Persistent Hyperinsulinemic Hypoglycemia Due to SUR1 (*ABCC8*) Mutation in Newborn Twins: An Eight-Year Follow-Up

Betül Ersoy[1], Nermin Tansuğ[2], Abdülkadir Genç[3], Deniz Kızılay[1], Seniha Kiremitçi[1], Pascale De Lonlay[4]

[1]Celal Bayar University Faculty of Medicine, Division of Pediatric Endocrinology and Metabolism, Manisa, Turkey

[2]Celal Bayar University Faculty of Medicine, Division of Neonatology, Manisa, Turkey

[3]Celal Bayar University Faculty of Medicine, Department of Pediatric Surgery, Manisa, Turkey

[4]University Paris Descartes, Hospital Necker Enfants Malades, APHP, Paris, France

Introduction

Congenital hyperinsulinism (CHI) is the most common reason for refractory hypoglycemia in newborns. CHI, characterized by dysregulated insulin secretion and hypoglycemia, is most commonly (40-50%) caused by dysfunction of one of the two subunits of the pancreatic ATP-sensitive K+ (K_{ATP}) channel: the sulfonylurea receptor 1 (SUR1) and the inward-rectifying potassium channel (Kir6.2). Mutations in the *ABCC8* gene are responsible for 40-50% of focal or diffuse CHI cases. Its management can be extremely complicated and may involve medical therapy and surgery. The main goal of the treatment is to maintain normoglycemia, since hypoglycemia during infancy can cause severe neurological consequences. In this study, we report an 8-year follow-up of twin patients who are diagnosed with CHI due to SUR1 (*ABCC8*) mutation in the neonatal period.

Case Report

Term male infants were born to consanguineous parents by caesarean section. Maternal antenatal screen was unremarkable. Their birth weights were 3.5 kg and 3.0 kg. The twins had hypoglycemia (20-30 mg/dL) since birth. Insulin levels of the patients were 50.9 µU/mL and 51.9 µU/mL during hypoglycemia attacks. In genetic analysis of both patients, homozygous mutation 2371G>T, E791X, in the *ABCC8* gene was identified. Both parents of the patients were found to be heterozygous carriers of the mutation. One of the twins responded to diazoxide (20 mg/kg/day) and octreotide (25 mg/kg/day) treatment. The other one did not respond to the medical therapy. This patient underwent subtotal pancreatectomy (95%) at the age of 60 days; also medical therapy was required after surgery due to persistent hypoglycemia. Pathologic analysis revealed marked increase in endocrine cells in some sections throughout the pancreas. The differential diagnosis between focal and diffuse hyperinsulinism could not be investigated further due to lack of our facility of ^{18}F-Dopa PET/CT scanning. Medical therapy was stopped at three years of age in both patients. After 8 years of follow-up, psychomotor development and growth of the patients were normal. Neurological and intellectual abilities were normal in both patients.

Conclusion

In these patients, despite severe clinical picture in the neonatal period, therapy was not necessary after 3 years. Neurological and intellectual abilities can be sustained by aggressive treatment.