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MRI of bilirubin encephalopathy (kernicterus): A case series of 4 patients from Sub-Saharan Africa, May 2017

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ABSTRACT
Characteristic magnetic resonance imaging (MRI) findings in patients with chronic kernicterus are bilateral and symmetric T2-weighted hyperintensities in the globus pallidus. We report 4 cases of infants with clinical, laboratory, and MRI findings of kernicterus in this case series. This is the first MRI report of kernicterus in Ethiopia. Awareness of the disease is raised in this report, and the role of magnetic resonance in detecting signal abnormalities associated with kernicterus in the globus pallidus is underscored. We recommend MRI to be part of the investigation in neonates with jaundice.

Introduction

Kernicterus, also known as chronic bilirubin encephalopathy, describes the chronic, toxic, and permanent sequelae of high levels of unconjugated bilirubin on the central nervous system of infants. It is part of the spectrum of bilirubin-induced neurologic dysfunction, which also includes acute bilirubin encephalopathy. Kernicterus is thought to be very rare and decreasing in incidence, although the exact number of incidence is unknown

Schmorl first used the term kernicterus in 1904 to describe the yellowish staining in the areas of the brain stem and basal ganglia at autopsy in babies who had marked hyperbilirubinemia before they died [1]. Kernicterus literally means yellow kern, in which kern indicates the commonly affected region of the brain, namely the nuclear regions. The basal ganglia, hippocampus, geniculate bodies, and cranial nerve nuclei including the oculomotor, vestibular, cochlea, and dentate nuclei are most commonly involved [2].

There is no disease-modifying treatment available for this condition, and prognosis is poor. Early management of...
neonatal hyperbilirubinemia, with therapies such as phototherapy and exchange transfusion, should be employed to prevent kernicterus.

Magnetic resonance imaging (MRI) has demonstrated high sensitivity in kernicterus and is the imaging modality of choice [3–5]. The posteromedial borders of the globus pallidi seem to be the most sensitive regions of the brain in detecting signal anomalies associated with kernicterus. These signal anomalies typically and initially show on T1-weighted sequences hyperintense signals in the acute phase but eventually become hyperintense on T2-weighted sequences as the disease progresses. Diffusion-weighted images show normal appearance. Magnetic resonance spectroscopy has been scantly mentioned in the literature in the diagnosis of kernicterus, and studies have reported increased levels of glutamate and decreased levels of choline and N-acetyl-aspartate [3–6].

Here we report 4 cases of patients with kernicterus who had perinatal hyperbilirubinemia and who subsequently had choreoathetoid and dystonic motor disorders. Brain MRI showed T2-weighted hyperintensities in the globus pallidi of the 4 cases.

Case I

A full-term male infant was born by spontaneous vaginal delivery after normal pregnancy. He was well till the fourth day of life when his mother noticed a yellowish discoloration in the eyes and skin, as well as failure to suck. Hyperbilirubinemia was the cause of A, B, O blood group incompatibility and the serum bilirubin level at that time was 40 mg/dL (normal bilirubin level is <12 mg/dL) with direct bilirubin level at 1.4 mg/dL. He needed an exchange transfusion and was discharged after a 5-day hospital course.

At 6 months of age, the patient presented with abnormal, contorting limb and torso movements, and delayed motor milestones—he was not able to roll over. It was found on physical examination that head circumference (HC) was 43.5 cm between the mean and two standard deviation (+2SD) for age and gender. His eyes were crossed, he had dystonic extremities, and subjective hearing loss. MRI of the brain taken at presentation (age of 6 months) to explain the dystonic motor disorders that the patient had showed T2-weighted hyperintensities in the globus pallidi bilaterally (Fig. 1), and diagnosis was confirmed on MRI.

Case II

A full-term female infant, who was born by cesarean section because of previous cesarean delivery of the mother, weighed 2 kg on the third day of life. Her mother noticed yellowish discoloration of the eyes and the skin. Serum bilirubin level at that time was reportedly greater than 50 mg/dL. On physical examination, her HC was 45.5 cm between the mean and +2SD for age and gender, and she had generalized dystonia with some oral movements. At 9 months of age, she presented with generalized dystonia with some oral movements. MRI, taken at the time of presentation, showed T2-weighted hyperintensities in the globus pallidus (Fig. 2).

The hyperbilirubinemia that the baby had after delivery was due to hemolysis caused by Rhesus factor (RH) incompatibility. Her mother’s blood type was O and RH-negative but she was RH-positive.

Fig. 1 – Case 1. Axial T2W magnetic resonance image showing bilateral T2 hyperintensities of the globus pallidus (arrows).

Fig. 2 – Case 2. Axial T2W magnetic resonance image showing symmetric hyperintensities in the globus Pallidus (arrows).
Case III

A full-term female infant was born by spontaneous vaginal delivery with assisted forceps. The delivery was complicated with cephalohematoma and several days later, she had yellow discoloration of the eyes and the skin. There was no major blood group incompatibility. Results of her bilirubin level could not be traced but she did have hospital admission and exchange transfusion. We had no way of excluding other differentials in the absence of laboratory findings. The outcome of the transfusion was not mentioned.

At 11 months of age, she presented with dystonic limbs and choreoathetoid movements. On physical examination, her HC was 42 cm (below 3SD for age and gender) and she weighed 6.2 kg. MRI taken at the time of presentation showed T2-weighted hyperintensities in the globus pallidus on both sides (Fig. 3).

Case IV

An 8-month-old female infant, with a birth weight of 3200 g and an HC of 31 cm, was born to a 25-year-old para 3 mother by spontaneous vaginal delivery. The mother was RH-negative, and the patient was RH-positive and developed discoloration of the skin and the eyes, dystonic limbs and choreoathetoid movement disorders on the fourth day of life. The total bilirubin level was 39 mg/dL. She had exchange transfusion. MRI taken at 8 months of age showed bilateral T2-weighted hyperintense signals in the globus pallidus (Fig. 4) and confirmed the diagnosis made on the basis of clinical and laboratory findings.

Discussion

Kernicterus is a term that refers to neuropathologic changes of the neonatal brain from neurotoxicity of the free serum or non-albumin-bound bilirubin (unconjugated), or bilirubin in excess to the plasma albumin binding capacity. Unconjugated bilirubin is toxic and the process of binding to plasma albumin renders it nontoxic. Histopathologically, elevated bilirubin leads to loss of neurons, proliferation of astrocytes, gliosis, and demyelination in the affected area. The neurologic manifestations of kernicterus appear when indirect serum bilirubin levels increase above 20 mg/dL. This tends to be lower for premature infants [7,8]. In 3 of 4 patients in this series, the bilirubin level exceeded this threshold.

The neurologic manifestations of kernicterus evolve with time and during the early periods of infancy and consist of hypotonia, hyper-reflexia, and delayed acquisition of motor milestones, which were seen in all our patients. In some cases, the extrapyramidal manifestations (dystonia, chorea-athetoid movement, etc.) can also be seen early in life, as is the case in our patients, although these symptoms did not fully manifest. In children, older than 1 years old, more familiar clinical features develop including abnormalities in the extrapyramidal, visual and auditory systems, and sometimes minor intellectual deficits [8].

The MRI findings of kernicterus are well documented and although various parts of the central nervous system are involved (brain stem, basal ganglia, thalami, subthalamic nuclei, hippocampus, dentate nucleus, and cranial nerves), only the globus pallidus demonstrates remarkable signal changes [2–5]. The most commonly reported and characteristic MRI finding after the acute phase is the bilateral hyperintense signal on...
T2-weighted sequences as is shown in all our patients. This corresponds to deposition of excess unconjugated bilirubin. The MRI appearances of kernicterus are nonspecific and the differential diagnosis includes hypoxic ischemic encephalopathy and toxic, metabolic, infectious, and inherited disorders [9]. Clinical and laboratory findings in conjunction with MRI findings clarify the diagnosis of kernicterus as in the presented cases.

Conclusion

Although prenatal screening of maternal blood group and subsequent determination of the baby’s blood group together with the advent of effective postnatal therapies, like phototherapy and exchange transfusion, have prevented kernicterus in high-risk patients in developed countries; developing countries like ours are still far behind in anticipating, recognizing, and properly managing such cases. Therefore, awareness of the disease and its risk factors are raised in this report, and the role of magnetic resonance in detecting signal abnormalities associated with kernicterus in the globus pallidi, which appear to be the most sensitive areas of the brain, is underscored. We recommend MRI to be part of the investigation in neonates with jaundice to help in the early detection and institution of appropriate treatment, and reduce severe, irreversible neurologic damage and intellectual impairment.