Ketosis-Prone Type 2 Diabetes in a Veteran Population

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Ketosis-prone type 2 diabetes is a unique and underrecognized clinical entity characterized by new adult onset of diabetes with severe hyperglycemia and ketosis similar to type 1 diabetes, but with clinical and biological features typical of type 2 diabetes (1). Hyperglycemic crisis with ketosis in these individuals appears to be related to acute and reversible β-cell dysfunction with subsequent insulin independence and acceptable glycemic control on diet and/or oral agents during follow-up (2).

In our retrospective study spanning from 1999 to 2011, we identified 62 adult veterans with new onset of diabetes presenting to the VA Greater Los Angeles Healthcare System (VAGLA) with diabetic ketoacidosis (DKA). Computerized medical records were used to identify DKA admissions. Diagnosis of DKA was established in the emergency room (3) in the absence of concomitant comorbidities that can lead to anion gap acidosis. All patients were hospitalized and treated with intravenous insulin, fluid, and electrolyte repletion. β-Cell recovery was defined as excellent glycemic control (A1C $<$6.3%, 45.4 mmol/mol) after discontinuation of insulin treatment for at least 1 year. Clinical and biochemical characteristics of patients with β-cell recovery were compared with patients who remained insulin dependent (Table 1). Only one patient was female, reflecting the predominantly male demographic served by the VA hospital. Three patients were lost in follow-up.

Patients from both groups were managed similarly during hospital admission and were discharged with similar doses of insulin. We found no difference in clinical, most biochemical, metabolic, or immunological characteristics comparing the recovery and insulin-dependent groups. A1C at presentation was significantly lower in the recovery group ($P = 0.01$), with subsequent further significant reduction after insulin discontinuation ($P < 0.001$). Fasting C-peptide levels were similar right after resolution of DKA, but only the recovery group showed a significant improvement in C-peptide level with time (first value reported 1 to 6 months after discharge, $P = 0.002$). After insulin discontinuation, the majority of patients were maintained on diet and/or oral anti-hyperglycemic agents.

Ours is the first report of ketosis-prone type 2 diabetes in the veteran population. Our observed rate of new-onset type 2 diabetes presenting with DKA is consistent with previous studies (2,4). Similarly, the rate of β-cell recovery, based on ability to achieve good glycemic control with insulin independence, is consistent with previous reports (2). In our veteran population, there was no single clinical characteristic at presentation that could identify ketosis-prone type 2 diabetic individuals who would become insulin independent. Rather, presence of three or more risk factors for type 2 diabetes (including overweight/obesity, hypertension, dyslipidemia, and positive family history), intact fasting C-peptide levels ($>$0.33 nmol/mL) 1 to 6 months after the initial DKA episode, and lower initial A1C all predicted β-cell recovery.

DKA has been classically considered pathognomonic of type 1 diabetes, or when type 2 diabetic patients are under extreme duress, yet we now know that a significant proportion of patients with type 2 diabetes present with DKA as their initial manifestation of disease.

Recognition of this digression from classic teaching is critical to facilitate future optimal care, including consideration of use of oral agents. Here, for the first time we report that in the veteran population more than 50% of the new onset of diabetes with ketosis is reversible, and early follow-up after discharge is essential to guide

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Table 1—Clinical and biochemical characteristics of veteran patients presenting with new onset of diabetes and DKA

	Recovery	Insulin dependent	*P*
Total number	33	26	NS
African American, *n*	24	19	NS
Hispanic, *n*	5	1	NS
Caucasian, *n*	3	4	NS
Other, *n*	1	1	NS
Mean age (SD), years	55 (9)	49 (4)	NS
BMI ≥30 kg/m^2, *n* (%)	22/33 (66)	15/26 (57)	0.38
Family history of diabetes, *n* (%)	20/29 (68)	16/24 (66)	NS
Hypertension, *n* (%)	25/33 (75)	15/25 (60)	NS
Dyslipidemia, *n* (%)	21/32 (65)	11/23 (47)	0.18
≥3 risk factors, *n* (%)†	20/28 (71)	10/26 (38)	0.015
BMI (SD), kg/m^2*	32 (5.7)	33 (6.3)	0.4
Glucose (SD), mmol/L*	40 (12.8)	38.2 (13.9)	NS
Anion gap (SD), mmol/L*	19.8 (5.7)	18.3 (4.7)	0.07
HCO_3 (SD), mmol/L*	19.9 (4.7)	19.1 (6.6)	NS
A1C (SD), %*	12 (2.3)	13.5 (2.9)	0.01
A1C (SD), mmol/mol*	107.7 (13.4)	124 (20)	0.01
Total cholesterol (SD), mmol/L*	4.8 (1.3)	3.9 (1.4)	0.054
Triglycerides (SD), mmol/L*	3.4 (2.3)	5.7 (7.9)	0.058
LDL (SD), mmol/L	2.8 (1.1)	2.9 (1.4)	NS
HDL (SD), mmol/L	0.9 (0.3)	0.9 (0.2)	NS
C-peptide (SD), nmol/L*	0.5 (0.36)	0.59 (0.49)	NS
Concurrent plasma glucose (SD), mg/dL‡	223.4 (80.4)	205 (62)	NS
C-peptide (SD), nmol/L**	1.19 (0.83)	0.59 (0.38)	0.017
Concurrent plasma glucose (SD), mg/dL‡	111 (23)	162.5 (31)	<0.01
GAD/ICA+, *n* (%)*	2/15 (13)	1/6 (16)	NS
β+, *n* (%)*	12/17 (70)	7/12 (58)	0.49
Insulin at discharge (SD), units/kg	0.5 (0.2)	0.56 (0.2)	NS

Results are expressed as mean ± SD (Student's *t* test; χ^2 test for categorical analysis). β+, preserved β-cell function defined as fasting C-peptide >0.33 nmol/L; ICA, islet cell antibodies. *, at presentation; **, at follow-up; †, risk factors: family history of diabetes, personal history of hypertension (historical diagnosis or treatment at patient presentation), personal history of dyslipidemia (historical diagnosis or treatment at presentation), and overweight/obesity (BMI >25 kg/m^2); ‡, plasma glucose checked concurrent with C-peptide at time of presentation or at time of follow-up.

appropriate management, including possible insulin discontinuation.

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