Hyperglycaemia in a boy of 13 years old: Not always Type 1 Diabetes Mellitus. A case report

Zacharoula Karabouta[1], Amalia Sertedaki [2]

[1] 2nd Paediatric Department, University General Hospital AHEPA, Thessaloniki, Greece
[2] Division of Endocrinology, Metabolism and Diabetes, First Department of Pediatrics, University of Athens Medical School, 'Aghia Sophia' Children's Hospital, Athens,Greece

Topic:Diabetes

Disclosure:No conflict of interest

Introduction

Type 1 Diabetes (T1D), the most frequent type of diabetes in Paediatrics, can be easily misdiagnosed.

Objectives

We report a 13 year old boy with monogenic diabetes, initially diagnosed and treated as T1D.

Methods

The patient presented at 7.5 years of age with a febrile illness and mild hyperglycaemia. An Oral Glucose Tolerance Test (OGTT) then was normal, HbA1c 6.3% (45 mmol/mol), (table 1). Slowly progressing T1D was diagnosed; he stayed under follow-up with routine BMstix measuring at home (max blood glucose (BG) 153 mg/dl (8.5mmol/l). A repeat OGTT at the age of 9y showed BG 127mg/dl (7.1mmol/l) at 0' and 258 mg/dl (14.3mmol/l) at 120', HbA1c 6.7% (50mmol/mol) (tabl. 2). He started on small doses of insulin. His glycaemic control was excellent; he remained on small doses of insulin (0.1U/Kg/d) for four years. The patient discontinued insulin without medical advice. Six months later, he had mild fasting hyperglycaemia, (BG 107-148mg/dl (6-8mmol/l)), HbA1c 6.2% (44 mmol/mol); Anti-GAD, ICA and IA2 were negative (tabl 3). OGTTs were normal for father and younger sister aged 2 years. His mother, 37 year old, had gestational diabetes, her OGTT showed BG 147mg/dl (8.2 mmol/l) at 0' and 121mg/dl (6.7mmol/l) at 120', HbA1c 6.4% (46mmol/l); negative anti-IA2 antibodies. DNA analysis was carried out for the presence of mutations in *HNF1A* and *GCK* genes employing bidirectional sequencing of the coding regions of the two genes. MLPA was employed to search for deletions in the genes *GCK, HNF1A, HNF4A, HNF1B*.

Table 1. Initial OGTT, age 7.5 y old

	0'	120'
Glu (mg/dl)	115 (6.4 mmol/l)	91 (5 mmol/l)
HBA1c (4.3-5.7%)	6.3% (45.4 mmol/l)	

Table 2. OGTT, age 9 y old

	0'	120'
Glu (mg/dl)	127 (7.0 mmol/l)	258 (14.3 mmol/l)
Ins (mIU/ml)	7.3	78
HbA1c (4.3-5.7%)	6.7% (49.7 mmol/l)	

Table 3. OGTT, 13y old

6 months after no insulin Tx	0'	60'	120
Glu (mg/dl)	120 (6.7 mmol/l)	170 (9.4 mmol/l)	97 (5.4 mmol/l)
Ins (2.6-25 mIU/ml)	8.3		
C-peptide (0.5-4.4ng/ml)	1.9		
HbA1c (4.3-5.7%)	6.2% (44/3 mmol/l)		

Results

Point mutations were not detected in the genes *GCK* and *HNF1A*. The MLPA revealed that the patient and his mother harbor a heterozygote *GCK* gene deletion (exons1-10), confirming the diagnosis of maturity onset diabetes of the young type 2 (MODY 2).

Conclusions

MODY is a heterogeneous group of monogenic diabetes that result in β-cell dysfunction (table 4, 5 &6). Diagnosis in paediatric patients may be challenging. It has an estimated prevalence of just 1%-2% of all diabetes in industrialized countries, however this prevalence is probably underestimated since large population screening studies have not been performed. MODY2 is characterized by mildly elevated fasting blood sugars and HbA1c ranging from 5.6–7.6% (38-60 mmol/mol). It is frequently unrecognized or misdiagnosed as T1D or T2D, resulting in unnecessary insulin treatment The suggested treatment for MODY 2 is normally a lifestyle modification with regular physical activity and a well balanced diet. Molecular diagnosis is, therefore, very important for recognising the type of MODY, deciding the appropriate treatment for the patient and providing a reliable long term prognosis for individual patients and their relatives.

Table 4. MODY types

MODY type	Frequency (% from MODYs)	Age at dg (y)	Hyperglycemia	Complications	Other features	Treatment
GKC	**15-20**	**newborn or older**	**Mild**	**Very rare**	**Mild hyperglycemia already from newborn, homozygote: PNDM**	**Diet**
HNF-4A	5	From puberty	Progressive	as T1D	Neonatal hyperinsulinemia, LGA, low triglyserides	OHA or insulin
HNF-1A	**almost 60**	**From puberty**	**Progressive**	**as T1D**	**reduced renal glucose treashhold**	**OHA or insulin**
HNF-1B	2	> 20	Progressive	as T1D	Renal anomalies, renal insufficiency, pancreatic hypoplasia, genital anomalies	OHA or insulin
Pdx1	< 1	> 35	Progressive	N.A	Homozygote: pancreatic agenesis	Diet or OHA or insulin
Ins	2	Infant to adult	Varies	Mild but can be as T1D	Can also present as PNDM	Diet or OHA or insulin
CEL	< 1	> 30	N.A	N.A	Exocrine insufficiency, lipomatosis	OHA or insulin
NeuroD	< 1	20-30	Progressive	N.A	Homozygote: PNDM and neurological abnormalities	OHA or insulin
KLF11	< 1	20-30	Variable	N.A	N.A.	OHA or insulin
Pax4	< 1	> 20	Progressive	N.A	N.A.	Diet or OHA or insulin
Kir6.2	< 1	From early puberty to adulthood	Variable	N.A	Homozygote: neonatal diabetes	Diet or OHA or insulin
SUR1	< 1	From early puberty to adulthood	Variable	N.A	Homozygote: permanent neonatal diabetes; heterozygote: transient neonatal diabetes	OHA (sulphonylurea)

Table 5. MODY2 pathophysiology

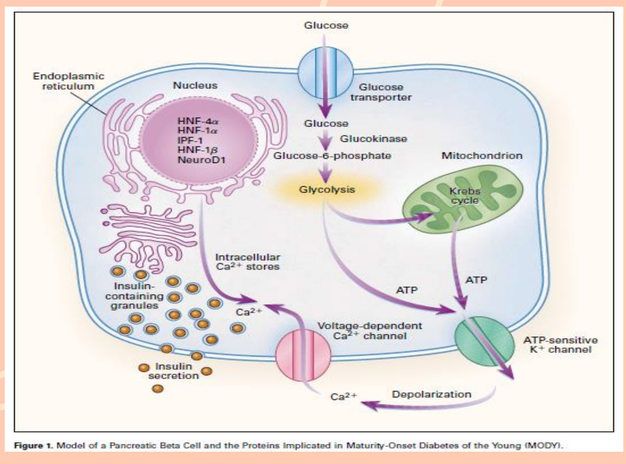

Figure 1. Model of a Pancreatic Beta Cell and the Proteins Implicated in Maturity-Onset Diabetes of the Young (MODY).

Table 6. MODY2 inheritance

References:

1. Afonso P, Ferraria N, Carvalho A, Castro SV. Maturity onset diabetes of young type 2 due to novel de novo GKC mutation. Arq Bras Endocrinol Metabol. 2014 Oct;58(7):772-5
2. Bacon S et al. The clinical management of hyperglycemia in pregnancy complicated by maturity-onset diabetes of the young. Am J Obstet Gynecol. 2015 Aug;213(2):236.e1-7. doi: 10.1016/j.ajog.2015.04.037. Epub 2015 Apr 30
3. Bosma AR et al..A genetic diagnosis of maturity-onset diabetes of the young (MODY): experiences of patients and family members. Diabet Med. 2015 Oct;32(10):1385-92. doi: 10.1111/dme.12742. Epub 2015 Mar 28
4. Flack JR, Ross GP, Cheung NW.GKC monogenic diabetes and gestational diabetes: possible diagnosis on clinical grounds. Diabet Med. 2015 Dec;32(12):1596-601. doi: 10.1111/dme.12830. Epub 2015 Jul 2
5. Kleinberger JW, Pollin T. Undiagnosed MODY: Time for action. Curr Diab Rep. 2015 Dec;15(12):110. doi: 10.1007/s11892-015-0681-7. Review
6. Langer S, Platz C, Waterstradt R, Baltrusch S. Characterization of two MODY2 mutations with different susceptibility to activation. Biochem Biophys Res Commun. 2015 Sep 4;464(4):1113-9. doi: 10.1016/j.bbrc.2015.07.088. Epub 2015 Jul 21

55th Annual ESPE Meeting, 10-12 September 2016, Paris, France

55ESPE 320--P2

Diabetes

Zacharoula Karabouta

DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS 10-12 SEPTEMBER