OBSERVATIONS

Association of Type B Insulin Resistance and Type 1 Diabetes Resulting in Ketoacidosis

Type B insulin resistance (IR) is a rare autoimmune disease characterized by the presence of autoantibodies directed against the insulin receptor, resulting in a marked IR inducing hyperglycemia (1,2). We describe here what we believe to be a case of type 1 diabetes and ketoacidosis associated with type B IR syndrome.

A 55-year-old Caucasian European man with mild obesity (BMI 32.4 kg/m^2) was diagnosed as having type 2 diabetes. Insulin therapy was introduced after 3 years of oral antidiabetic therapy when weight loss suggested lack of insulin secretion. Four years after diagnosis, he developed a severe metabolic ketoacidosis. Continuous insulin infusion was promptly introduced, but ketones disappeared only after 6 days. Insulin requirement was exceptionally high (up to 5 units/kg/day for a 21.5 kg/m^2 BMI) despite the use of a continuous subcutaneous insulin infusion associated with metformin. Clinically, there was neither acanthosis nigricans nor lipodystrophy. Antiglutamic acid decarboxylase 65 (anti-GAD) antibodies were positive on two dosages (3,335 and 3,418 cpm). Triglycerides level was 1.35 mM. Serum IGF-1 was 193 ng/mL (normal range, 55–186 ng/mL) and serum adiponectin was 7.4 μg/mL (normal range, 2.5–6 μg/mL). Soluble nuclear antigen–specific antibodies, antineutrophilic cytoplasmic antibodies, antinuclear antibody, anticardiolipin antibodies, serum assay for tumoral tracers, HIV, and viral hepatitis serologies were negative. Pelvic thoracoabdominal computed tomography was normal. Breath test, serologies, and research in feces of *Helicobacter pylori* were negative.

Anti-insulin receptor autoantibodies, evaluated by their ability to compete with insulin for binding to its receptor in Chinese hamster ovary cells overexpressing the insulin receptor (3), were significantly positive. Half-maximal inhibition of insulin binding was observed at a serum dilution of 1:3 and confirmed using two successive samples from the patient.

In addition to the presence of insulin receptor autoantibodies, the major weight loss, the extreme IR, the clinical course of hyperglycemia, the unusual low triglyceride levels, and the paradoxical increase level of IGF-1 and adiponectin are compatible with the usual presentation of type B IR syndrome (2). In particular, although most states of IR are associated with low serum levels of adiponectin, it is not the case for insulin receptoropathies (4).

Systemic lupus erythematosus and other autoimmune features are common in type B IR syndrome (2). Recently, helicobacter pylori infection was reported to be involved in the development of insulin receptor autoantibodies, but it was not present in our patient. Poor glycemic control and weight loss after diabetes diagnosis and positivity of anti-GAD antibodies suggested diagnosis of latent autoimmune diabetes. Although some reports described the presence of insulin receptor autoantibodies in patients with type 1 diabetes, they were not associated with type B IR syndrome and could represent an anti-idiotypic response to anti-insulin autoantibodies (5). Interestingly, our patient did not present with anti-insulin antibodies.

One year later, insulin requirement spontaneously decreased to 0.5 unit/kg/day and HbA_{1c} was 6.8%. At the same time, anti-insulin receptor antibodies dosage became negative, whereas anti-GAD65 antibodies were still highly positive at 1,536 cpm. We suggest that spontaneous disappearance of circulating anti-insulin receptor autoantibodies explained the insulin sensitivity improvement (2).

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