Congenital hyperinsulinism

There are many types of congenital hyperinsulinism (CHI), each treated differently and with different outcomes. Below are CHI diagnoses that we treat.

Genetic forms of congenital hyperinsulinism

There are many genetic forms of CHI with more being discovered each year. Typically, 60 percent of patients with genetic forms will present in the first week of life with hypoglycemia. These patients will have hypoglycemia that requires a combination of feeding frequently and/or glucose infusion to keep the blood glucose above 70 mg/dl. Some may respond to diazoxide, but more than 50 percent will not and will require surgery to cure the hypoglycemia. Current best practices suggest that pediatric endocrinologists make a diagnosis of the different forms of CHI and determine whether the infant has autosomal recessive diffuse hyperinsulinism or non-mendelian genetic focal disease. This diagnosis is confirmed by running genetic and special imaging studies, which are only available in special hyperinsulinism centers with research studies and a multidisciplinary CHI team, like Cook Children's Hyperinsulinism Center. Early identification and treatment of these genetic forms of CHI is critical to preventing the 20-40 percent incidence of brain damage seen in these children.

Diffuse hyperinsulinism

Diffuse hyperinsulinism is a form of ATP sensitive potassium channel congenital hyperinsulinism (Di-K_{ATP} HI) caused by autosomal recessive mutations in ABCC8 or KCNJ11. Infants diagnosed with Di-K_{ATP} HI have an abnormal pancreas where all beta cells are abnormal and secrete insulin. When medical therapy fails, surgery is usually required to remove up to 98 percent of the pancreas. Most of these patients will develop diabetes or persistent hypoglycemia and will need to be managed by an endocrinologist long-term.

Focal hyperinsulinism

Focal hyperinsulinism is another form of ATP sensitive potassium channel congenital hyperinsulinism (Fo-K_{ATP} HI) that is caused by an unusual genetic abnormality. These infants have an autosomal recessive mutation in ABCC8 or KCNJ11 from the father and a loss of the normal maternal allele. This causes a small part of the pancreas to secrete insulin during hypoglycemia. Because a small portion of the pancreas is affected while the rest of the pancreas is normal, diagnosing patients with Fo-K_{ATP} HI allows us to identify which part of the pancreas is affected and remove it. As a result, some patients are cured and have a very low risk of diabetes.

Glutamate dehydrogenase hyperinsulinism

Glutamate dehydrogenase hyperinsulinism (GDH-HI) is the second most common type of hyperinsulinism and may be referred to as protein sensitive hypoglycemia. With GDH-HI, the pancreas releases an abnormal amount of insulin in response to both fasting and protein ingestion. Children diagnosed with GDH-HI have elevated ammonia levels at all times and low blood sugar levels after eating protein and after an overnight fast. Most diagnoses occur in children more than 3 months old when their diet becomes exposed to a higher protein intake. These children usually respond to diazoxide and rarely need surgery.

Glucokinase hyperinsulinism

Glucokinase hyperinsulinism is one of the least common forms of CHI. It is caused by activating mutations in the glucokinase gene, the glucose sensor of the beta cells. With this form of CHI, the beta cells do not recognize that the glucose levels are <70 mg/dl so they continue to secrete insulin and cause hypoglycemia. The age of onset varies from newborn to adulthood. These children often respond to diazoxide and only the most severe will require surgery, which is a 98 percent pancreatectomy.

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Transient neonatal hyperinsulinism

Transient neonatal hyperinsulinism (TNHI) is one of the most common forms of hyperinsulinism (HI) with an estimated 1:10,000 babies affected. Typically, hypoglycemia begins within 24 hours of birth and can last from three to 10 days up to 6 months. Often this form of CHI is caused by a diabetic mother, perinatal stress, perinatal hypertension, IUGR or LGA; however, some babies appear to have no risk factors.

The hypoglycemia may be mild, with hypoglycemia occurring two to four hours after eating or it may be more severe with hypoglycemia occurring despite intravenous glucose infusion and/or high-calorie feedings every three hours.

Although TNHI is temporary, it can cause brain damage if left untreated. In order for infants with TNHI lasting longer than seven days to be discharged from the medical center, they will need treatment with diazoxide and proof that the illness is controlled by demonstrating the ability to fast for eight to nine hours. Most of these patients will need regular visits to an endocrinologist specializing in hyperinsulinism for the next six to 12 months. Hypoglycemia will typically resolve itself during that time frame.

Other forms of hypoglycemia treated by our team include:

- Idiopathic ketotic hypoglycemia
- Nissen fundoplication induced hypoglycemia