Patient Care Services / Nursing

"Flatbush" Diabetes: A Variant of the Typical Classification

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Why "Flatbush" Diabetes?

- The term "Flatbush" Diabetes was first applied to the African Americans residing in the ethnically diverse, Brooklyn, New York neighborhood of Flatbush, who presented in DKA at the time of their diabetes diagnosis.
- While presenting in DKA, these patients ultimately experience a clinical course resembling type 2 diabetes (T2DM).

Proliferation of Terms

- The traditional classification of diabetes was challenged with the emergence of patients demonstrating characteristics of both T1DM and T2DM.
- Terms such as **"Atypical Diabetes," "Type 1.5 Diabetes Mellitus," "Idiopathic Type 1 Diabetes," "Diabetes Mellitus Type 1B," "Temporary Diabetes," "Ketosis Prone Diabetes," "Ketosis Prone Type 2 Diabetes"** evolved.
- With the expanding ethnic reach of this presentation of diabetes, current literature more commonly references **"ketosis prone diabetes" (KPDM)**.

KPDM Classification System

- Developed to: (1) address the heterogeneity of KPDM patients and (2) predict long term β cell function and insulin independence.
- Based on autoimmunity (A) and beta cell function (β).
  - Autoimmunity = β cell autoantibodies (glutamic acid decarboxylase)
  - β cell function = fasting C-peptide > 1.0 ng/ml or peak glucagon stimulated C-peptide response > 1.5 ng/ml
- Found to have both high sensitivity and specificity.

Classification System			
KPDM Type	Autoimmunity (A)	β Cell Function (β)	Characteristics
Type 1A	+	-	A+β- (type 1A DM); require lifelong exogenous insulin
Type 1B	-	-	A-β- (type 1B DM); require lifelong exogenous insulin
Type 2A	+	+	A+β+ (LADA); ultimately lose β cell reserve & require lifelong exogenous insulin
Type 2B	-	+	**A-β+ (Flatbush DM); majority can discontinue exogenous insulin & manage with oral antihyperglycemic agents

- A+β- and A-β-: immunologically and genetically distinct, but share clinical characteristics of T1DM (low/no β cell function)
- A+β+ and A-β+: immunologically and genetically distinct, but share clinical characteristics of T2DM (preserved β cell function)

Clinical Presentation A-β+:

- Severe hyperglycemia following a period of polyuria/polydipsia/weight loss
  - BG > 500 mg/dl
  - Mean A1c > 10%
- Often "unprovoked" DKA
  - New or pre-existing DM diagnosis with DKA presentation
  - pH < 7.30
  - β-hydroxybutyrate: > 3 mmol/l
- Lack of HLA genetic association
- GAD and IA-2 antibody negative
- Measurable pancreatic insulin reserve
- Mean age at diagnosis 40 years
- Physical signs consistent with T2DM: obesity, abdominal adiposity, acanthosis nigrans
- (+) family history of T2DM

Pathophysiology

- The occurrence of ketoacidosis, despite the physical characteristics of T2DM, is a unique aspect.
- Despite five decades of KPDM case investigation, the etiology for the decompensation of β cell function and subsequent recovery is unknown, and the propensity for ketosis is poorly understood.
- Recent follow-up research disputes several theories proposed in earlier decades.
  - Investigation of an autoimmune etiology yielded discrepant findings.
  - A viral etiology was investigated, but in recent literary reports, unproven.
  - No unique genetic etiology has been found.

Management

- Acute management is focused on reversing the ketoacidosis:
  - Electrolyte replacement
  - Fluid repletion
  - Insulin administration (IV)
- Transition to a SQ insulin regimen occurs with resolution of ketosis. A starting dose of 0.8-1.2 u/kg/day is often needed due to insulin resistance.
- Intensified DM management results in improved β cell function and insulin sensitivity within several weeks to a few months, thereby enabling discontinuation of insulin.
- Near normoglycemic remission (insulin independence) may last months to years, although oral antihyperglycemics are necessary to address insulin resistance and maintain glucose control. Ketotic relapses may necessitate a temporary return to insulin use.
- Research from the 1990s demonstrated the value of using sulfonylureas to prolong the period of insulin independence, with more recent studies suggesting that Metformin® or Sitagliptin® may be equally efficacious.
- Long term β cell functional decline ultimately mirrors that seen in T2DM, often necessitating escalation of therapy to insulin use.

Incidence

- The exact incidence is not well known, and very likely underestimated and under reported.
- KPDM has been well described in Blacks of African and Caribbean descent, and may account for up to 50% of the newly diagnosed Black and Hispanic patients presenting with DKA.
- The highest numbers of cases are found in the populations at high risk for T2DM: Native American, Hispanic, Chinese, Japanese, South Asian, and Caucasian.
- Men are afflicted three times more than women.

CASE EXAMPLE

58 year old Caucasian female with a hyperglycemic history that dates back to 2002.

August 2006: Patient was admitted to a large, northeastern Pennsylvania teaching hospital after being found unresponsive. Initial lab work revealed DKA: BG: 358 mg/dl; anion gap: 31; bicarbonate: 5; arterial pH: 6.95; pCO2: 7; acetone: (+); A1c: 16.2%. A diagnosis of T1DM vs LADA was made. She was discharged with a basal/bolus insulin regimen, after only taking Avandia® prior to admission.

Over the course of the next 7 years patient enjoyed insulin independence, attaining an A1c low of 6.4%, taking only a gliptin/biguanide combination. Her medical record was amended to "T2DM."

January 2014: Patient again experienced unprovoked DKA: BG: 543 mg/dl; anion gap: 31; bicarbonate: 6; arterial pH: 6.94; βHB: 9.99; A1c: 12%. Endocrinology was consulted to address T2DM vs LADA. Insulin was resumed. "Flatbush" Diabetes is noted in follow-up one week after discharge, along with her (-) GAD antibodies and "detectable" c-peptide level. Management included "pancreatic rest with insulin for a few weeks or months, as needed," with hope of transition to an oral treatment plan thereafter.

April 2014: A1c 6.4%. All insulin doses discontinued; gliptin/biguanide combination resumed.

September 2016: Patient experienced a brisk worsening of glucose control (A1c 8.1% → 11.4% in 7 months). Basal insulin was added to her gliptin/biguanide combination.

November 2016: Within seven weeks after insulin re-initiated, her A1c had decreased to 8.9%.

May 2017: A1c 7.7%. Treatment with basal insulin + gliptin/biguanide continues. Endocrinology notes indicate that prior DKA episodes may be predictors of "future pancreatic function decline" and that "she may need to consider basal/bolus insulin in the future."

Role of the Diabetes Educator

- A specific role for the diabetes educator is notably absent in the KPDM medical literature
- The diabetes educator, with an awareness of KPDM, can provide information and support to address the questions and anxiety anticipated with the mixed symptom presentation and the poorly understood pathophysiology.
- Given the potential for relapsing and remitting ketosis, reinforcement of the need for treatment adherence, defined BG and ketone monitoring habits, and symptom recognition of hyperglycemia through evolving ketosis are essential components of teaching.
- Antibody testing and c-peptide monitoring can be suggested by the educator for patients after an unprovoked DKA episode, particularly for patients from general medical practices where KPDM may not be recognized.

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