Letter to the Editor

Magnetic resonance imaging features in twin neonates with nonketotic hyperglycinemia

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Nonketotic hyperglycinemia (NKH) is an autosomal recessive inborn error of metabolism caused by a defect in the glycine cleavage system [1]. Magnetic resonance imaging (MRI) findings of neonatal nonketotic hyperglycinemia have rarely been described in the literature, with only a few individual cases or small series reported. In this article, we present twin cases of neonatal onset nonketotic hyperglycinemia, imaged at 3 days of age, and discuss characteristic MRI findings. To our knowledge, this is the only report of such complete MRI analysis in twin neonates.

The female monochorionic diamniotic twin patients were born at 34 weeks gestation by spontaneous vaginal delivery. The pregnancy was uncomplicated. Their parents were nonconsanguineous, with no family history of metabolic or neurologic disease. The Apgar score for the first patient was 7/9 and for the second patient was 6/9. The birth weight of the first patient was 2400 g and that of the second patient was 2150 g. At 2 days old, they were transferred to our Neonatal Intensive Care Unit for hypotonia, cyanosis, poor feeding, and myoclonic seizures. They were hypotonic and lethargic and had unresponsive neonatal reflexes. The first patient had persistent hiccups and myoclonic convulsions. The second patient had myoclonic convulsions and respiratory depression.

The diagnosis of NKH was made based on a markedly elevated CSF/plasma glycine ratio (0.24, 0.19 respectively) at age 7 days. The normal ratio is less than 0.08 [2]. Brain MRI was performed at 3 days of age in our patients. Both patients had progressive cortical and white matter atrophy. The corpus callosum was thin and volume loss was both supra- and infratentorial. In T2-weighted images the appearance of the white matter myelination was inappropriate for age. In the first patient, there were subependymal T1-hyperintense and T2-hypointense areas and ventriculomegaly congruent with germinal matrix grade 3 hemorrhage. Hypoplasia of the corpus callosum, cystic dilatation of the fourth ventricle that may hemorrhage and cerebellar volume loss were also present (Figure 1). The second patient's MRI also showed lack of normal myelination for age, hypoplasia of the corpus callosum, ventriculomegaly, retrocerebellar cystic dilatation and cerebellar volume loss (Figure 2). However, intracranial hemorrhage was not observed.

Structural cerebral abnormalities observed in NKH include cerebral atrophy, callosal dysgenesis, posterior fossa cysts and ventriculomegaly [3, 4]. The improvement of hydrocephalus in patients with NKH has been in particular associated with the existence of large retrocerebellar cysts

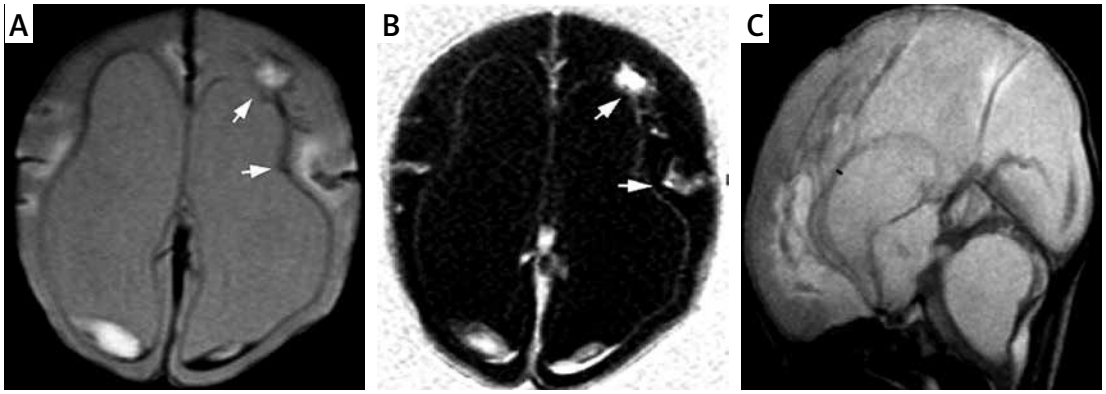

Figure 1. In the first patient, axial T2-weighted (**A**) and T1-weighted (**B**) images show progressive cortical and white matter atrophy. Subependymal T1-hyperintense and T2-hypointense areas (arrow) and ventriculomegaly congruent with germinal matrix grade 3 hemorrhage are observed. In the sagittal T2-weighted images (**C**) the hypoplasia of the corpus callosum and cystic dilatation of the fourth ventricular are clearly visible

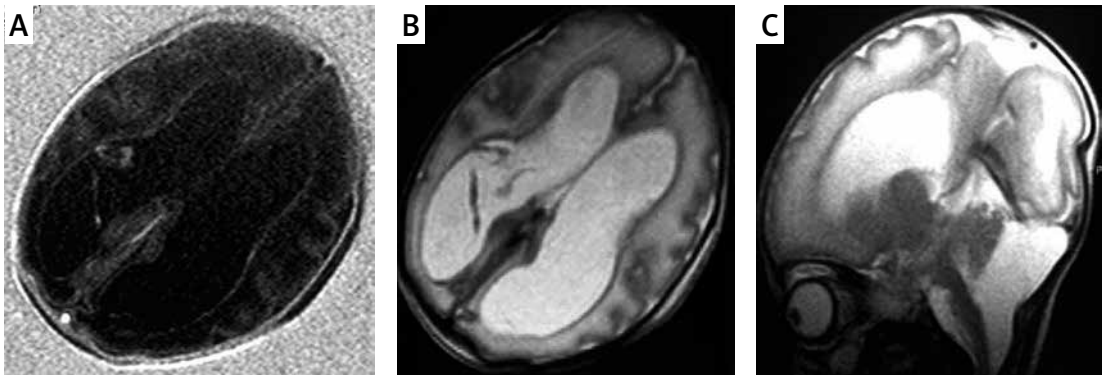

Figure 2. In the second patient, axial T1-weighted (**A**) and T2-weighted (**B**) images also showed lack of normal myelination for age, ventriculomegaly, hypoplasia of the corpus callosum, and retrocerebellar cystic dilatation (**C**)

[4, 5]. On the third day of life, cranial MRI of the twins showed callosal hypoplasia and ventriculomegaly. Germinal matrix hemorrhage was observed in just one of the twins. In the literature, the relation between germinal matrix hemorrhage and NKH has not been reported yet. Because of that, the germinal matrix hemorrhage was not associated with either prematurity or NKH.

Brain MRI shows clear pathological changes in children with NKH. The MRI data of 3-day-old twin neonates with NKH show structural cerebral abnormalities. An early diagnosis, though it does not change the disease course, allows proper genetic counseling, with the possibility of prenatal diagnosis. Another benefit of diagnosis is that having a definite diagnosis with this phenotype prevents further excessive investigations for other genetic or metabolic etiologies.

Conflict of interest

The authors declare no conflict of interest.

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