Un caso poco habitual de diabetes
An uncommon cause of diabetes

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ABSTRACT

Patients with Maturity Onset Diabetes of the Young (MODY) are often misclassified as having type 1 or type 2 diabetes and, as a result, are given inappropriate therapy. This case report aims to draw attention to MODY as a possible diagnosis in young diabetic patients. Biomarkers in combination with clinical characteristics, can help identify patients who should receive genetic testing. Rapid referral for genetic testing can avoid insulin use and establish optimal treatment. Furthermore, the knowledge of the genetic etiology will enable more-appropriate treatment, better prediction of disease progression, screening of family members and genetic counseling.

Keywords: Diabetes, Genetics, Disease

INTRODUCTION

Maturity Onset Diabetes of the Young (MODY) is a rare but increasingly recognized cause of diabetes among young people\(^1\). It is likely to account for 1% to 2% of all cases of diabetes\(^1,2,3\). MODY is the most common form of monogenic diabetes and is the result of mutations in genes that are responsible for the development or function of beta cells\(^3\). Accurate, population-based prevalence estimates of MODY are difficult to obtain because the majority of cases are misclassified as type 1 or type 2 diabetes\(^1\).

CASE REPORT

A 34-year-old diabetic woman with asthma and hypertension was diagnosed with type 1 diabetes at the age of 16. At that time, she had no symptoms of insulin deficiency and had normal renal function. Because she maintained a very poor metabolic control for years (despite being treated with high dosage of insulin) she developed microvascular complications (bilateral diabetic retinopathy, stage 3 chronic kidney disease and distal sensorimotor neuropathy) with no evidence of macrovascular complications. Family history displayed diabetes in three consecutive generations (Figure 1). Physical examination revealed an oriented and collaborative patient, with uncharacteristic facies, impaired visual acuity and her body mass index was 22kg/m\(^2\). Blood pressure was 130/80mmHg, cardiovascular and respiratory examination were unremarkable. Peripheral pulses of the feet were absent and distal sensorimotor neuropathy and ankle edema were present.

In June of 2014, laboratory test results revealed a HbA1c of 14% with no records of hypoglycemia. The pancreatic autoantibodies (AntiGlutamic Acid Decarboxylase 65; Islet cell antibodies; Insulin antibodies) were negative. C peptide, a marker of endogenous insulin production, co-secreted with insulin, was 7,03ng/mL (reference range 1,1-4,4ng/mL). Gliclazide 30 mg once daily was commenced in July 2014 with good response. Regular contact was maintained. A mutation in HNF1A gene was identified, confirming the diagnosis of HNF1A-MODY. Her mother and sister presented the same mutation. This patient is currently (August, 2018) undergoing hemodialysis, has a HbA1c of 6% and requires no pharmacological treatment for diabetes.

DISCUSSION

MODY is an autosomal dominant disease, with a multigenerational family history of diabetes\(^1\). The onset is usually before the age of 25 and the affected patients don’t have pancreatic autoimmunity or insulin resistance\(^1,2\). A typical patient with MODY presents with diabetes in the second to fourth decade of life and have a subacute or incidental presentation without ketosis. He is usually non-obese and doesn’t have features of insulin resistance or other conditions as dyslipidemia, hypertension or fatty liver disease\(^2,4\). Absence of autoantibodies for pancreatic antigens and evidence of endogenous insulin production with the detection of measurable of normal C-peptide are characteristic of MODY\(^5\).

Several different genetic abnormalities have been identified\(^4\). The most common are mutations in the hepatic nuclear factors 1A and 4A and glucokinase (GCK), each leading to a different phenotype\(^1\). GCK and HNF1A mutations account for roughly 70% of all cases of MODY\(^6\). HNF1A-MODY and HNF4A-MODY have very similar clinical features and...
patients can be successfully treated with a small dose of sulfonylurea in monotherapy as opposed to injected insulin\textsuperscript{2}. Most patients respond well to this treatment, with HbA1c remaining at target for many years\textsuperscript{2}. GCK-MODY, caused by an altered set point for glucose sensing, may not require any treatment or alterations in diet\textsuperscript{5,6}. It is characterized for mild asymptomatic hyperglycemia without significant postprandial glucose increment\textsuperscript{2}.

In some cases, other clinical features are present besides diabetes. For instance, mitochondrial diabetes is associated with deafness and HNF1B mutations with renal cysts and genitourinary abnormalities\textsuperscript{3}. In conclusion, the authors emphasize that although MODY is a rare diagnosis, it has important implications. Individually, it allows a better treatment option (eg, sulphonylureas in HNF1A and HNF4A mutations) or obviates the need of treatment (in the case of mild hyperglycemia in GCK mutations)\textsuperscript{3}. It also predicts future course of the illness. Furthermore, family members of affected MODY patients can be screened for their carrier status to predict disease\textsuperscript{6,7}. In a young patient with non-acute presentation of diabetes, absence of beta cell autoimmunity and no signs of insulin resistance it is important to consider monogenic diabetes.

**REFERENCES**