Parsing Brittle Diabetes Takes Detective Work

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Diabetes patients whose lives are frequently disrupted by glycemic episodes requiring hospitalization need a multifaceted work-up to identify the cause of their brittle diabetes, Dr. Irl B. Hirsch said.

Compared with diabetes patients who have relatively stable and well-controlled glucose levels, patients with brittle diabetes tend to be younger and are more likely to be female, Dr. Hirsch said at a meeting sponsored by the American Diabetes Association. They also tend to have higher hemoglobin A_{1c} values and to use more insulin, and are more likely to have psychiatric disorders or psychosocial problems, including family disruption, adolescent crises, and personality disturbances, said Dr. Hirsch, professor of medicine at the University of Washington, Seattle.

Both physical and psychiatric problems can result in brittle diabetes. Look for the following to identify contributing factors, he said:

► **Counterregulatory hormone excess.** This can cause insulin resistance and make diabetes very difficult to control. Cushing's disease, acromegaly, pheochromocytoma, and glucagonoma are rare causes of insulin resistance to consider in the work-up of brittle diabetes.

► **Insulin antibodies.** These are worth measuring but have a low yield in these patients. "Unless the physical exam suggests a diagnosis of Cushing's disease or acromegaly or some endocrine disorder like that," go ahead and measure insulin antibodies, he said.

A potentially more productive approach is to measure both free and total insulin levels in a patient. A discrepancy in the results suggests that there's something binding up the insulin.

Be sure to use a clinical laboratory that knows how to measure free insulin, Dr. Hirsch cautioned. After the blood is drawn, several preparatory steps must be completed within 30 seconds before the sample is sent out to be assayed. "Not all labs do that," he said.

► **Celiac disease.** This occurs in approximately 7%-8% of childhood-onset type 1 diabetes patients and can lead to brittle diabetes. Screening for celiac disease typically focuses on identifying the transglutaminase IgA antibody, but 5% of the population lacks IgA, Dr. Hirsch warned. Before looking for the antibody, measure IgA levels to make sure they're normal. If IgA is absent, the antibody test "becomes worthless," he said.

Patients with brittle diabetes are more likely to have psychiatric disorders compared with patients whose glucose levels are relatively stable.

► **Gastroparesis.** Considering this "makes sense. If you have a mismatching of food and insulin, it makes the diabetes that much more difficult to control," Dr. Hirsch said.

► **Injection and pump sites.** Check these, because lipodystrophy may cause severe insulin resistance. Although the use of protease inhibitors is the most common cause of lipodystrophy in the general population, congenital lipodystrophy is the most frequent cause in Dr. Hirsch's patient population. Patients with congenital lipodystrophy typically get referred to him from a lipid clinic for severe hypertriglyceridemia and insulin resistance.

► **Timing of insulin injections.** Bad timing in relation to food intake probably is the most common mistake made in insulin therapy, he said. Problems with timing of injections usually won't disrupt a patient's life to the point of frequent hospitalizations, but they "certainly will cause glycemic instability," he said.

► **Psychological or psychiatric problems.** These can interfere with diabetes management, so a mental health evaluation is a key part of the work-up for most patients with brittle diabetes. Frequent episodes of diabetic ketoacidosis usually result from patients' not taking their insulin, Dr. Hirsch said. Severe depression can make it difficult for a patient to manage diabetes.

The mental health evaluation "is best performed by someone knowledgeable about diabetes, particularly with experience in eating disorders, because that's the big issue, especially in adolescents," he said. ■

Pages 16a—16b