OBSERVATIONS

Diabetic Ketosis Caused by the Insulin Analog Aspart–Induced Anti-Insulin Antibody: Successful Treatment With the Newest Insulin Analog Glulisine

Anti-insulin antibodies induce immunological insulin resistance and poor diabetic control in insulin-treated diabetic patients. Recently, the prevalence and levels of anti-insulin antibodies have remarkably decreased as a consequence of the purity of insulin preparations and human insulin (1). The insulin analog insulin aspart exists as hexamers that rapidly dissociate into monomers and dimmers after the subcutaneous injection; therefore, insulin aspart is supposed to be less immunogenic than human recombinant insulin (2).

Here we report a type 1 diabetic patient who developed diabetic ketosis induced by severe insulin resistance caused by anti-insulin antibody after 6 years of insulin aspart use. He was treated with the newest insulin analog, insulin glulisine, which resulted in ameliorated glycemic control, reduced requirement of daily insulin, and decreased insulin binding rate by anti-insulin antibody.

A 48-year-old man developed type 1 diabetes in 2000. For the last 6 years, he has been treated with four daily insulin injections: three injections of insulin aspart before breakfast (6–8 units), lunch (6–8 units), and dinner (6–8 units) and one of insulin glargine (6 units) at bedtime. Home monitoring of blood glucose has not been performed for the last 3 years. He was admitted to hospital because of hypoglycemia in November 2009 and in July 2010. In August 2010, he was admitted to our hospital because of nausea and disturbed consciousness. His body weight was 49.4 kg and height 179.3 cm (BMI 15.4 kg/m^2). Plasma glucose (868 mg/dL) and HbA_{1c} (13.1%) levels were significantly elevated. A blood test revealed elevated serum total ketone bodies (5,770 μmol/L; normal, <130 μmol/L) and normal pH (pH = 7.366), suggesting the development of diabetic ketosis. Anti-insulin antibody (^{125}I-insulin binding rate, 43.9%; normal, <0.4%) level was significantly elevated. Switching from insulin aspart to insulin glulisine ameliorated his blood glucose levels. His blood glucose levels were 130–160 mg/dL by using 4, 4, and 6 units of insulin glulisine before breakfast, lunch, and dinner, respectively, and 6 units of insulin glargine at bedtime, and he was discharged in September 2010. His HbA_{1c} level and ^{125}I-insulin binding rate by anti-insulin antibody significantly decreased to 11.3 and 35.3%, respectively, after 4 months of insulin glulisine use.

The insulin glulisine molecule is more stable and less likely to self-associate, compared with human insulin, by the modification of the amino acid sequence at positions 3 and 29 in the B chain of human insulin (3). Therefore, unlike other insulin analogs, insulin glulisine allows for a viable drug product in the absence of hexamer-promoting zinc, which may provide immediate availability of insulin glulisine at the injection site for absorption (3). The characteristics of insulin glulisine such as the rapid absorption and being zinc-free may be associated with amelioration in anti-insulin antibody–mediated immunogenic insulin resistance in our case.

In summary, we suggest that insulin glulisine may be suitable for the treatment of patients with other insulin analog–mediated immunogenic insulin resistance.

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