ABCC8 MODY in an Obese Adolescent Misdiagnosed with Type 2 Diabetes

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Background-Aim

The *ABCC8* gene encodes the sulfonylurea receptor 1 (SUR1) subunit of the pancreatic beta cell ATP-sensitive potassium (KATP) channel. Activating mutations in the *ABCC8* gene cause both transient and permanent neonatal diabetes mellitus (DM) or MODY 12. In relation to the variant in the *ABCC8* gene, patients may also present with either neonatal hyperinsulinism and/or DM later in life. Besides, the same variant can cause different phenotypic features among family members. Response to the sulfonylurea treatment may vary between patients.

Aim: To present the clinical features and response to sulfonylurea treatment in an obese adolescent misdiagnosed with type 2 DM, who was later found to have a heterozygous variant in the *ABCC8* gene.

Case

13 years old, girl
Complaint: Hyperglycemia in routine laboratory examinations, no additional complaints (polyuria, polydipsia, nocturia, weight loss etc.)
Medical history: Term, 4500 g birth weight, no chronic disease and hypoglycemia/hyperglysemia in the neonatal period
Family history: Unrelated parents
Mother,diabetes mellitus for 3 years, oral anti-diabetic treatment
Father, diabetes mellitus for 6 years, insulin treatment
Grandmother, diabetes mellitus, oral anti-diabetic treatment

Physical examination

- **Weight +3.43 SDS**
- Height +1.22 SDS
- **BMI +2.63 SDS**
- Puberty Tanner stage V
- **Acanthosis nigricans +**
- Rest of the physical examination normal

Laboratory findings (at diagnosis)

- **Fasting serum glucose: 332 mg/dL** (N, 60-100)
- **Fasting insulin: 37.4 mIU/mL** (N, 2.6-24.9)
- C-peptide: 5.69 ng/mL (N, 0.9-7.1)
- **HbA1c: 10.4%** (N, 4-6%)
- Anti-glutamic acid decarboxylase: Negative
- Anti insulin antibody: Negative
- Urine ketones: Negative
- Blood gas analysis: Normal

Clinical Follow-up

- Type 2 diabetes mellitus
  Metformin
  (2x 1000 mg)
  Insulin glargine
  (0.25 U/kg/day)
- High blood glucose measurements
  High HbA1c
  Insulin aspart
- Diabetes in three generations
  Negative diabetes antibodies
  Unable to discontinue insulin
  MODY?
- **NGS of MODY genes**
  (*GCK*, *HNF1A*, *HNF1B*, *HNF4A*, *KCNJ11*, *INS* and *ABCC8* genes)
  c.1252 T>C heterozygous variant in the *ABCC8* gene (previously defined)
- Discontinuation of metformin and insulin aspart
  Gliclazide (120 mg/day)
  Insulin glargine (0.7 U/kg/day)

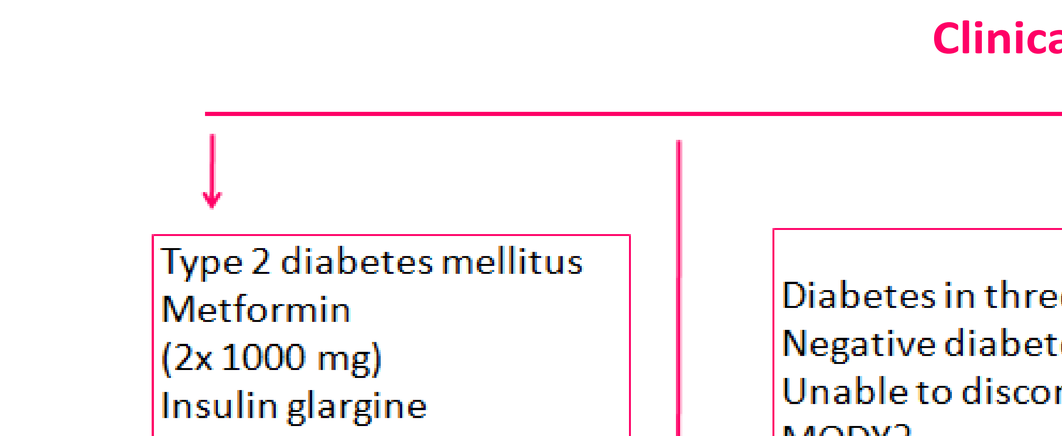

Figure 1. Pedigree

Conclusion

Identification of a MODY subtype is crucial for the choice of adequate treatment. Molecular genetic analyses of MODY genes in patients with apparent type 2 DM, who have a strong family history of DM and on-going need for insulin treatment, may provide accurate diagnosis. Diabetic patients with mutations in *ABCC8* are usually responsive to treatment with sulfonylurea. In these cases, transition from insulin to sulfonylurea therapy may allow better glycemic control and improvement in the quality of life.