dL. The cause of the encephalopathic hyperbilirubinemia is unknown, but was presumed to be hemolytic in nature.

Because of the increased risk of hearing loss in infants with hyperbilirubinemia, a brain-stem evoked response examination was performed. This examination was consistent with bilateral severe sensorineural hearing loss. The question of possible brain-stem injury was also raised. An MR examination was obtained at 18 days of age (Fig 1A). T2-weighted images showed symmetric high signal in the globus pallidus bilaterally. Another MR examination was performed 6 months later in this infant, who now exhibited hypotonia, early signs of choreoathetosis, developmental delay, nystagmus, and suspected seizure activity (Fig 1B). High signal on T2-weighted images was again found in the globus pallidus bilaterally, with no evidence of mass effect. Follow-up MR at 1 year of age was unchanged (Fig 1C).

Discussion

Kernicterus is a neurologic condition resulting from the deposition of unconjugated bilirubin within the brain. Bilirubin encephalopathy was described in 1904 by Schmorl (3), who reported the postmortem pathologic finding of yellow staining of the basal ganglia in infants to be associated with neonatal jaundice.

Causes of kernicterus (hyperbilirubinemia) include erythroblastosis fetalis or other hemolytic anemias such as glucose 6-phosphate dehydrogenase deficiency. Phototherapy and exchange transfusions are two therapeutic options in the neonate with hyperbilirubinemia that have significantly reduced the prevalence of bilirubin encephalopathy (2).

The neurologic manifestations of hyperbilirubinemia usually appear by 2 to 5 days of age as serum bilirubin levels rise over 20 mg/dL in the term neonate, lower in the more susceptible premature neonate (4). Characteristic neurologic symptoms include somnolence, hypotonia, opisthotonus, rigidity, and a high-pitched cry. Early in the course of the disease, the symptoms may be subtle, mimicking sepsis, asphyxia, or hypoglycemia (1). Initially, seizures are uncommon. Once the neurologic complications appear, the prognosis is poor. Posticteric encephalopathy often develops in the few survivors of kernicterus. Neurologic symptoms of posticteric encephalopathy are mostly related to the basal ganglia and include
choreoathetoid movements, asymmetric spasticity, rigidity, opisthotonus, neurogenie hearing loss, and ataxia (5, 6).

Bilirubin is usually bound to plasma albumin, rendering it nontoxic. However, free bilirubin is toxic and can enter the brain when the concentration of bilirubin exceeds normal albumin binding capacity. Hence, exchange transfusions are usually performed when bilirubin levels approach 18 to 20 mg/dL (7). Reduced albumin levels can also lead to increased free bilirubin levels, perhaps explaining the occurrence of kernicterus at lower serum bilirubin levels in the premature neonate (8).

Pathologic findings of kernicterus have classically been described as preferential bilirubin (icteric) discoloration of the basal ganglia, with relative sparing of the cerebral cortex and white matter (2). The pattern of involvement is symmetric and highly selective. The most common sites affected are the pallidum, subthalamic nucleus, and horn of Ammon; staining of the thalamus and striatum is less common. Brain-stem involvement mainly affects cranial nerve nuclei of the tegmentum, particularly the oculomotor and dentate nuclei, and the cerebellar flocculi. Associated destructive lesions in the white matter, such as periventricular infarcts, have also been reported (1). Microscopic evaluation of icteric stained sections reveals bilirubin pigment within neurons, neuronal processes, and microglia. The selective pattern of involvement of specific nuclear groups and the nature of the cytotoxic action of bilirubin are not well understood. The entrance of bilirubin into the brain tissue was attributed to disturbances of the albumin-bilirubin equilibrium, resulting in prolonged high concentrations of bilirubin in the bloodstream, as well as to the greater permeability of the immature blood-brain barrier. Another proposed mechanism is that bilirubin enters the brain after damage of certain nuclear groups by asphyxia, increasing the permeability of the blood-brain barrier in the damaged regions (1). In autopsy specimens of children past the newborn period, chronic changes of neuronal loss, gliosis, and demyelination can be seen in the basal ganglia (9).

The MR findings in this neonate reflect the characteristic pathologic findings of kernicterus. High signal seen in the globus pallidus bilaterally corresponds to known areas of preferential deposition of unconjugated bilirubin. A recent review of imaging of bilateral basal ganglia lesions in the pediatric population (10) describes a differential that lists acute causes such as hypoxia, hypoglycemia, carbon monoxide poisoning, and encephalitis versus chronic con-

Fig 1. Kernicterus.
A. Axial T2-weighted MR image (spin-echo 3000/110/2 [repetition time/echo time/excitations]) obtained at 18 days of age shows bilateral hyperintense lesions involving the globi pallidi (arrows).
B and C. Subsequent T2-weighted MR images obtained at ages 6 months (B) (fast spin-echo 2500/119/2) and 1 year (C) (spin-echo 3000/110) show persistence of the lesions (arrows). Low T2 signal of the further myelinated internal capsule outlines better the preferential involvement of the globi pallidi.
ditions that include inborn errors of metabolism, dysmyelinating disorders, and degenerative diseases. To this list, we should add kernicterus (bilirubin encephalopathy).

Although the MR findings of high signal in the basal ganglia are nonspecific, they do demonstrate evidence of irreversible central nervous system toxicity from the hyperbilirubinemia. Imaging findings along with the appropriate clinical presentation and laboratory values could establish the correct diagnosis of kernicterus.

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References


