

# A case of congenital hyperinsulinism due to ABCC8 mutation: A challenge to diagnosis, management and treatment

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Topic: Diabetes and insulin

## Objectives:

Congenital hyperinsulinism (CHI) is a rare complex disorder of hypoglycaemia attributable to inappropriate and dysregulated insulin secretion from the pancreas with an incidence of 1:50 000 (1:2500 in consanguineous populations). Genetics involves defects mainly in the KATP channel genes ABCC8 and KCNJ11. We describe a male infant, presented with refractory hypoglycaemia the first week of life.

## Methods:

The patient was admitted to the Paediatric Department with lethargy and reduced breastfeeding. He was the first child of healthy unrelated parents, born at term, birth weight 4.180gr; no history of perinatal asphyxia, no dysmorphic features. His mother had a normal oral glucose tolerance test (OGTT) during pregnancy. A low blood sugar (BG) 35mg/dl (1.9 mmol/l) on day one resolved with oral feeding. On admission, serum BG was 19 mg/dl (1.0 mmol/l), treated with intravenous (iv) dextrose. Consequently, he was started on iv Dextrose infusion and antibiotics, was monitored with hourly BGs (BMstixs) and had regularly 2-hourly feeds by mouth and nasogastric tube (NGT). A hypoglycaemia screen performed when BG was 23mg/dl (1.3 mmol/l); insulin and C-peptide levels were inappropriately high (10,6µU/l and 3,3 ng/ml respectively), blood and urine ketones were negative confirming the hyperinsulinaemic hypoglycaemia. Septic screen was negative, cortisol, thyroid function tests, growth hormone levels, metabolic screen, carnitine and acylcarnitine were all normal. A central line was inserted to deliver concentrated dextrose infusion 12.5% (max 13.1mg glucose/kg/min), oral feeds were enriched with carbohydrate supplements; oral diazoxide and chlorthalidone were started, with progressively increasing doses of diazoxide (up to 15mg/kg/day) to maintain normoglycaemia (BG >60mg/dl (3.3 mmol/l)). Gradually, the infant was released from iv fluids, central catheter and NGT were removed. He was discharged home on oral feeds with carbohydrate supplements with occasional hypoglycaemic episodes (figs 1 & 2). Currently, he is outgrowing the doses of oral diazoxide and chlorthalidone while growth and development are appropriate for age. He has though developed excessive body hair as side effect of the treatment with diazoxide (pics 1 & 2)

Figs 1 & 2. Course of disease and treatment

Day of life	6 <sup>th</sup>	9 <sup>th</sup>	10 <sup>th</sup>	18 <sup>th</sup>	21 <sup>th</sup> (on treatment)	27 <sup>th</sup>	37 <sup>th</sup>	42 <sup>nd</sup>	49 <sup>th</sup>
Glucose (70-100mg/dl)	19	64	51	66	86	90	99	94	104
Insulin (2,6-24,9µU/ml)	10,6	14,2	32,1	26,2	4,7	3,6	7,2	7,2	7,8
C-peptide (1,1-4,4ng/ml)	3,3	3,37	4,09	2,60	1,14	1,46	1,85	1,58	1,69

Day of life	12 <sup>th</sup>	15 <sup>th</sup>	17 <sup>th</sup>	20 <sup>th</sup>	21 <sup>st</sup>	22 <sup>nd</sup>	36 <sup>th</sup>	42 <sup>nd</sup>
Glucose requirements (N 4-6 mg/kg/min)	10,57	11,017	11,1	12,1	12,15	13,13		
Dextrose solution(%)	10%	10%	12,5%	12,5%	12,5%	12,5%		
			Insertion of Hickmann line & rinogastric tube					
Feeding (oral / i.v (%)				20/80	30/70	40/60	.....	100 / 0
Treatment				Diazoxide (5mg/kg/d) hydrochlorothiazide (7mg/kg/d)				Diazoxide (15mg/kg/d) hydrochlorothiazide (7mg/kg/d)
					Carbohydrate supplement (95% carbohydrate)			

Pics 1 & 2. excess body hair



## Results:

Genetic testing showed that the infant was compound heterozygous for two pathogenic ABCC8 variants, a diagnosis of autosomal recessive CHI, subtype ABCC8 (hyperinsulinism and diffuse disease).

## Conclusions:

CHI is a high-morbidity disease with lifelong consequences that require sustained medical input. It is important to optimize treatment to safeguard brain function and quality of life. Homozygous and compound heterozygous mutations are likely to suggest permanent forms of CHI. Recent experience suggests a reduction in the severity of hyperinsulinism over time. However, the management of CHI still remains a challenge.

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