A novel variant HNF1A gene (HNF1A-MODY) in a patient presenting with hyperglycaemia and glucosuria

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INTRODUCTION

HNF1A-MODY (MODY3) is a common subtype of the Maturity Onset Diabetes of the Young (MODY), a monogenic autosomal dominant disease presenting as a nonketotic diabetes with onset usually during adolescence, or early adulthood.

HNF1A-MODY is less common among children as the hyperglycaemia usually manifests after 10th year of life.

AIM

We describe a young girl presented with hyperglycaemia and glucosuria.

METHOD

Presentation: An 8.5-year-old girl presented with abdominal pain, nausea, elevated serum blood glucose (BG) 288 mg/dl (16 mmol/l), glucosuria (+++), hyperglycaemia and glucosuria first appeared at 60 months of age.

Clinical course: Pre-and post-prandial BMStix returned to normal range, urine was negative for glucose.

Treatment: intravenous N/S 0.9%, no insulin.

Laboratory tests on admission:
- Oral glucose tolerance tests (OGTT) (table 1)
- Blood gas: pH 7.44, HCO3, 22.4 mmol/l, BE -2.3 mmol/L
- Urine: glucosuria, no ketones; later normal.

RESULTS

Initial diagnosis: newly developing type 1 Diabetes (T1D).

Further screening:
- Autoantibody screen: Anti-GAD, IAA, ICA negative

Previous history:
- one of dizygotic twins, born at 36 wks gestation

Unrelated parents

Growth on the 50th percentile, prepubertal

Family history:
- Father, 51 years old, on treatment for arterial hypertension and presumed type 2 Diabetes (T2D) for the last decade

- Mother and twin brother healthy

Patient was discharged home on glucose self-monitoring (BMStix), OGTT periodically (table 2), and follow up in clinic.

Genetic testing: both patient and her father are heterozygous in HNF1A gene for a novel variant c.454>C (p.T152P ) that was confirmed by Sanger Sequencing exon 2 of HNF1A gene.

HFN1A is expressed in pancreatic β cells and hepatocytes. While the underlying mechanism is not well understood, the mutations relate to reduced insulin secretion in response to rising blood glucose levels.

CONCLUSIONS

- HNF1A-MODY patients could easily be misclassified as T1D or T2D

- Most patients will need pharmacological treatment as they show progressive deterioration in glycaemic control.

- Patients are extremely sensitive to sulfonylureas.

- Molecular genetic diagnosis of the MODY subtype is of utmost importance for clinical diagnosis, disease progression, prognosis and family counselling.

REFERENCES


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