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Case Report / Olgu sunumu

A Case of Maturity Onset Diabetes of the Young: Just Keep of Mind

MODY Tip Diyabet Olgu Sunumu: Sadece Akılda Tutun

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Abstract

Maturity onset diabetes of the young (MODY) is a monogenic, autosomal dominant form of diabetes characterised by mutations in genes resulting in dysfunction of pancreatic β-cells and subsequent insulin production. HNF1A-MODY is nonketotic diabetes with onset during childhood, adolescence, or early adulthood, progressive character of hyperglycemia with a high risk for chronic microvascular diabetes complications.[1] We present a child with HNF1A-MODY due to a likely pathogenic mutation HNF1-A gene (c,787C > T(p.R263C) (c.Arg263ys)) diagnosed incidentally.

Keywords: MODY, hyperglycemia, diabetes

Öz

MODY tip diyabet , pankreas β hücrelerinin işlev bozukluğu ve ardından insülin üretimi ile sonuçlanan , monojenik, otozomal dominant bir diyabet formudur. MODY, kronik mikrovasküler diyabet komplikasyonları açısından yüksek riskli, hipergliseminin ilerleyici karakterde olduğu , çocukluk, ergenlik veya erken yetişkinlik döneminde başlayan, ketotik olmayan diyabet tipidir.[1] Bu yazıda rastlantısal tanı alan HNF1-A genine (c, 787C> T (p.R263C) (c.Arg263ys)) gen mutasyonuna bağlı HNF1A-MODY'li bir hasta sunuldu.

Anahtar kelimeler: MODY, hiperglisemi, diyabet

INTRODUCTION

Diabetes mellitus is commonly known to be divided into type 1 and type 2, both with etiologies involving complex interplay between multiple genetic and environmental factors. In addition and less well-known, there is a third category of diabetes with specific etiologies including diabetes secondary to a drug, transplant, injury, or other genetic or non-genetic illness; and syndromic and non-syndromic forms caused by a mutation in a single gene. MODY is one of the most well-known forms of monogenic diabetes.[2] Genetic variants of 13 known genes cause MODY through pancreatic beta cell dysfunction that leads to elevated blood glucose. MODY is estimated to make up at least 1% of all cases of diabetes. The three most common forms of MODY are caused by mutations in HNF4A, GCK, and HNF1A, and they make up the majority of all MODY cases.[3,4]

CASE REPORT

A 13 year old male syrian refugee patient referred from ophtalmology department because of hyperglycemia. He was hospitalized with the diagnosis of iridocyclitis. His blood glucose level was 1066 mg/dl in the absence of ketoacidosis. There was no ketonuria or glycosuria. He had not any complaint or symptoms. Initial glycosylated haemoglobin (HbA1c) was 20.7%. His body weight was 52 kg (0.16 sds), with a height of 162 cm (0.72 sds).He was at Tanner stage III. The rest of the physical examination were normal. Treatment was started in the form of multiple-dose insulin with basal insulin (glargine) and bolus insulin (aspart), resulting in acceptable blood glucose levels. The celiac disease markers were negative, and the thyroid profile was normal. Microalbuminuria proved negative. The other study findings at the start of diabetes, with cardiological, ophthalmological

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and neurological evaluations were normal. The family history revealed type 2 diabetes mellitus in the father and grandmother. GAD autoantibodies and AI2 autoantibodies were negative.After negative antibodies were confirmed, and together with the described family history, absence of ketoacidosis unusually with extreme hyperglicemia a MODY study was made, which revealed a heterozygote mutation on HNF1-A gene (c,787C > T(p.R263C) (c.Arg263ys)).

With the confirmed diagnosis of MODY-3,we planned to change treatment with sulfonylureas.We tried to reach the patient, but could not succeed because of lack of contact information. The current status of the patient is unknown.

DISCUSSION

Maturity onset diabetes of the young comprises a distinct group of monogenic and autosomal dominant inherited forms of diabetes mellitus due to β-cell dysfunction with onset at a young age.

MODY is caused by mutations resulting in pancreatic β-cell dysfunction in the production or excretion of insulin.

As MODY shares clinical features with the more common forms of diabetes mellitus, the true prevalence is probably underestimated but but is estimated to be responsible for at least 1% of cases of diabetes mellitus.[3,4]

At present, mutations in 13 genes linked to different types of MODY have been identified. In general, GCK-MODY and HNF1A-MODY each represent 20-70% of all cases.

Mutations in the GCK gene cause a mild, asymptomatic and non-progressive fasting hyperglycaemia from birth usually requiring no treatment. In contrast, mutations in the genes encoding the transcription factors HNF1A cause a progressive insulin secretory defect and hyperglycaemia that can lead to vascular complications.[5]

The diabetes in HNF1A-MODY typically presents in adolescence or early adulthood before the age of 25 years These patients are born with normal glycaemia, tend to be slim and have normal insulin sensitivity.[6,7]

Microvascular and macrovascular complications are observed in HNF1A-MODY and are related to poor glycaemic control.[8]

Patients with HNF1A MODY have some interesting extra-pancreatic features reflecting that the HNF1A gene is expressed in tissues outside the pancreas.

These patients have glycosuria because of a low renal threshold for glucose, thought to be due to reduced expression of the sodiumglucose cotransporter 2 (SGLT-2) and reduced glucose reabsorption in the proximal tubule.[9]

In addition, these patients have a higher than normal high density lipoprotein (HDL) cholesterol concentration.This observation may be predicted to decrease cardiovascular risk, but despite the high HDL cholesterol, incidence of coronary heart disease is greater in HNF1A-MODY than in patients with Type 1 diabetes but less than those with Type 2 diabetes.[10]

Patients with HNF1A mutations show marked sensitivity to the oral sulphonylurea. Despite the efficacy of sulfonylurea derivative treatment insulin therapy may be required in some patients as β-cell dysfunction progresses.[5]

Since MODY-3 is an unusual form of diabetes in paediatric patients, we consider the publication of this case. We underline the importance of clinical suspicion in establishing a proper diagnosis. As progression of diabetes is generally slow in MODY patients, early diagnosis and start of appropriate treatment might reduce the risk of diabetic complications.

ETHICAL CONSIDERATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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