Congenital hyperinsulinism: a curable case in an infant

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Severe, early onset congenital hyperinsulinism (CHI) consists of two broad subtypes: on the one hand focal adenomatous hyperplasia associated with Ch. 11p15 gene defects, and on the other diffuse β-cell abnormalities associated with Ch. 11p15, 7p15-p13, 10q23.3, and 4q22-q26 (1). In a considerable percentage of CHI patients pharmacological treatment "fails", and surgical intervention is the only remaining treatment option. Since focal disease is potentially curable through a limited surgical intervention (removal of just the focal lesion) carrying a much lower risk of disturbing endocrine and exocrine function than near-total pancreatectomy, the clinical, biochemical and genetic distinction between focal and diffuse disease has become increasingly important.

Here we discuss the medical history of a term, male newborn who presented with severe hypoglycemia 1 hour after birth, and who was subsequently diagnosed and treated for HI in the Academic Medical Center according to the guideline published in 2000 (2).

Because the inappropriate insulin release was not responsive to treatment with diazoxide or nifedipine, and normoglycemia could only be maintained by continuous, subcutaneous somatostatin and glucagon administration, the child was transferred to Hospital Necker Enfants Malades in Paris for transhepatic portal venous insulin sampling which proved positive. After surgical removal of a focal lesion in the tail of the pancreas at the age of 2.7 months, the child remains normoglycemic without any medication or special measures.

Chromosome analysis of the index patient showed a pericentric inversion of chromosome 11. DNA sequencing demonstrated a heterozygous C deletion in exon 36 of the ABCC8 gene (ΔC4321) leading to a frameshift and a premature stop codon in the Sur1 protein, while the KCNJ11 gene was unaffected. The significance of these findings will be discussed.

(1) Dunne MJ, et al. (2004) Physiol Rev. 84(1): 239-275
(2) Aynsley-Green A, et al., (2000) Arch. Dis. Child Fetal Neonatal. 82(2): F98-F107

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