Glycogen-Storage Disease Type VI in a girl presenting with Recurrent Ketotic Hypoglycaemia but no Hepatomegaly

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Background

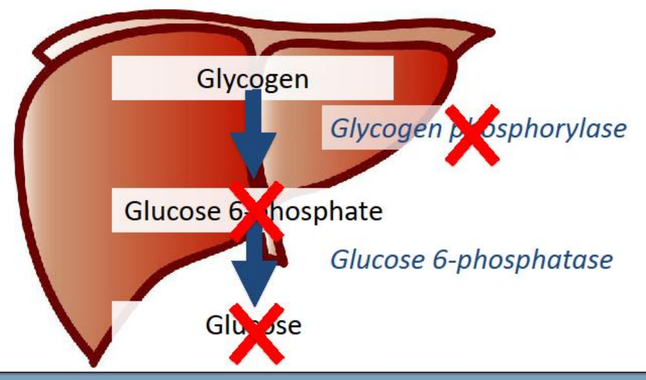
Glucose homeostasis:

- Glycogen, the stored form of glucose, is formed in periods of dietary carbohydrate loading, and broken down during fasting to maintain euglycaemia
- This process is called glycogenolysis and relies on numerous enzymes, including glycogen phosphorylase
- Inborn errors of metabolism resulting from mutations in genes involved in glycogen synthesis, degradation or regulation cause a group of conditions called Glycogen Storage Diseases
- Glycogen is most abundant in liver and muscle, the organs most affected by glycogen storage diseases (GSDs)
- Ketotic hypoglycaemia is a relatively common diagnosis in children presenting with hypoglycaemia, but it is a diagnosis of exclusion

Glycogen Storage Disease type VI (GSD VI):

- Autosomal recessive
- Deficiency of the liver isoform of glycogen phosphorylase
- Results in abnormal accumulation of glycogen
- Typical presentation - early childhood with growth retardation, hepatomegaly, hypoglycaemia and ketosis

Fasted state



Case

- 3-year-old girl , born at term, birth weight 3.14kg
- Presented with episodes of recurrent hypoglycaemia not associated with intercurrent illness
- Non-consanguineous Caucasian parents
- Uneventful past medical history
- Height SDS -2.5
- Normal examination with no dysmorphic features or hepatomegaly

1. Investigations:

Glucose (mmol/L)	Insulin (pmol/L)	C-peptide (pmol/L)	Free fatty acids (µmol/L)	B-hydroxy-butyrate (µmol/L)	Bedside blood Ketones (mmol/L)	Cortisol (mmol/L)
2.4	<14	51	3640	3965		
2.3	<24.8				2.5	1065

- Plasma amino acids, lactate, blood ammonia, blood spot acylcarnitine profile and urine organic acids - no abnormalities
- Suggestive of ketotic hypoglycaemia

2. Further results:

- IGF1 5.4 (2-32 nmol/L)
- Prolactin 77 (0-500 mU/L)
- TSH 1.04 (0.3-3.8 mu/L)
- T4 14.3 (9-19 pmol/L)
- Normal bone profile
- 46XX karyotype

3. Glucagon stimulation test:

- Suboptimal growth hormone response of 4.7µg/L

Glucagon Stimulation Test			
Time (min)	GH (ug/L)	CORT (nmol/L)	GLUC (mmol/L)
0	3.06	334	3.3
30	2.65	337	4.7
60	4.79	303	3.2
90	3.77	309	2.4
120	0.99	596	2.7
180	0.45	458	9.7

- Commenced on growth hormone

4.

- Continued to have symptomatic ketotic hypoglycaemic episodes
- Not triggered by intercurrent illness

➔ Further genetic analysis undertaken

5. Metabolic mutation analysis:

Heterozygous *PYGL* mutation

- Suggests a diagnosis of probable GSD VI with an unidentified second mutation
- Presence of exonic deletions or deep intronic variations in the PYGL gene cannot be ruled out as these were not analysed

Conclusion

- We report a case of probable GSD VI who presented with recurrent ketotic hypoglycaemia without hepatomegaly.
- Ketotic hypoglycaemia is a diagnosis of exclusion.
- It is important to consider alternative diagnoses especially in the presence of recurrent hypoglycaemic episodes with atypical features for ketotic hypoglycaemia.
- Genetic evaluation may be warranted in selected cases of ketotic hypoglycaemia.

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