B/L Basal Ganglia Lesions in a Child Leading to a Diagnosis of Glucose-6-Phosphate Dehydrogenase Deficiency

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Keywords

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Abstract

Bilateral basal ganglia lesions are a common non-specific finding seen in many diseases. One of the differential diagnoses for it, in a child, is kernicterus occurring due to hyperbilirubinemia. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common cause of severe hyperbilirubinemia. A 1-year old child presented to the hospital with history of generalized dystonia in the previous 3 days. MRI showed evidence of symmetrical lesions in bilateral globus pallidus, which were hyperintense on T2/FLAIR and isointense on T1. Patient's blood test revealed G6PD deficiency. Hence, a diagnosis of G6PD deficiency leading to kernicterus was made. In a child, the diseases that may affect the basal ganglia symmetrically and bilaterally include kernicterus, hypoxia, carbon monoxide poisoning, hypoglycemia, inherited metabolic and dysmyelinating disorders like Leigh disorder, Canavan and Krabbe, Neurofibromatosis, Herpes encephalitis, congenital HIV infection, manganese poisoning and extrapontine myelinolysis. Important causes of kernicterus are Rh incompatibility, ABO incompatibility, sepsis, hemolytic anaemia and G6PD deficiency. G6PD deficiency leading to

kernicterus should be considered a differential diagnosis of bilateral basal ganglia lesions in children. Proper elicitation of history with appropriate blood biochemical tests will help in arriving at a proper diagnosis.

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Introduction

Bilateral basal ganglia lesions are a common non-specific finding seen in many diseases [1]. One of the differential diagnoses for it, in a child, is kernicterus occurring due to hyperbilirubinemia. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common cause of severe hyperbilirubinemia [2]. In this article, we present a case of a child who showed bilateral basal ganglia lesions on MRI, due to kernicterus and on investigation, and was diagnosed to be a case of G6PD deficiency.

Case Report

A 1-year old child presented to the hospital with history of generalized dystonia for the last 3 days. MRI showed evidence of symmetrical lesions in bilateral globus pallidus, which were hyperintense on T2/FLAIR and isointense on T1 (Fig. 1a, b). There was no contrast enhancement seen in them. There was no diffusion restriction.

Fig. 1. Axial MRI images of brain of 1-year old child showing symmetrical lesions in bilateral globus pallidus. **a** T2-weighted images showing lesions are hyperintense. **b** T1-weighted images showing lesions are isointense.

Parents of the patient were asked about the birth and neonatal history of the patient. The child was born at term and with normal vaginal delivery. He had spontaneous cry at birth. However, patient had jaundice on the 10th day with peak total serum bilirubin levels of 24 mg/dL. Exchange transfusion brought down the total serum bilirubin level to normal. Patient was discharged after 5 days. No other work up was done.

The patient's blood test revealed G6PD deficiency. Hence, a diagnosis of G6PD deficiency leading to kernicterus was established.

Discussion

The term basal ganglia includes caudate and lentiform nuclei. Lentiform nuclei consist of globus pallidus and putamen. Basal ganglia, substantia nigra and subthalamic nuclei belong to the extrapyramidal system. There are a number of diseases, which may affect bilateral basal ganglia. MRI characteristics of the basal ganglia lesions, along with the age and clinical symptoms of the patient, aid in arriving at a diagnosis.

In a child, the diseases that may affect the basal ganglia symmetrically and bilaterally include kernicterus, hypoxia, carbon monoxide poisoning, hypoglycemia, inherited metabolic and dysmyelinating disorders like Leigh disorder, Canavan and Krabbe, Neurofibromatosis, Herpes

encephalitis, congenital HIV infection, manganese poisoning and extrapontine myelinolysis [1].

Kernicterus is an important cause and should be considered in the differential diagnosis. "Kernicterus" word was coined by Schmorl in 1903, on discovering the pathologic finding of canary yellow staining of basal ganglia in infants who had neonatal jaundice. It is caused due to the deposition of unconjugated bilirubin within the brain [3]. The most commonly affected areas are the basal ganglia (predominantly globus pallidus), subthalamic nuclei, dentate nuclei, hippocampus (sector H2, H3), cerebellar vermis and cranial nerve nuclei (oculomotor, vestibular and cochlear). Periventricular infarcts may also be present. However, cortex is spared [4]. On MRI, this deposition is seen as hyperintensity on T1 in acute cases and T2 hyperintensity in chronic lesions. Thalami are spared in kernicterus. This may help in differentiating between hypoxia and metabolic disorders, which commonly affect the thalami also.

Important causes of kernicterus are Rh incompatibility, ABO incompatibility, sepsis, hemolytic anaemia and G6PD deficiency [5]. G6PD deficiency was discovered in 1957 [6]. G6PD enzyme is important in the glycolytic cycle (Embden Meyerhof), which converts glucose to lactate, with production of ATP. The first step in the cycle is catalyzed by this enzyme, with production of NADPH.

NADPH leads to reduction of glutathione to GSH and methemoglobin to oxyhemoglobin. Deficient G6PD enzyme leads to reduced production of GSH and ATP. GSH is a substrate of Glutathione peroxidase, which protects cell from toxic effects of H₂O₂, which is produced by some drugs [7]. Some drugs also lead to the damage of RBC cell membrane, with increased permeability to cations, which is compensated by an ATP-dependent transport mechanism. If ATP is deficient, there is failure of compensation, loss of osmotic equilibrium and hemolysis [8]. The increased hemolysis leads to increased unconjugated bilirubin and consequently kernicterus.

G6PD deficiency disease is gender linked. The gene for this is present on X chromosome. It usually gets manifested in hemizygous males, homozygous females and a few heterozygous females.

About 400 million people are affected worldwide, with increased prevalence in Africa, Middle East, tropical and subtropical Asia, Mediterranean, Papua and New Guinea [9]. About 24 million children are born in India annually and 390,000 out of them are affected by this disease [10].

G6PD deficiency usually manifests in newborn as jaundice. Jaundice occurs after 24–48 h of neonatal life. Some even manifest in 3rd to 4th week. If jaundice leads to kernicterus, patient usually presents with athetoid cerebral palsy, speech or hearing impairment. In older pa-

tients, it presents as acute hemolytic crisis, on taking drugs like chloramphenicol, primaquin, chloroquin, sulphonamides, chemicals like naphthalene and henna and exposure to viral and bacterial infections.

Prevention of kernicterus is important in neonates with hyperbilirubinemia. Phototherapy and exchange transfusion are used to bring down the bilirubin levels. It is important to avoid drugs that may predispose to hemolytic crisis in patients of G6PD deficiency.

In conclusion, G6PD deficiency resulting in kernicterus could be considered a differential diagnosis of bilateral basal ganglia lesions in children. Detailed history with appropriate blood biochemical tests may help in arriving at a proper diagnosis.

Disclosure Statement

Authors declare no conflict of interest. The manuscript complies with ICMJE.

Authorship Contributions

Imaging was done by Dr. Chirag Ahuja. Manuscript preparation was done by Dr. Nidhi Prabhakar. Manuscript Editing was done by Dr. Chirag Ahuja, Dr. Niranjana Khandelwal.

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