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Idiopathic Ketotic Hypoglycemia, An Abnormal Presentation

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Introduction

Idiopathic ketotic hypoglycemia (IKH) is the most common cause of fasting hypoglycemia in children, classically presenting between 18 months and 6 years of age. It results from limited hepatic glycogen reserves and an exaggerated reliance on fat metabolism during periods of fasting. Presentation beyond early childhood is uncommon and often triggers extensive evaluation for endocrine or metabolic disorders. Correct diagnosis depends on biochemical interpretation of a critical sample obtained during hypoglycemia, allowing differentiation from hyperinsulinism, fatty acid oxidation disorders, glycogen storage diseases, and hormonal deficiencies.

Methods :

We report a case of an 11-year-old girl presented with recurrent episodes of fasting hypoglycemia, manifesting predominantly as neuroglycopenic symptoms without typical features of ketosis. She was underweight (24.8 kg), but normal height, and bone age (height 140 cm ≈ 25th centile), with no hepatomegaly on examination. Due to recurrent episodes of hypoglycemia, she was admitted for a supervised inpatient diagnostic workup. A fasting study was conducted with hourly capillary glucose monitoring until hypoglycemia (≤55 mg/dL) was reached, at which point critical blood and urine samples were obtained.

Results :

Hypoglycemia occurred at a blood glucose level of 47 mg/dL (2.8 mmol/L). Results demonstrated elevated ketone levels and an appropriate counter-regulatory response, including elevated cortisol, with normal lactate, ammonia, and acid–base status. (Table 1)

Table 1: Critical Sample During Hypoglycemia (BG 47 mg/dL):

Four Main Groups of Causes of hypoglycemia in Non-diabetic Children

Discussion :

Hypoglycemia occurred at a blood glucose level of 47 mg/dL (2.8 mmol/L). Results demonstrated elevated ketone levels and an appropriate counter-regulatory response, including elevated cortisol, with normal lactate, ammonia, and acid–base status. (Table 1)

Four major categories were considered. (Table 2)

1. Hyperinsulism State
2. Hormonal deficiencies (Growth Hormone, Adrenal Insufficiency)
3. Metabolic disorders (Glycogen storage disease, fatty acid oxidation disorders)
4. Idiopathic Ketotic Hypoglycemia.

Why Idiopathic Ketotic Hypoglycemia was Most Likely?

- Hypoglycemia with ketosis
- Normal lactate and ammonia→ argues against GSD
- No hepatomegaly→ argues against GSD
- Increased ketone production→ excludes FAOD
- Low insulin and C-peptide→ excludes hyperinsulinism states
- Elevated cortisol→ excludes adrenal insufficiency

This case represents an atypical late presentation of IKH:

- Age 11 years (IKH usually presents around 2 years)
- Absence of classic ketosis symptoms; only neuroglycopenic symptoms
- Low IGF-1
- Low GH level during hypoglycemia: 2.5 mmol/L (reference range 0-10 mmol/L)

Primary growth hormone deficiency (GHD) is unlikely given the isolated hypoglycemic presentation without prior auxological abnormalities at this age; instead, the low IGF-1 likely reflects secondary suppression from recurrent fasting vulnerability and chronic hypoglycemia rather than intrinsic pituitary dysfunction, corroborated by normal height, and bone age.

Current biochemical and clinical parameters do not warrant GH stimulation testing, which would be low-yield and potentially misleading; instead, clinical follow-up every 4-6 months should monitor height, growth velocity, weight/BMI, and pubertal progression (Tanner staging), while laboratory reassessment of IGF-1 should occur only when the child is clinically well, adequately nourished, and 1-2 weeks post-hypoglycemia—typically normalizing in such secondary cases.

Formal GH axis evaluation becomes indicated only if declining growth velocity, downward crossing of height percentiles, delayed puberty, or persistently low IGF-1 despite optimal nutrition emerges; if needed, this would entail repeat IGF-1 and IGFBP-3, followed by formal GH stimulation testing (not random GH levels), bone age reassessment, and pituitary MRI solely if biochemical GHD is confirmed.

Conclusion :

Idiopathic ketotic hypoglycemia can present beyond early childhood and should be considered in older children with fasting hypoglycemia and normal growth.

References:

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