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Case Report

A Curious Case of New-Onset Diabetes

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A B S T R A C T

New-onset type 1 diabetes most frequently presents with diabetic ketoacidosis in young patients. A subset of patients with autoimmune type 1 diabetes may present with a slower progression to insulin deficiency and are frequently misdiagnosed with type 2 diabetes. Clinicians should screen for type 1 diabetes in patients who present with hyperglycemia and do not have obvious signs of insulin resistance or obesity. This case report presents an adult patient with hyperglycemia after a hospital admission for coronavirus disease 2019 and the evidence used to diagnose type 1 diabetes with atypical presentation.

During the initial stages of the coronavirus disease 2019 (COVID-19) pandemic in 2020, a significant number of patients with severe infections of COVID-19 had diabetes. The initial presumption was that diabetes increased the risk and severity of infection because of compromised immunity from a hyperglycemic, hypercoagulable, and proinflammatory state. Systemic complications such as kidney disease, hypertension, obesity, and cardiovascular disease were also attributed to the increased risk for severe COVID infection. Since 2020, the interrelationship between COVID-19 and diabetes has become more convoluted, and it is now proposed that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) itself (the virus causing COVID-19) may play a role in the etiology of diabetes. Determining the etiology of diabetes due to COVID versus a predisposition for diabetes (type 1 and type 2) has become more challenging to determine in patients newly found to have diabetes during an active COVID infection.

This case report presents an adult patient who was incidentally found to have hyperglycemia after admission for COVID-19 pneumonia and the evidence used to appropriately diagnose type 1 diabetes with atypical presentation. Patients with newly diagnosed type 1 diabetes most frequently present to the emergency department in diabetic ketoacidosis (DKA). However, a subset of patients with autoimmune type 1 diabetes may present with a slower progression to insulin deficiency with temporary remission from the need for insulin, sometimes referred to as latent autoimmune diabetes in adults (LADA).

Case Presentation

A 32-year-old white man presented to the emergency department with a 4-day history of fever, cough, dyspnea, and diarrhea. He was subsequently admitted to the medical-surgical unit for sepsis with acute hypoxemic respiratory failure caused by COVID-19 pneumonia. The patient was unvaccinated for COVID-19 and stated other members of his household had recently tested positive. He was found incidentally to have hyperglycemia on admission labs with an initial serum glucose of 226 mg/dL (before the initiation of steroids). He was started on the standard of care therapy for acute COVID-19 pneumonia including antiviral remdesivir 200 mg daily for 5 days, supplemental oxygen with a 30-L high-flow nasal cannula, prophylactic anticoagulation with Lovenox (Sanofi-Aventis) 40 mg twice a day, and prone therapy. Because the patient was requiring greater than 3-L nasal cannula of supplemental oxygen, he was started on a steroid course of dexamethasone 6 mg daily per hospital protocol. He had a significant uptrend in blood glucose after the initiation of steroids. The admitting hospitalist physician placed a consult for glycemic management, and the patient was seen by nurse practitioners (NPs) of the hospital's inpatient glycemic team.

Past Medical History

The patient had a history of appendectomy about 1 year before admission and had no other significant past medical history. He stated that he did not have a primary care provider and did not follow up for regular medical screenings.

Allergies

The patient had no known allergies.

Home Medication List

The patient was not taking any medications before admission.

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Table
A Full Diagnostic Panel of Autoantibodies to Evaluate for Type 1 Diabetes

Autoimmune Antibodies	Reference Range
Glutamic acid decarboxylase	< 5 nmol/L
Insulin autoantibodies	< 5 nmol/L
Tyrosine phosphatases	< 0.02 nmol/L
Zinc transporter 8	< 15 U/mL
Islet cell antibodies	< 1.4 nmol/L

Family History

According to the patient, his paternal uncle and paternal grandmother had diabetes. He did not know if they had type 1 or type 2 diabetes but stated both were obese.

Social History

The patient denied alcohol and the use of tobacco. He reported a distant history of marijuana use and denied using any other substances. He stated he was employed full-time as an engineer and lived with his fiancé. The patient stated he regularly exercised several days per week including weight lifting and followed a healthy diet.

Review of Systems

The patient endorsed 8 days of decreased appetite, fatigue, fevers, chills, and malaise. He reported cough, dyspnea, and diarrhea starting 4 days before presentation to the emergency department. He denied polyuria, nocturia, polydipsia, polyphagia, and recent weight loss. All other systems were negative.

Physical Examination

The patient was well-developed and muscular. He was 6'1" and weighed 100 kg with a body mass index (BMI) of 29. Although his BMI 29 is classified as overweight, the patient appeared muscular and lean without central obesity and no obvious signs of insulin resistance such as acanthosis nigricans.

Diagnostic Studies

Because of the patient's young age and lean body habitus, NPs of the inpatient glycemic team ordered hemoglobin A1C and glutamic acid decarboxylase (GAD 65) antibody tests to test for type 1 diabetes. A C-peptide level was also ordered to assess the level of insulin production by beta cells.

GAD 65 autoantibodies are the most prevalent in patients with type 1 diabetes, although other autoantibodies may also be present (Table). The GAD 65 antibody level was 106 nmol/L, which is suggestive of autoimmune type 1 diabetes; the normal value for people without diabetes is < 5 nmol/L. The patient's C-peptide level was within normal limits, albeit at the low end of normal at 1.0 with concomitant glucose of 201 mg/dL. Hemoglobin A1C was drawn on the day of the patient's admission and resulted at 6.5%, correlating to an average blood glucose level of about 140 mg/dL. The patient's chest X-ray showed bilateral infiltrates related to COVID-19 pneumonia.

Case Outcome

The patient's blood glucose was managed according to the standard of care for inpatient management. A basal-bolus insulin regimen was initiated using weight-based dosing. The patient's insulin regimen included basal insulin glargine once daily and short-acting insulin apart with nutritional and correctional scale doses given 3 times daily before meals. Insulin doses were titrated daily based on point-of-care blood glucose trends and insulin requirements. While on dexamethasone, the patient's point-of-care blood glucose ranged from 291 to 393 mg/dL, and his insulin doses were titrated up to a maximum of 133 U received in a 24-hour period. After the discontinuation of steroids, hyperglycemia persisted, and the patient continued to require about 50 U insulin in 24 hours with blood glucose ranging 78 to 216 mg/dL.

After 4 days of aggressive pulmonary hygiene and treatment, the patient was successfully weaned off supplemental oxygen and the course of dexamethasone was discontinued early. Before discharge, an NP provided diabetes education including diabetes survival skills and teaching on diabetes diet and counting carbohydrates with a registered dietician. Diabetes survival skills include education on the type of diabetes, self-monitoring of glucose, the signs and treatment of hypoglycemia and hyperglycemia, the insulin regimen, and follow-up. The patient was also determined to have a high literacy level and motivation for learning and thus was also provided with teaching on following an insulin regimen with an insulin-to-carbohydrate ratio with carbohydrate counting and a correctional scale.

At discharge, he was prescribed multiple daily insulin injections to manage his diabetes. His discharge regimen included basal insulin glargine 20 U once daily and short-acting lispro 3 times daily before meals dosed with an insulin-to-carbohydrate ratio of 1 U insulin for every 10 g carbohydrates (1:10) and a correctional scale of 1 U insulin for every 50 mg/dL greater than 150 mg/dL. A referral to endocrinology was also sent before discharge. He was discharged 8 days after admission and instructed to continue quarantine at home and follow up with his primary care provider. Unfortunately, the patient was lost to follow-up after hospital discharge.

Discussion

Type 1 diabetes is distinguished by an autoimmune process in which pancreatic beta cells are destroyed, leading to near complete insulin deficiency. Notably, the patient in this case study was not in DKA at the initial presentation, which is atypical for new-onset type 1 diabetes. This atypical presentation of type 1 Diabetes is more common in adults than children and is sometimes referred to as LADA. Patients presenting with atypical onset of autoimmune type 1 diabetes are frequently misdiagnosed as having type 2 diabetes. This is problematic because insulin deficiency is shown to progress more quickly than with type 2 diabetes; thus, insulin should be considered sooner. This case highlights the importance of completing a thorough evaluation for type 1 diabetes in adult patients who are less than age 40 years old and without obvious signs of insulin resistance (acanthosis nigricans and obesity). Distinguishing between type 1 and type 2 diabetes is necessary to prescribe the appropriate therapy and maintain optimal glucose levels, thereby decreasing the risk for diabetes complications. The treatment for patients with type 1 diabetes is strictly insulin with multiple daily injections or an insulin pump because of complete insulin deficiency. Patients with type 2 diabetes continue to make some insulin but have decreased sensitivity because of insulin resistance; thus, oral diabetes agents are typically first-line therapy.

Several factors led to the diagnosis of LADA in this patient. The patient's young age; body habitus; and lack of prior medical history of prediabetes, metabolic syndrome, or hypercholesteremia prompted NPs to order GAD autoantibodies, which were positive. LADA is a form of autoimmune type 1 diabetes in which the immune system gradually attacks the insulin-producing beta cells of the pancreas, sometimes resulting in a temporary remission from

the need for insulin.[1-3] The gradual attack on the beta cells leads to a slower decline in insulin production compared with the more typical presentation of type 1 diabetes with sudden onset that manifests as DKA at the initial presentation. However, compared with patients with type 2 diabetes, patients with LADA have a faster progression to insulin deficiency and should be monitored closely. Per American Diabetes Association guidelines, a patient with LADA should be treated with insulin, although there is literature to support the use of noninsulin diabetes medications as adjunct therapy.[1,4,5] Specifically, dipeptidyl peptidase 4 inhibitors have been shown to improve islet beta-cell function with a lower risk for hypoglycemia.[4] Metformin, glucagon-like peptide-1, and thiazolidinediones may also be beneficial, although the literature regarding the use of these medications to treat LADA is not as robust.[5] When risk factors for type 1 diabetes are present, providers can order autoimmune antibodies (Table) and C-peptide levels to distinguish between type 1 and Type 2 diabetes. Specifically, providers can order GAD65 as the first-line antibody test because patients with type 1 diabetes are predominantly positive for GAD autoantibodies.[6,7] Risk factors include age < 40 years; a low or normal BMI; a family history of type 1 diabetes; and a history of other autoimmune disorders, such as vitiligo, celiac disease, and autoimmune thyroid disease.[8,9] Patients diagnosed with LADA or type 1 diabetes should be referred to an endocrinology clinic for further management.

Another notable factor in this case is that the patient presented with acute COVID-19 infection. Since the start of the COVID-19 pandemic, a bidirectional relationship between COVID-19 and diabetes has been observed. Diabetes was identified as a significant predictor of poor outcomes for SARS-CoV-2 infection, and it is hypothesized that SARS-CoV-2 may play a role in inducing hyperglycemia and diabetes.[3,10-12] Generally, viral infections have long been suspected to play a role in the development of autoimmune type 1 diabetes through the process of binding and replication in pancreatic beta cells, although exact mechanisms are unknown.[12] Specifically, SARS-CoV-2 has been shown to bind to angiotensin-converting enzyme 2 receptors, which are expressed on the pancreas.[12] Thus, mechanisms of particular interest include the possibility that this binding process may directly damage beta cells or lead to an autoimmune reaction that causes severe insulin deficiency as in type 1 diabetes.[12,13] It is also suspected that inflammation caused by SARS-CoV2 infection may lead to insulin resistance, the underlying mechanism in type 2 diabetes.[14] In patients with insulin resistance, the body continues to make some insulin, but fat, muscle, and liver cells cannot fully utilize the available insulin because of lowered sensitivity. Significantly, the patient in this case report displayed marked insulin resistance, requiring 50 to 133 U insulin in a 24-hour period to manage hyperglycemia. Even considering the effect of steroids, this is significant, especially for an insulin-naive patient.

New information is ongoing regarding the incidence and prevalence of new-onset diabetes after COVID-19 infection. The current literature supports an increased risk and burden of diabetes after COVID-19 infection.[13,15-17] A recent study of national databases from the United States Department of Veterans Affairs concluded that increased risks for diabetes persists beyond 30 days after infection among nonhospitalized and hospitalized patients.[16] Also, a retrospective analysis of more than 2.5 million children concluded that the incidence of new-onset diabetes after COVID-19 infection was 116% more likely to occur among those with COVID-19 infection than those with acute respiratory infection prepandemic.[17] Questions regarding the full scope of pancreatic damage, either transient or permanent, inflicted by SARS-CoV-2 have yet to be determined. For clinicians, it raises awareness of screening for diabetes after COVID-19 infection, especially in the presence of other signs and risk factors.

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