A novel genetic mutation in a Turkish family with GCK-MODY

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Background

Maturity-onset diabetes of the young type 2 (MODY2) is an autosomal dominant inherited disease caused by heterozygous inactivating mutations in the glucokinase (GCK) gene. It mostly presents with mild noninsulin-dependent fasting hyperglycemia. MODY2 accounts for 2%–5% of all diabetes cases. It is treated with diet only, and complications are extremely rare. We presented here a family with MODY2 caused by a novel heterozygous p.E51*(c.151.G>T) mutation of the GCK gene

Case

A 17-year-old girl was admitted to our department because of fasting hyperglycemia. Parents had no consanguinity. Father and grandfather were diagnosed with diabetes. On physical examination Body mass Index was 30.2 kg/m² (>95 p).She had not acanthosis nigricans. Pubertal assesment revealed Tanner V. Serum autoantibodies against glutamic acid decarboxylase, islet cell antibodies, and anti-insulin autoantibodies were negative. Blood glucose level was repeatedly checked and showed fasting hyperglycemia (130 mg/dl) as well as an elevated hemoglobin A1c level (6.6 % ; reference range, 4.8 % – 5.9 %). A standard oral glucose tolerance test with 75 g of glucose equivalent was performed with a fasting glucose of 130 mg/dl and a 2-hour glucose of 159 mg/dl. The fasting insulin concentration was 6.9 µU/mL and 27 µU/mL after two hours.

Methods

Considering the clinical and family history, mutation analysis of the GCK gene was performed. Complete sequencing of coding exons and intron-exon boundaries of the GCK gene was carried out in the patient. Genetic analaysis of case identified a heterozygous mutation (c.151.G>T) leading to stop codon (p.E51*) in GCK gene Family members were screened for this mutation. The same mutation and mild hyperglycemia were found in the patient's father and the two-sisters but was absent in the mother

Conclusion

GCK mutation screening should be considered in patients with mild early-onset hyperglycemia, family history of impaired glycemia, and negative ß-cell antibodies. In addition family members of patients with MODY should be screened

Table I. Laboratory characterization of patients with MODY 2

	Proband	Sister 1	Sister 2	Father
Age (year)	$16^{7/12}$	$7^{9/12}$	$14^{8/12}$	40
Fasting Glucose (mg/dl)	130	129	135	161
HbA1c(%)	6.6	6.4	6.4	6,9
Diabetes Auto-antibodies	Negative	Negative	Negative	Negative

Table II. Glucose and insulin concentrations during a standard oral glucose tolerance test with 75 g glucose equivalent

Time (min)	Proband		Sister 1		Sister 2	
	Glucose (mg/dl)	Insulin (µIU/mL)	Glucose (mg/dl)	Insulin (µIU/mL)	Glucose (mg/dl)	Insulin (µIU/mL)
0	131	6,9	121	3	122	11
30	153	20	187	16	139	24
60	178	20	201	28	179	51
90	176	29	170	20	159	40
120	159	27	146	18	150	31

ESPE 2015 707--P3
Diabetes 1
SEYIT AHMET UCAKTURK
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology