TYPE 2 DIABETES WITH KETOSIS TENDENCY: A CASE REPORT

DIABETES TIPO 2 COM TENDÊNCIA À CETOSE: RELATO DE CASO

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ABSTRACT

In the United States, in recent years, a growing number of cases of ketosis-prone type 2 diabetes (KPTD) have been reported. In Brazil, this is still a rare condition and its exact prevalence is still unknown. The typical initial presentation is diabetic ketoacidosis (DKA) without apparent triggering factor but a within a few weeks or few months it is possible to withdraw insulin therapy and to maintain an adequate glycemic control only with oral drugs or even with diet therapy. Antibodies against beta cell antigens are negative and most patients are obese Afro-american or Hispanic men with a strong family history of type 2 diabetes mellitus. In the article, it was reported a case of KPTD in a 31-year-old man, in whom it was possible to discontinue insulin therapy 3 months after the DKA episode, with maintenance of metformin. Eighteen months after DKA, the patient remained well controlled with diet only (fasting glucose of 102 mg/dL and HbA1c of 5.7%).

Keywords: Diabetes *mellitus*. Diabetes *Flatbush*. Diabetes *mellitus* com tendência à Ketosis-prone type 2 diabetes. diabetic ketoacidosis

RESUMO

Nos Estados Unidos, nos últimos anos, tem sido descrito um número crescente de casos de Diabetes Mellitus tipo 2 com tendência à cetose. No Brasil, trata-se de condição ainda rara, e sua prevalência exata ainda é desconhecida. Os pacientes, em geral, abrem o quadro com cetoacidose diabética sem fator desencadeante perceptível e, dentro de algumas semanas, é possível a suspensão da terapia insulínica e um controle glicêmico adequado apenas com drogas orais ou mesmo somente dietoterapia. Os anticorpos contra antígenos da célula beta são negativos, e a maioria dos pacientes são homens negros ou hispânicos obesos, com forte história familiar de Diabetes Mellitus tipo 2. No artigo, é relatado o caso de Diabetes Mellitus tipo 2 com tendência à cetose em um homem de 31 anos, no qual foi possível a suspensão da terapia insulínica três meses após o episódio da cetoacidose diabética, com manutenção da metformina. Dezoito meses após a cetoacidose diabética, o paciente se mantinha bem controlado apenas com dietoterapia (glicemia de jejum de 102 mg/dL e HbA1c de 5,7%).

Palavras-chave: Diabetes *mellitus*; Diabetes *Flatbush*; Diabetes *mellitus* com tendência à cetose; Cetoacidose diabética

INTRODUCTION

Diabetic ketoacidosis (DKA) is the most characteristic acute metabolic complication of type 1 diabetes mellitus (T1DM) and often represents the initial manifestation of this disease[1]. This complication is uncommon in type 2 diabetes (T2DM)[1,2].

In recent years, particularly in the United States, a subgroup of patients has been increasingly described. They are mostly obese, Black or Hispanic, and present DKA as the initial manifestation of DM, with an atypical progression and no apparent triggering factor. Insulin therapy can often be discontinued within months, and patients can be managed with oral hypoglycemic agents or with diet alone[3,6]. This variant of T2DM was initially called Flatbush diabetes, in reference to a community in Brooklyn (New York), where the first cases were reported[5,10]. Other proposed names have included atypical diabetes, type 1 1/2 diabetes, and, more recently, ketosis-prone type 2 diabetes (KPT2D)[2,6].

Data on the prevalence of KPT2D in Brazil are scarce[2], evidencing the importance of this case report.

CASE REPORT

J.S.F., a 31-year-old white male with a body mass index (BMI) of 28.6 kg/m^2, with no previous history of DM, attended the emergency room with disorientation, decreased level of consciousness, dyspnea, and tachycardia. Family members reported that the patient was not taking any medication, and for the last three to four days had been experiencing polyuria and polydipsia. The patient was torpid, dehydrated (++/4+), afebrile, with ketonic breath, blood pressure levels of 120/80 mmHg, a heart rate of 112 beats/minute, a respiratory rate of 28 breaths/minute, a regular heart rhythm, universally audible vesicular murmurs, and an abdomen without visible changes. Abdominal palpation showed diffuse pain without signs of peritoneal irritation. Laboratory tests revealed arterial blood gas metabolic acidosis (pH 7.0), ketonuria, and hyperglycemia (430 mg/dL). The complete blood count described leukocytosis (18,000 leukocytes) with a left shift (8% rods), and the abdominal ultrasound was normal. A case of DKA was diagnosed with no apparent triggering factor, and the treatment encompassed intravenous hydration (0.9% saline infusion), potassium replacement, and insulin therapy, initially with continuous intravenous infusion, followed by intermittent subcutaneous injections. The response to treatment was satisfactory, with rapid resolution of the DKA. After one week, the patient was discharged with a prescription for a basal-bolus regimen of insulin glargine U-300 (30 units in the morning) and preprandial insulin aspart. He was also advised on diet and the need to consult an endocrinologist.

Despite presenting occasional hyperglycemic spikes for 15 days after hospital discharge, the patient began experiencing frequent hypoglycemia, resulting in a progressive reduction in the insulin dose. C-peptide levels were measured after stimulation with one milligram of glucagon, and anti-GAD and anti-IA2 autoantibodies were tested, revealing preserved pancreatic function (C-peptide of 5.5 ng/mL). Autoantibody levels were negative. HLA class II DRB1/DQB1 typing was performed on genomic DNA using polymerase chain reaction, suggesting DRB1*03/DRB1*13 alleles. Three months after the DKA episode, metformin was introduced, and insulin aspart was discontinued. The patient presented a BMI of 25.7 kg/m^2, and tests revealed fasting glucose of 78 mg/dL and HbA1c of 6.4%. Therefore, insulin glargine treatment was discontinued. In July 2017, metformin was discontinued, and the patient was maintained solely on diet therapy and physical activity. The patient has maintained adequate glycemic and lipid control, and tests from June 2018 revealed fasting glucose of 102 mg/dL and HbA1c of 5.7%.

COMMENTS

KPT2D is currently considered a subgroup of "ketosis-prone diabetes," which encompasses a heterogeneous group of patients classified by the Aβ system according to the presence or absence of autoantibodies (A), especially anti-GAD65 and anti-IA2 (A+ or A–, respectively), and the functional reserve of pancreatic beta cells (β), assessed by measuring C-peptide levels in the fasting state and after stimulation with 1 mg of glucagon (β+ or β–)[5,6]. This assessment should be performed one to three weeks after DKA resolution[5,6]. Patients with KPT2D belong to the A–β+ subgroup, characterized by the absence of autoantibodies and the presence of beta-cell function (fasting C-peptide ≥ 1 ng/mL or peak after glucagon stimulation ≥ 1.5 ng/mL) (5,6).[3,4] HLA class II antigens DRB1*03 and/or DRB1*04 are present in up to 63% of cases[7], as observed in this case. Patients with KPT2D are generally obese, with a mean age of 40 years (between 33 and 53 years), and most are Black or Hispanic, but its incidence has been increasing in all ethnicities[3-6]. In the United States, KPT2D accounts for 20 to 50% of cases in Black and Hispanic individuals, and about 10% in White and Asian individuals[4-6]. This condition is more common in males, with a ratio ranging from 2:1 to 8:1[4,5]. In Brazil, data on the clinical and epidemiological characteristics of the disease are scarce[2].

The pathophysiology of KPT2D is not completely understood, but glucotoxicity likely plays an important role, while the role of lipotoxicity remains controversial[2,6].

Although some patients can maintain the condition controlled by diet alone in the medium or long term, recurrence of hyperglycemia appears to be greater than in those who are treated with oral hypoglycemic agents[6].

This case illustrates a variant of T2DM that has been diagnosed with increasing frequency in some countries but remains rare in Brazil. Recognition is important because initial presentation with DKA suggests the diagnosis of T1DM, which requires lifelong insulin therapy. Patients with KPT2D

can remain well controlled with oral drugs alone for several years after a period of weeks to months of insulin dependence.

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