

Case Study: Atypical Presentation of Diabetic Ketoacidosis in an Obese African-American Man

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Presentation

T.R., an obese 40-year-old African-American man with a medical history significant for hypertension, presented to the emergency department complaining of 5 days of weakness, abdominal pain, and upper respiratory symptoms. On further questioning, he also reported ~ 1 month of polyuria, polydipsia, and polyphagia accompanied by a 5-lb weight loss. No visual symptoms were noted.

His medical history included hypertension with antihypertensive noncompliance, an exploratory laparotomy for a gunshot wound, and a remote appendectomy. He denied the use of alcohol, tobacco, or illicit drugs. His family history was strongly positive for adult-onset diabetes, including one sibling who died of related complications.

On initial physical examination, he was afebrile, with a blood pressure of 140/90 mmHg and a heart rate in the 120 bpm range. Physical findings were remarkable for abdominal obesity and acanthosis nigricans.

Arterial blood gas revealed a pH of 7.31 and partial pressure of carbon dioxide of 22 and bicarbonate of 3. Serum chemistries revealed the following: serum sodium 144 mEq/l, potassium 6.9 mEq/l, bicarbonate 7 mEq/l, blood urea nitrogen 50 mg/dl, and creatinine 3.5 mg/dl. Serum glucose was 1,200 mg/dl. Serum acetone was detectable in moderate quantity. C-peptide was nondetectable. Urinalysis demonstrated glycosuria with moderate ketones and negative protein. Complete blood count was consistent with hemocentration and otherwise unremark-

able. Amylase, lipase, and thyroid-stimulating hormone were within normal limits. Hemoglobin A_{1c} (A1C) was 13.6%, and antibodies to GAD-65 were not detected. Myocardial ischemia and infectious processes were excluded.

T.R. was initially admitted to the medical intensive care unit and treated with intravenous fluid hydration and intravenous insulin infusion. His condition quickly stabilized, and he was converted to intensive subcutaneous insulin therapy with a regimen of glargine and aspart. Over a period of several days, the regimen was titrated according to blood glucose values, and he was discharged to home on a regimen of 85 units glargine before bedtime and 30 units of aspart before each meal, for a total daily insulin dose of 175 units. Fingerstick glucose readings were stable in the mid-100 mg/dl range. At discharge, he was also on an ACE inhibitor and statin therapy.

Questions

1. How would one classify T.R.'s type of diabetes based on his initial presentation? In what ways does this differ from traditional type 1 diabetes?
2. Will T.R. require lifelong treatment with multiple daily insulin injections? What are some other treatment options?
3. Was there an obvious precipitating cause for the ketoacidosis? What was the likely reason for his metabolic decompensation?
4. What is the importance of recognizing this type of presentation of diabetic ketoacidosis (DKA)?

Commentary

DKA was once thought to be specific to type 1 diabetes. However, it has more recently been recognized to occur in individuals with type 2 diabetes as well, especially in obese members of ethnic minority groups including Latinos and African Americans. The presentation is atypical and includes features of both classic type 1 and type 2 diabetes.

T.R. presented with marked dehydration and uncontrolled hyperglycemia, along with acidosis and ketosis resulting from deficient insulin secretion, as evidenced by a lack of detectable C-peptide. However, the phenotypic features of obesity, acanthosis nigricans, and marked insulin resistance are classically associated with type 2 diabetes.

The pathophysiology of traditional type 1 diabetes is an absolute insulin deficiency resulting from β -cell destruction, without significant insulin resistance. Exogenous insulin therapy is required for the prevention of ketosis and for survival.^{1,2} In contrast, the pathophysiology of type 2 diabetes is believed to be a relative insulin deficiency, with insulin resistance at the level of the adipocyte and skeletal muscle coupled with defective insulin secretion and progressive loss of β -cell function.

It is sometimes difficult to evaluate β -cell function in patients with diabetes, especially in the presence of DKA and the acute effects of glucotoxicity. One prospective study of patients presenting with DKA demonstrated a lower glucagon-mediated C-peptide response in obese patients with DKA versus those with only hyperglycemia. This suggests that reduced insulin secretion in the face

of progressive hyperglycemia and insulin resistance may lead to the development of ketosis in these patients.³

Patients with atypical or “idiopathic” type 1 diabetes often present with unprovoked ketosis and DKA consistent with classical type 1 diabetes. However, after initial insulinization, the clinical course is often very different, with recovery of β -cell function and maintenance of normal or near-normal glycemic control with diet control, lifestyle change, and/or oral hypoglycemic agents.^{3–6} In fact, it has been reported that initial intensive glycemic control results in β -cell recovery with remission of the hyperglycemia and maintenance of normal A1C levels resulting from removal of a “critical component” of glucotoxicity and lipotoxicity at the level of the β -cell and/or peripheral tissues.⁵

One large prospective study conducted at an inner-city hospital found that the majority of obese African-American patients who presented with DKA had a variant of diabetes characterized by a higher insulin secretion demonstrated by C-peptide response to glucagon infusion, the absence of autoimmune markers (antibodies to GAD-65, islet cell antibodies, insulin autoantibodies, and antibodies to IA2 proteins), and a lack of HLA association.³ In contrast, another study of patients with similar clinical presentations and phenotypes had negative autoimmune markers of type 1 diabetes but did have an increased frequency of the HLA DR3 and HLA DR4 haplotypes.^{7,8}

The recognition of clinical, metabolic, immunological, and genetic markers associated with classical type 1 diabetes is important because patients with typical phenotypical features and positive autoimmunity are likely to fail diet and oral therapy and will require continued

treatment with exogenous insulin. On the other hand, patients with a more classical type 2–like phenotype may maintain good glycemic control with lifestyle measures or oral agents after initial insulin therapy to overcome the profound glucotoxicity and insulin resistance that are seen with hyperglycemic metabolic decompensation.

Another consideration is whether to maintain these individuals with idiopathic type 1 diabetes with a type 2 phenotype on long-term insulin therapy regardless of whether they have positive antibodies to GAD-65 or ICA. The rationale for this is preservation of β -cell mass and function and slowing of disease progression.

The mainstay of therapy for these patients is lifestyle change, with proper diet, exercise, and weight loss as indicated being important in the maintenance of glycemic control. Attention should be paid to treating not only hyperglycemia, but also blood pressure and lipid abnormalities to targets outlined in established guidelines. It is also important to remember that during long-term follow-up, maintenance of near-normal glycemic control is very important because progressive hyperglycemia can lead to deterioration of insulin secretion and recurrent ketoacidosis.

Clinical Pearls

- Atypical or idiopathic type 1 diabetes encompasses clinical, metabolic, and phenotypical features of both type 1 and type 2 diabetes. Often the first presentation is unprovoked ketoacidosis.
- There is often marked insulin resistance resulting from glucotoxicity as well as obesity, and often aggressive insulin therapy is initially required to reverse the ketosis and hyperglycemia.
- Recognition of this type of patient is

important and has implications for appropriate long-term management and follow-up.

- Lifestyle changes, including diet, weight loss, and exercise, are an important part of the treatment regimen to help improve insulin sensitivity and maintain good glycemic control.

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