COMMENT ON WĘDRYCHOWICZ ET AL.

Like-Triple Diabetes as First Manifestation of MODY2 in an Overweight Teenager With Transient Multiple Antibodies. Diabetes Care 2014;37:e66–e67

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We read with interest the article by Wędrychowicz et al. (1). Maturity-onset diabetes of the young (MODY) is a heterogeneous group of monogenic forms of diabetes. Differential diagnosis with common forms such as type 1 and type 2 diabetes frequently poses a challenge to clinicians, especially in MODY forms caused by transcription factors. Glucokinase (*GCK*)-MODY stands out in this regard for displaying a rather constant phenotype (2).

We agree with the authors that the incidental association of obesity with *GCK* mutations can act as a diagnostic confounder. Moreover, coexistence of clinical features of both type 1 and type 2 diabetes is well described in the form of double diabetes. Individuals with type 1 diabetes can show a broad range of cardiovascular risk factors, such as dyslipidemia and hypertension, correlated with different degrees of glycemic control (3). Nevertheless, we feel some key elements to establish a causal role for both a *GCK* mutation and persistent islet autoimmunity are lacking from this patient description.

GCK-MODY phenotype is firmly established as a syndrome of early-onset mild fasting hyperglycemia, frequently in the nondiabetic or prediabetic range (2). Glucose excursions after an oral glucose challenge are closer to normal individuals than other types of diabetes. Therefore, the absence of available fasting glucose values for the patient and the relatively high 2-h value partially undermine the clinical hypothesis of *GCK*-MODY. Moreover, a detailed description of base and amino acid substitutions in the mutation would be necessary, as there is the possibility of a single nucleotide polymorphism. A previous description of functional studies of the mutation would also be helpful to establish the *GCK* mutation's causal role in this complex case. A more detailed description of clinical characteristics of other relatives with diabetes would be likewise necessary as it could simply reflect a pattern typical of type 2 diabetes, compatible with the finding of hyperinsulinemia and dyslipidemia. Furthermore, risperidone use also shows a frequent association with hyperglycemia, obesity, and dyslipidemia (4).

Islet autoantibodies may be present in asymptomatic individuals, mainly in relatives of patients with type 1 diabetes. Prospective studies demonstrated that appearance of multiple antibodies is usually sequential rather than simultaneous and that the number (two or more) of positive antibodies is a strong predictor of progression to overt type 1 diabetes. Patients with low titers of a single antibody may fluctuate, transiently showing negative values. However, remission of all antibodies in a patient with three different types of antibodies present is virtually unheard of, thus raising the possibility of methodological problems (5). This could render transient autoimmunity unlikely at this moment of the patient's history.

In conclusion, this can be regarded as a complex case of diabetes in the young. Previous obesity, hereditary predisposition to type 2 diabetes, and antipsychotic use may possibly converge in its pathogenesis. However, some diagnostic caveats should be solved and interpreted with caution, along with a longer clinical follow-up, before a diagnosis of triple diabetes is confirmed.

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