OBSERVATIONS

Sulfonylrea Treatment in Permanent Neonatal Diabetes Due to G53D Mutation in the *KCNJ11* Gene

Improvement in glycemic control and neurological function

Previous studies have reported the successful switch from insulin to sulfonylrea therapy in some patients who have neonatal diabetes due to *KCNJ11* mutations (1); however, data on adults are limited (2,3). Also, it has not yet been determined whether neurological symptoms can be improved by the action of sulfonylrea therapy.

Here, we report the glycemic and neurological responses in an adult patient with the G53D mutation in the *KCNJ11* gene who was transferred from insulin to sulfonylurea.

A 26-year-old male patient was diagnosed with diabetes in the third month of life, and insulin treatment was initiated. Islet cell antibodies were negative. He showed severe learning difficulties and very poor attention. Crisis of generalized seizures started at age 5 years during episodes of hypoglycemia; his electroencephalogram was normal.

In 2006, the proband was found to have a heterozygous G53D mutation in the *KCNJ11* gene. In an attempt to switch from insulin to sulfonylrea therapy, glibenclamide was introduced. After 4 weeks, the patient no longer required insulin and was using 0.8 mg · kg^{-1} · day^{-1} glibenclamide; subsequently, the dose was reduced to 0.68 mg · kg^{-1} · day^{-1}.

Capillary glucose measurements showed that 3 months after starting glibenclamide therapy, mean glucose levels before lunch and dinner reduced from 185 ± 100 to 107 ± 45 mg/dl (P = 0.036) and from 225 ± 110 to 111 ± 41 mg/dl (P = 0.006), respectively. A 72-h continuous glucose monitoring showed that 76% of glycemic values were between 71 and 199 mg/dl. Postprandial C-peptide level was <0.05 ng/ml before sulfonylrea therapy and increased to 1.3 ng/ml during glibenclamide treatment.

The patient was given an identical battery of neuropsychological tests before and after initiating sulfonylrea therapy. At baseline, the patient showed low intellectual level (IQ: 52) and global impairment on cognitive functions. Retesting 3 months after initiating glibenclamide showed an important improvement in verbal performance, such as episodic verbal memory, visual naming ability, verbal learning, and long-term memory.

Here, we showed the effectiveness of sulfonylrea therapy in an adult patient carrying the G53D mutation in the *KCNJ11* gene. The change to sulfonylrea resulted in a marked improvement in diabetes control and quality of life. Also, an improvement on verbal performance was observed. It is very likely that the improvement observed in our patients' neurological status is related to the action of glibenclamide on sulfonylrea receptor 1 present in the neurons. However, we cannot exclude the possibility that the reduction of hypoglycemia may also have contributed.

In summary, this case illustrates that sulfonylrea treatment can be effective even in adult patients with neonatal diabetes due to *KCNJ11* mutations. Besides improvements on metabolic control and quality of life, sulfonylrea therapy also showed beneficial effect on neurological functions.

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