

OBSERVATIONS

Long-Standing Sulfonylurea Therapy After Pubertal Relapse of Neonatal Diabetes in a Case of Uniparental Paternal Isodisomy of Chromosome 6

Approximately 30% of cases of transient (relapsing) neonatal diabetes can be diagnosed by identifying anomalies of chromosome 6 (6q24). At the time of relapse of diabetes, β -cell function appears to be intact and β -cells able to secrete insulin while exhibiting a specific defect of insulin secretion after glucose stimulation similar to that in patients with mutations of the ATP-sensitive K^+ channel (1,2,3). However, in contrast with patients with mutations of the ATP-sensitive K^+ channel, 6q24 patients are usually treated with insulin or diet alone and not with oral agents (4).

We report on a patient with uniparental paternal isodisomy of chromosome 6 (UPD6) with good-to-fair glycemic control during long-standing sulfonylurea therapy started after diabetes relapsed at the age of 15 years. The boy was born at term with low birth weight (2,060 g) and no family history of diabetes except for a grandmother with type 2 diabetes. Diabetes was diagnosed within the first days of life and treated with insulin until he was 7 months of age. Postnatal growth and psychomotor development were normal. Finally, at the age of 15 years, he had an incidentally measured fasting glucose of up to 11 mmol/l. At that point, he was not ketotic and reported no symptoms of di-

abetes. At the time of relapse, he tested negatively for islet cell antibodies and for glukokinase gene mutations. Testing for anomalies of chromosome 6 indicated UPD6.

After having been incidentally given a dose of glibenclamide by his family doctor for the first time, the patient suffered an episode of symptomatic hypoglycemia. Because he declined insulin treatment and was obviously sensitive to sulfonylureas, we started him on 2 mg gliclazide daily (~ 0.04 mg/kg body wt). Glycemic control remained good for over 10 years with A1C levels between 5.7 and 7.8% (mean \pm SD $5.2 \pm 0.47\%$), and there were no episodes of symptomatic or severe hypoglycemia. Fasting blood glucose values were initially ~ 10 mmol/l with postprandial values up to 16 mmol/l. There were no episodes of ketosis. The patient is still treated with 2 mg gliclazide, and he has recently shown elevated A1C levels up to 8.5%. We suggested that his gliclazide dose be raised to 3 mg daily.

At his most recent follow-up at the age of 26 years, the patient was in good clinical condition without any signs of diabetes complications. Random levels of C-peptide were in the normal range (0.92, [range 0.36–1.45 nmol/l]), and his BMI was 26 kg/m². Until presently, only one other case of UPD6 treated with sulfonylurea has been reported, but, unfortunately, this second patient did not adhere to therapy and subsequently developed diabetes complications (2).

To our knowledge, this report presents the first case of relapsing transient neonatal diabetes caused by UPD6 and successfully treated with sulfonylurea for more than 11 years. Our case shows excellent long-term performance with oral sulfonylurea treatment and should encourage the use of this treatment for UPD6 patients after clinical relapse of diabetes.

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