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20 cases of congenital hyperinsulinism in Ukraine

E.Globa[1], N.Zelinska[1], S.E. Flanagan[2], S. Ellard[2], Henrik Christesen[3]

[1] Ukrainian Scientific Centre of Endocrine Surgery, Kyiv, Ukraine
[2] University of Exeter Medical School, UK.
[3] Hans Christian Andersen Children's Hospital, Odense University Hospital, Denmark

Background

Congenital hyperinsulinism (CHI) is a rare heterogeneous disease. Genetic testing is crucial as identifying the underlying aetiology can guide clinical management.

Objective and hypotheses

We investigated the clinical characteristics and genetics of 20 Ukrainian patients with CHI.

Methods

Routine clinical and laboratory investigations were performed on 20 patients with hypoglycemia and unsuppressed C-peptide and p-insulin, diagnostic for CHI. Patients were subgrouped according to whether the hypoglycemia was persistent (n=12) or transient (n=8). *KCNJ11* and *ABCC8* were sequenced in all patients. tNGS of all the known CHI genes was undertaken in 2 patients with persistent CHI. In one case features of Beckwith-Wiedemann Syndrome prompted methylation and dosage analysis of chromosome 11p15.5. ^{18}F-DOPA PET-CT scanning was performed on 9 cases (75%) with persistent CHI.

Results

Table 1. Clinical characteristics and genetic causes of patients with CHI

	Persistent CHI (n=12)	Transient CHI (n=8)	p*
Date of manifestation, days	22.5 [1,8; 54]	89.5 [1.75; 284]	p=0.01
Birth weight, g	3845 [3625; 4373]	3475 [3205; 3937]	p=0.001
Genetic causes	83.3% *ABCC8* (n=9), *KCNJ11* (n=1)	25% *ABCC8* (n=1), pUPD 11p15.5 (n=1)	p=0.004

* There was no difference in gender, blood glucose levels, p-insulin or C-peptide at presentation between the groups (p>0.05).

Of the 9 patients who underwent ^{18}F-DOPA PET-CT scan 5 cases with a paternally inherited KATP channel mutation had a focal lesion, whilst diffuse disease was observed in 2 cases with a compound heterozygous *ABCC8* mutation and one case with a dominant *ABCC8* mutation. Two patients without a mutation had atypical histology.

11 patients with persistent CHI (91.6%) were treated with short-acting octreotide and/or diazoxide vs 5 patients with transient CHI (62.5%), p>0.05. Nine (75%) patients with persistent CHI underwent surgery due to poor response to medical therapy.

Postoperative complications included transient fasting hyperglycemia (n=1), subclinical exocrine insufficiency (n=1) and a cicatricial hernia (n=1). Hypoglycaemia persisted following surgery in 2 patients (with atypical and diffuse disease). Both are currently treated with long acting release octreotide.

Conclusions

Despite persistent CHI being associated with an earlier age at diagnosis and higher birth weight, the overlap in the range of these features between those with persistent and transient CHI means that it is not possible to use clinical characteristics to predict disease duration. Genetic testing should therefore be performed in all individuals with CHI to ensure optimal treatment.

References:

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