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Oral Therapy in a Diabetic Patient With History of Infantile Hyperinsulinism

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Dear editor,

Hyperinsulinism is the most common cause of persistent hypoglycemia in early infancy (1). Loss of function mutation in HNF4A gene is an unusual cause of this disease (2). HNF4A protein is a homodimer nuclear transcription factor with 474 amino acids which plays a role in 22 identified pathways. Mutations in this gene cause deficiency in regulation of beta-cell development and nuclear receptors transcription pathways, associated with maturity onset diabetes of Young (MODY) and HNF4A-related hyperinsulinism (3, 4).

Association of hyperinsulinemia in infancy and diabetes in adolescence has been reported only in patients with HNF4A mutations (4).

We present a patient with hyperinsulinmia in infancy and diabetes in adolescence without HNF4A mutation and with good response to oral hypoglycemic agents.

In infancy, this patient presented with persistent hyperinsulinemic hypoglycemia. He was on oral diazoxide until 3 years of age when this drug was tapered and discontinued. Genetic study was not performed at that time due to limitation of facilities. After that time, his blood sugar was normal until 15 years of age when he presented with diabetes mellitus. Starting HbA1c was 9.5%.

In addition, fasting triglyceride level and cholesterol level was 66 mg/dL and 168 mg/dL, respectively. Other routine laboratory studies were within the normal range. Pancreas anatomy was also normal in ultrasonography.

At the time of manifestation of diabetes, he was 162 cm tall (about 25th percentile for sex and age) and 51 kg (about 25th percentile for sex and age). He did not have any family history of diabetes.

Insulin therapy associated with oral sylfonylurea (Glibenclamid) was started with impression of monogenic diabetes. As he responded, insulin dose was gradually tapered and discontinued, and an α-glucodisase inhibitor (Acarbose) was started to improve his mild postprandial hyperglycemia. The treatment was continued with 0.1 mg/kg/day Glibenclamid and 50 mg Acarbose before each meal. Self-monitoring of blood glucose by the patient and most of the measurements were in the target range (70-130 mg/dL). After 4 months of treatment, HbA1c was 6.7%. He tolerated the medications well without any side effect.

According to previous history of the patient, the most probable diagnosis was HNF4α mutation. However, the results of HNF4α gene study by DNA sequencing method revealed no mutation and only a previously reported variant rs745975 C > T determined in nucleotide 5 of intron 1 (5). This variant was associated with Stearoyl-CoA desaturase 1 activity (6) and with type 2 diabetes mellitus (7).

History of hyperinsulinism in infancy, diabetes mellitus in adolescence, low plasma triglyceride level, and good response to oral hypoglycemic agents has been reported in previous cases of MODY type 1 with HNF4A mutation (8). Mutation in HNF4A was not found in the presented case and due to shortage of facilities, more genetic study was not performed, however, his clinical course is in favor of a type of monogenic diabetes. This case showed that some adolescent diabetic patients, even without family history of diabetes, and without clinical characteristics of type 2 diabetes may have good response to oral hypoglycemic agents. Further studies are needed to find more cases of monogenic diabetes in adolescents, and to determine which diabetic adolescent can be treated with oral agents. Also, it is recommended that in every patient whose diabetes commences in adolescence, a precise history about hypoglycemia of infancy should be obtained.

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Authors' Contributions

Hossein Moravej and Zohreh Karamizadeh contributed substantially to conception and design, acquisition of data, analysis and interpretation of data AND drafted the article. Omid Aryani contributed to laboratory analysis.

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