Maturity Onset Diabetes of Youth (MODY) in a patient with VATER syndrome

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Introduction

- VATER syndrome is a rare, usually sporadic, entity, including ≥2 of the following: vertebral defects (V), anal atresia (A), tracheoesophageal fistula, esophageal atresia (TE) and radial or renal dysplasia (R).

- Maturity Onset Diabetes of Youth (MODY) is a usually non-insulin-dependent type of monogenic diabetes mellitus (DM), usually in adults <25 years, with autosomal dominant inheritance, without the features of metabolic syndrome.

Case report

At admission:
A 25-year-old Caucasian male with VATER syndrome was admitted to our department due to newly diagnosed DM on occasion of polydipsia and polyuria, without ketoacidosis [fasting plasma glucose (FPG) levels: 355 mg/dl, glycosylated hemoglobin (HbA1c): 12.6%].

Medical history and physical examination:
Clinical examination was remarkable for a low body mass index (18.28 kg/m²), muscular weakness of the extremities and hearing loss.
His family history was positive for non-insulin dependent DM (diagnosed at 35 years, without the classical features of metabolic syndrome).

Laboratory findings:
Investigation for autoantibodies to glutamic acid decarboxylase (GAD), insulin, islet cells and tyrosine phosphatase (IA2) was negative.
During an oral-glucose-tolerance-test (OGTT), FPG, fasting insulin and C-peptide levels at baseline were: 150 mg/dl, 2 mIU/ml (normal: 6-27) and 1.07 ng/ml (normal: 0.9-7.1), and 2h after glucose 75 g: 256 mg/dl, 11.7 mIU/ml and 3.38 ng/ml, respectively.

Management and patient’s clinical course:
He was treated with glimepiride 2 mg/day. At 3 months, HbA1c fell to 5.9%.
He remained on glimepiride for 1 year, when due to glucose control deterioration, insulin was started.

He fulfills the 5 criteria of MODY:
- early-age newly DM with normal insulin and C-peptide levels
- positive family history for DM
- >90 mg/dl increase in plasma glucose during OGTT
- glycosuria with relatively normal FPG
- responsiveness to sulfonylureas

Genetic analysis for MODY 3 (the most common) was negative. Further testing to rule out mitochondrial diabetes is under way.

Conclusions

This is the first case reporting the co-existence of MODY with VATER syndrome.
The exact pathogenetic mechanisms linking these entities are currently unknown.

References