MUTATION IN *UCP2* GENE: A RARE CAUSE OF HYPERINSULINEMIC HYPOGLYCAEMIA SYNDROME IN A SMALL-FOR-GESTATIONAL AGE NEWBORN

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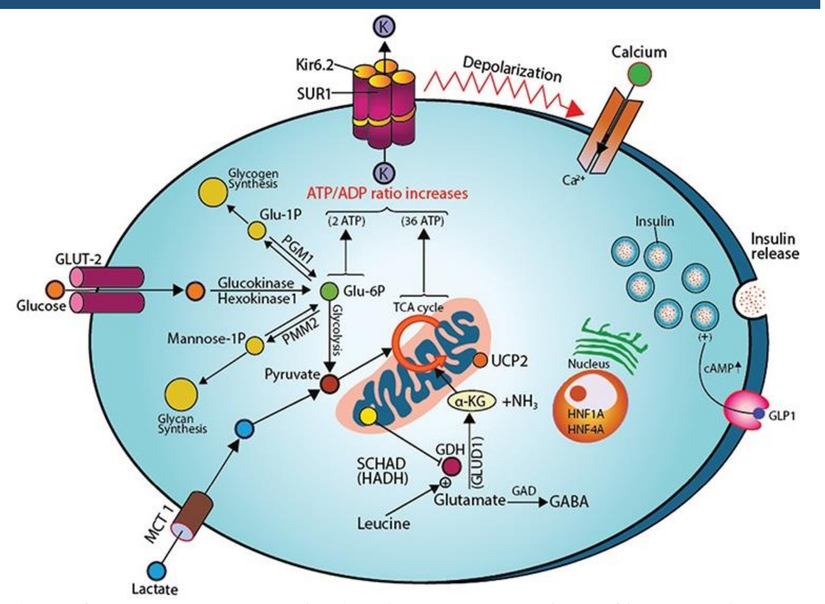
INTRODUCTION

Hyperinsulinism is a common cause of severe and persistent hypoglycaemia during the neonatal period. Eleven genes have been identified that lead to unregulated insulin secretion and hyperinsulinemic hypoglycaemia (HH). Inactivating mutations in *UCP2* gene have been described in a very small number of patients with HH. UCP2 protein is an inner mitochondrial carrier protein and its loss of function causes enhanced glucose oxidation and increased intracellular ATP synthesis leading to HH.



Sites of gene mutations involved in the genetics etiology of hyperinsulinaemic hypoglycaemia. (Figure from Demirbilek H, Hussain K)[3]

CASE REPORT

Male newborn who presented hypoglycaemia since the first hour of life.

Family history: no consanguinity. Mother with hypertension. No history of hypoglycaemia nor diabetes mellitus.

Obstetric history: First gestation of 34 weeks' duration. O´Sullivan test and TORCH serologies were normal.

Third trimester ultrasound detected intrauterine growth restriction (IUGR) and signs of hemodynamic redistribution.

Birth by caesarean section. Apgar 8/9, weight 1630g (-1.92 SD), length 41cm (-2.23 SD) and cephalic perimeter 29cm (−1.28 SD).

Physical examination was normal with the exception of an umbilical hernia of less than 1cm.

The patient presented persistent asymptomatic hypoglycaemia that required administration of intravenous glucose boluses and continuous enteral feeding by nasogastric tube. **Carbohydrates were progressively increased up to 17.4 mg/kg/min.** There were no clinical-biochemical markers of infection.

Complementary Tests

Results at 12 days of life under hypoglicaemia (35mg/dL)		
		normal value
Insulin	1.72	3 - 25 mU/mL
Serum ammonium	88	< 53 µmol/L
Total free fatty acids	0.18	0.6 - 1.3 mmol/L
β-Hidroxibutirat	140	15 - 700 µmol/L
Lactate	1.2	0.3 - 2.1 mmol/L
Cortisol	16	5.27 - 22-45 µg/dL

Genetic study

Included *ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, HNF4A, HNF1A, UCP2, HK1* and *PGM1* genes.

Finding an **inactivating mutation in *UCP2 (*c.127-1G>T), a splicing mutation that had not been previously reported.**

Serum amino acids, urine organic acids, acid-base equilibrium, liver and renal function tests were normal.
Echocardiogram and abdominal ultrasound were also normal.

Evolution and treatment

Diazoxide was started at a dose of 5 mg/kg/day at the age of one month with a positive response. It allowed carbohydrate requirements to be significantly reduced, withdrawing the feeding by gastroclysis and prolonging the interval between takes. Diazoxide was well tolerated and suspended with a dose < 3.5mg/kg/day at the age of 3 months. Currently the patient has 13 months and tolerates normal fasting time for age.

CONCLUSION

We have described the case of a small-for-gestational age newborn who presented transitory HH caused by mutation in *UCP2* gene, who responded to diazoxide treatment.

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