Hyperinsulinemic hypoglycemia in congenital disorder of glycosylation type-Ia (CDG-1a)

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INTRODUCTION

Congenital disorder of glycosylation type-Ia is a multi-system disease involving neurological, gastrointestinal, ophthalmologic, cardiac or endocrine systems. In addition to hypothyroidism and hypergonadotropic hypogonadism, rare occurrences of hyperinsulinemic hypoglycemia in CDG patients have been reported. In the present report, we describe a patient diagnosed with CDG type-1a accompanied by hyperinsulinemic hypoglycemia, and whose responsive to diazoxide.

CASE

The female patient was referred to our hospital at the age of 8 months with the complaint of failure to thrive. She was born at term as the first child of healthy non-consanguineous parents with a birth weight of 2.7 kg. Her weight:6 kg(<3p), height:63 cm (3p), head circumference: 41 cm (3p). She had strabismus, axial hypotonia, a hepatomegaly of 3 cm below the margin, inverted nipples and an abnormal distribution of subcutaneous fat such as unusual fat pads in supragluteal region.

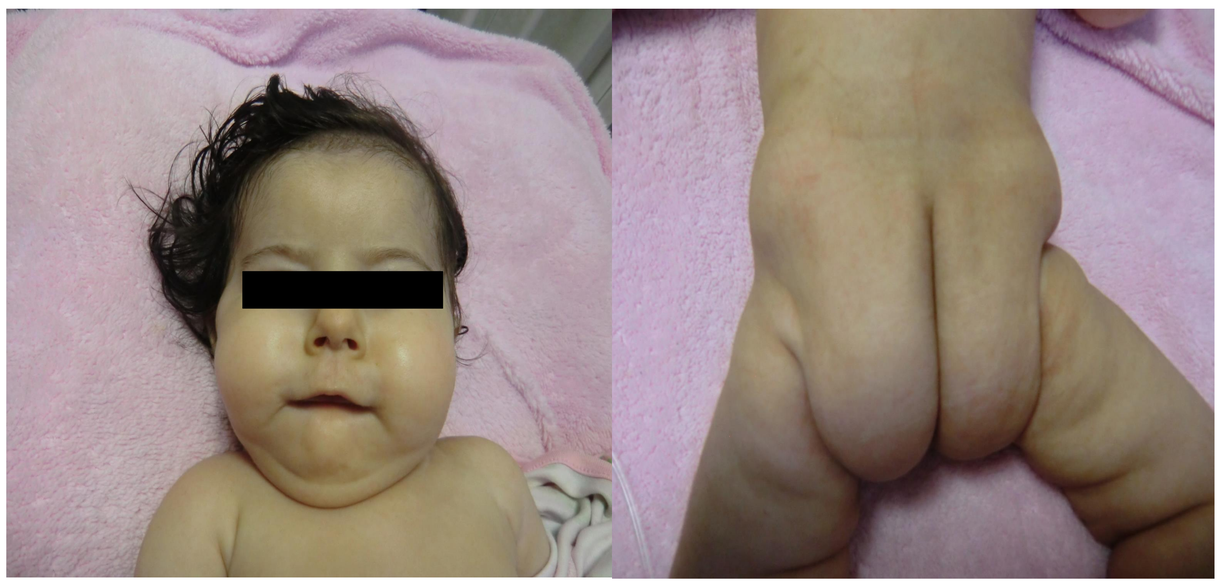

Table 1. Laboratory investigations

Hb: 10.9 gr/dl (11.1-14.1)	Na: 136 mEq/L (136-146)	AST: 218 IU/L (<56)
Rbc: 4.06 x 10^6/µL (3.9-5.1x 10^6/µL)	K: 4.94 mEq/L (4.1-5.3)	ALT: 156 IU/L (<57)
Wbc: 12.5 x 10^3/µL (6-16 x 10^3/µL	BUN: 5.99 mg/dl (5-18)	ALP: 256 IU/L (124-341)
Plt: 249 x 10^3/µL (200-550 x10^3/µL)	Cr: 0.16 mg/dl (0.16-0.39)	GGT: 37 IU/L (1-39)
MCV: 77.9 fL (72-84)	Uric acid: 5.29 mg/dl (2.6-6)	LDL: 54.84 mg/dl (<130)
RDW: 15.9 % (11.7-14.6)	Total Protein: 5.28 g/dl (5.1-7.3)	HDL: 14.26 mg/dl (40-60)
	Albumin: 3.1 g/dl (3.5-5.2)	Triglyceride: 307 mg/dl (<150)

Prothrombin time (PTZ): 16.6 sec(10.4-12.6)	Free T4 13.67 pmol/L (7.86-14.41)
Activated prothrombin time (aPTT): 42.7 sec (22.5-32)	Frees T3: 5.8 pmol/L (3.8-6)
INR: 1.42 (0.8-1.2)	TSH: 4.33 µIU/L ((0.38-5.33)

Table 2. Critical blood evaluations during hypoglycemia

Glucose : 36 mg/dl (70-100)

Insulin: 3.1 µIU/ml (1.9-23)

C-peptide: 1 ng/ml (0.9-7.1)

ACTH: 25.8 pg/ml (0-46)

Cortisol: 6.19 µg/dl (6.7-22.6)

Growth hormone: 8.01 ng/ml (>10)

Lactic acid: 14 mg/dl (4.5-19.8)

Ammonia: 33 µg/dl (20-120)

Urine ketone: Negatif

Tandem mass spectrometry: Normal

Plasma and urine amino acid profiles: Normal

Urine organic acid analysis: Normal

Low dose ACTH stimulation test peak cortisol: 21.1 µg/dl

As the patient was hypoglycemic, an IV glucose infusion was given at a rate of 8 mg/kg/min. Hyperinsulinism was considered, since the levels of insulin and c-peptide were elevated while the patient was hypoglycemic, and exaggerated glucose response was seen in a glucagon test, and so the patient was started on diazoxide. The patient experienced no new episodes of hypoglycemia after treatment with diazoxide. Transferrin isoform electrophoresis, requested following a preliminary diagnosis of CDG, based on the appearance of bilateral inverted nipples and abnormal distribution of subcutaneous fat, was abnormal with type 1 pattern. A homozygous mutation was detected in a PMM2 gene analysis (c.385G>A). Cranial MRI showed cerebellar atrophy and diffuse volume loss in the brainstem, echocardiography demonstrated pericardial effusion and increased echogenicity in the myocardium, and the lipid profile showed hypertriglyceridemia and low HDL levels, which were consistent with the CDG.

CONCLUSION

Hyperinsulinemic hypoglycemia accompanying CDG type-1a has been reported in very few cases, and its etiology is still to be clarified. Based on a previously suggested hypothesis, an abnormal glycosylation of the KATP channels may result in hyperinsulinism, and so patients respond well to diazoxide, as an agent with proven activity in KATP channels.

REFERENCES

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