Unusual congenital hyperinsulinism case in a patient with a pathogenic *GCK* mutation

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OBJECTIVES

Dominant activating mutations in GCK gene are known to be the cause of congenital hyperinsulinism (CHI).

Patients with GCK mutations show a wide range of clinical presentations varying from asymptomatic adult onset hypoglycemia to medically unresponsive severe neonatal onset HI.

METHODS

Here we report a severe GCK-HI case which required pancreatectomy.

The diagnosis of CHI was based on persistenting hypoglycemia and confirmed biochemically by the presence of detectable serum insulin during hypoglycemia.

NGS was made on Ion Torrent platform and included analysis of the following genes: *GCG*, *GLUD1*, *WFS1*, *HNF1A*, *GCK*, *INS*, *HNF1B*, *ABCC8*, *HNF4A*, *RFX6*, *PTF1A*, *NEUROD1*, *AKT2*, *ZFP57*, *INSR*, *EIF2AK3*, *PPARG*, *PAX4*, *PDX1*, *GLIS3*, *KCNJ11*, *SLC16A1*, *FOXP3*, *BLK*, *CEL*, *KLF11*, *SCHAD*, *GCGR*.

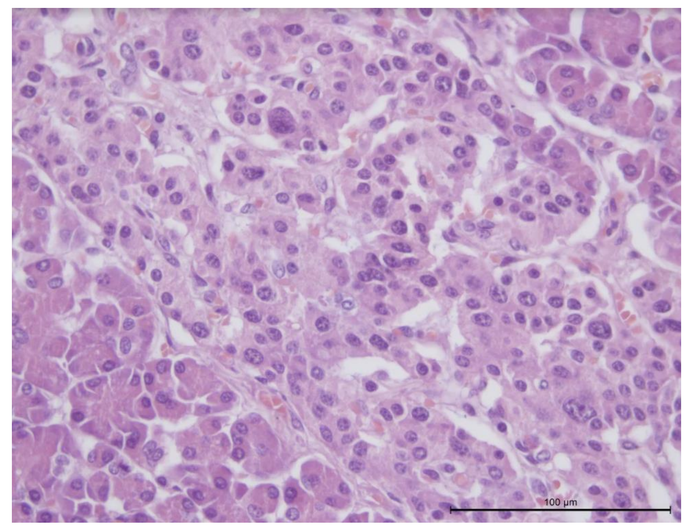
RESULTS

14 months
- first hypoglycemic seizures

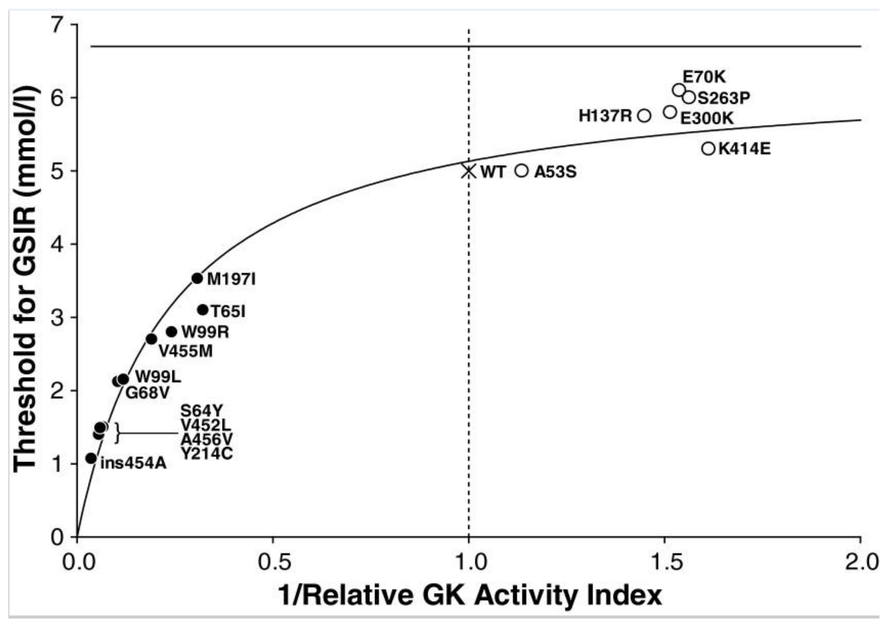
16 months
- diagnosed with persistent hyperinsulinemic hypoglycemia
- poor response to 20 mg/kg/day Diazoxide and 18 μg/kg/day Octreotide
- stable euglycemia was achieved at 19 mg/kg/min glucose infusion
- heterozygous mutation c.1361_1363dupCGG (=ins454A) in GCK gene was found in 11% of reads in the blood sample

18 months
- near-total pancreatectomy
- persistent hypoglycemic episodes reoccurred. Low glucose diet with fructose intake and 12 mg/kg/day Diazoxide treatment – ineffective

21 months
- 10 μg/kg/day Octreodite in combination with Nifedepine – partial response
- Frequent feeds, corn starch
- **normal neurological status**



Histopathology. Islet cell nuclei are polymorphic and moderately enlarged.
(hematoxylin and eosin stain,
original magnification ×250).



Calculated thresholds for glucose-stimulated insulin release in activating and inactivating mutations of glucokinase.
● glucokinase hyperinsulinism mutations;
○ MODY2 mutations;
X wild type.

Sayed S., Langdon D. R., Odili S. et al. (2009). Extremes of clinical and enzymatic phenotypes in children with hyperinsulinism caused by glucokinase activating mutations. Diabetes 58, 1419–1427. 10.2337/db08-1792

CONCLUSIONS

In summary, near-total pancreatectomy led to some improvement, although did not completely cure the patient. The necessity of near-total pancreatectomy in GCK-HI patients is debatable.
Activating mutations of the GCK gene, which is also expressed in the brain, may possibly have some protective effects by keeping the neuronal cells active even during hypoglycemia.

We have no conflict of interest to declare

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Fetal, neonatal endocrinology and metabolism (to include hypoglycaemia)

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