MATURITY ONSET DIABETES OF THE YOUNG: JUST THINK ABOUT IT

A. MESSAAOUI, S. TENOUTASSE, H. DORCHY
UNIVERSITY CHILDREN'S HOSPITAL QUEEN FABIOLA, UNIVERSITÉ LIBRE DE BRUXELLES, BRUSSELS, BELGIUM

- **INTRODUCTION:** Maturity Onset Diabetes of the Young (MODY) is a monogenic form of diabetes with onset in patients aged less than 25 years. It is a heterogeneous disorder due to heterozygous monogenic mutations with an autosomal dominant transmission. It represents 2 to 5 percent of diabetes but is often underdiagnosed. We report three different cases of MODY.

- **CASE REPORT 1:** a nine-year-old boy with a BMI of 24.5 kg/m² (> P97) presented with diabetes: glucose level was 283 mg/dl and HbA1c 9.7% (83 mmol/mol; N 4.0-6.2%). He was born to non consanguineous Armenian parents. The mother has diabetes insulin treated. His sister has diabetes and obesity treated with metformin. IAA, ICA, GADA and IA2A were negative. HLA-DQ was not at risk for type 1 diabetes. Mutation c.392G>A (p.Arg131Gln) was found in the hepatocyte nuclear factor-1-alpha, which causes MODY 3. Initial treatment consisted of Repaglinide but after two years, the patient requires insulin (0.8 U/kg/d). The same mutation was found in his mother and his sister.

- **CASE REPORT 2:** thirteen-year-old girl with a BMI of 22.8 kg/m² (P 90-97) presented with pre-diabetes: fasting glucose level was 115 mg/dl. She was born to non consanguineous Bolivian parents. The mother has diabetes treated with oral diabetes medications. There were no insulin resistance with fasting insulin 6.1 µUI/ml and HOMA-IR 1.71 (P75-90). IAA, ICA, GADA and IA2A were negative. Mutation c.898G>A (p.Glu300Lys) was found in the glucokinase gene, which causes MODY 2. Metformin was given three times a day and, currently, her HbA1c is 6.7 % (50 mmol/mol). The mutation was not found in the mother.

- **CASE REPORT 3:** a nine-year-old Caucasian girl presented with polyurodipsia. Serum glucose level was 275 mg/dl and HbA1c 6.2% (44 mmol/mol). Medical history revealed bilateral renal dysplasia with renal insufficiency and renal graft. Homozygous mutation c.1235C>G (p.Pro412Arg) was found in the hepatocyte nuclear factor-1-beta gene, which causes MODY 5. Insulin was given twice daily (0.5 U/kg/d).

Type of MODY	1	2	3
Genetic defect	HNF-4-alpha	Glucokinase gene	HNF-1-alpha
Chromosome	20	7	12
Frequency	< 10%	15-30 %	52-65%
Age of diagnosis	Adolescents, young adults	From birth	Adolescents, young adults
Hyperglycemia	Severe	Mild and stable	Severe
Clinical features	Diabetes	Diabetes	Glycosuria and diabetes
Optimal traitement	Sulfonylurea - insulin	Diet	Sulfonylurea - insulin
Risk of complications	Yes	Rare	Yes

- **DISCUSSION:** We highlight here the features of three subtypes of MODY, two without associated abnormalities and one with renal disorder. Mutations concern genes that are directly involved in the beta cell function. In patients with nonsyndromic diabetes, more than 99 % of MODY result from mutations in hepatocyte nuclear factor-1-alpha (formerly MODY 3), glucokinase (MODY 2), or HNF-4-alpha (MODY 1). The symptoms manifest slowly with the absence of obesity and ketosis in most cases. MODY is usually treated by diet, oral diabetes medications and insulin. Treatment and prognosis vary depending on the genetic mutation.

CONCLUSION: Clinicians should keep in mind the possibility of MODY, especially in antibody-negative youth with familial diabetes. To make a diagnosis of MODY can have important implications for the guidance of appropriate treatment, prognosis and genetic counselling.

AM2015

ESPE 2015 763--P3

Diabetes 2

Anissa Messaaoui

DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology

PosterSessionOnline.com