Long-term follow-up in a case with congenital hyperinsulinemic hypoglycemia with a novel p.Ser1389Pro mutation in ABCC8 gene

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INTRODUCTION

Hyperinsulinemic hypoglycemia is one of the most common causes of severe and persistent hypoglycemia in neonates and children (1). Early diagnosis and treatment of the disease are important for the future neurodevelopmental outcomes Genetic examination often can guide the treatment. The most common affected genes are the ABCC8 and KCNJ11 genes, which encode the SUR1 and Kir6.2 K_{ATP} channels, respectively (2).

AIM

Here, we present the case whose genetic analysis was reported as an otosomal dominant diazoxide unresponsive missense variant, had a partial diazoxide response and diazoxide was discontinued after LAR treatment at the age of three years. Also, genotype-phenotype relationship and treatment experience will be discussed.

CASE PRESENTATION

A female patient born from a 33-year-old mother with a birth weight of 1990 g (0.91 SDS) by C / S was admitted to our clinic because of hypoglycemia in the first hours of follow-up in the newborn intensive care (she was hospitalized due to respiratory distress). The laboratory results at the time of hypoglycemia were given in Table-1.

At first, glucose replacement was started with an infusion rate (GIR) of 5-8 mg/kg/min. Since her hypoglycemia continued after increasing GIR, diazoxide (5 mg/kg/d) was added the treatment. As the hypoglycemia continued in the follow-up, the dose of diazoxide was gradually increased (10 mg/kg/d). Thiazide (7 mg/kg/g) was added to the treatment due to the fluid retention side effect of diazoxide. Octreotide (10 mcg/kg/d) was started as the patient continued to have hypoglycemia

Her genetic analysis (novel p.Ser1389Pro (c.4165T> C) heterozygous de novo variant) was reported as an diazoxide unresponsive missense mutation, due to previous neighbor mutations. Discontinuation of diazoxide treatment was made based on genetic result but she had hypoglycemia again. Hypoglycemia improved when diazoxide was added to therapy. She was followed up as normoglycemic with diazoxide and octreotide until the age of three. When she was three years-old, octreotide treatment was switched to a long-acting release form.. Diazoxide was discontinued six months after this treatment. Also, long-acting release form octreotide (LAR) dose requirement decreased over time. Now, she is five years-old and neurodevelopment is appropriate for the age, and the follow-up continues without drug-related side effects. Anthropometric and laboratory findings in the last control are given in Table-2.

Table-1: Laboratory datas at admission

Glucose (mg/dl)	47
Insulin (µIU/mL)	11.3
C-peptide (ng/mL)	1.43
ACTH (pg/mL)	10.9
Cortisol (µg/dL)	16.27
Growth hormone (ng/mL)	7.5
Ketone	Negative

Table-2: The anthropometric and laboratory results in the last control

Anthropometric		Laboratory	
Height (cm)	107.5	**Glucose (mg/dL)**	89
Height SDS	-0.62	**SGOT/SGPT (U/L)**	37/17
Bodyweight (kg)	17.1	**IGF-1 (ng/mL)**	103 (-0.29 SDS)
Bodyweight SDS	-0.69	**IGFBP3 (ng/mL)**	3580 (0.4 SDS)
BMI (kg/m²)	14.8	**TSH (µIU/mL)**	3.5
BMI SDS	-0.46	**fT4 (ng/dL)**	1.31

CONCLUSIONS

As a result, the genetic examination is important in guiding treatment in patients with HH. However, the genotype-phenotype relationship may not always be clear. After the partial response to diazoxide, LAR treatment was started and diazoxide was not needed anymore in our case. This situation is thought to be due to the decrease in the severity of the disease with age, or an unknown mechanism of action of LAR treatment on the K_{ATP} channel. It is very important to discuss the cases with HH in terms of guiding clinical follow-up and treatment.

REFERENCES

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