Diabetic Ketoacidosis Among Obese African-American Adolescents With NIDDM

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OBJECTIVE — To determine whether ketosis at the time of presentation occurs among African-American adolescents with NIDDM.

RESEARCH DESIGN AND METHODS — We reviewed the charts of all islet cell antibody (ICA) negative patients diagnosed with NIDDM at Children's Hospital Medical Center (CHMC) between 1982 and 1995.

RESULTS — Between 1982 and 1985, 70 adolescents were diagnosed with NIDDM. Of these, ICA determinations were available and negative on 42 subjects (28 African-American, 12 white). Twelve of 28 (42%) African-American patients presented with ketonuria, and seven of 28 (25%) presented with DKA. In comparison, none of the 12 white adolescents with NIDDM had ketonuria at presentation or during their subsequent course. Mean follow-up time for patients with ketosis at presentation was 24 months. There was no difference between the age, BMI, or sex distribution of patients with and without ketosis. Previously diagnosed hypertension was present in 42% of patients presenting with ketosis, compared with 17% of the general NIDDM population at CHMC.

CONCLUSIONS — We conclude that ketosis may occur among African-American adolescents with NIDDM, as has been previously reported among African-American adults with NIDDM. Therefore, ketosis in obese young African-American patients with new-onset diabetes does not necessarily imply the presence of IDDM and insulin dependence.

Diabetic ketoacidosis (DKA) is considered a cardinal feature of IDDM. However, a recent report has indicated that among obese African-American adults, ketosis can occur in patients with NIDDM and that DKA can be a presentation of NIDDM in this population (1).

We have recently reported that the incidence of NIDDM is increasing markedly among adolescents in greater Cincinnati (2). These adolescent patients share characteristics common among the adult NIDDM population: they are disproportionately African-American, they are markedly obese, and they have a strong family history of NIDDM. We report here that, like adults, African-American adolescents with NIDDM may present with ketosis and DKA.

RESEARCH DESIGN AND METHODS

Patient population

We reviewed the charts of patients diagnosed with NIDDM at Children's Hospital Medical Center (CHMC) Cincinnati, OH according to the National Diabetes Data Group (1979) (3) between 1982 and 1995. A detailed population-based study of these adolescent NIDDM patients has been reported previously (2). NIDDM was diagnosed when a patient *1)* met oral glucose tolerance test or random glucose criteria (2 values >11 mmol/l; 200 mg/dl), *2)* was not ketosis prone under basal conditions, *3)* did not require exogenous insulin for extended periods of time, and *4)* did not have illnesses or medications predisposing to the development of secondary diabetes.

Although the absence of islet cell antibodies (ICA) is not part of the criteria for the diagnosis of NIDDM, only patients in whom ICA determinations were performed (Barbara Davis Diabetes Center, Denver, CO) were included in the current study. Beginning in 1994, ICA determination included measurement of anti-ICA512, anti-GAD, and insulin autoantibodies. ICA were negative in all patients included in this study who were diagnosed with NIDDM on clinical grounds.

Ketosis

Ketonuria was defined as urinary ketones >15 mg/dl ("small"). DKA was defined as an arterial pH <7.3, a bicarbonate value <15 meq/l, and a glucose level >250 mg/dl with ketonuria (4)

RESULTS

— Between 1982 and 1995, 70 adolescent patients were diagnosed with NIDDM at CHMC. Of these 70 patients, ICA determinations were available on 42 (60%). All ICA determinations performed on this group of patients were negative. The clinical features of this group are presented in Table 1 and compared with the entire group of 70 patients diagnosed with NIDDM. There was no statistical difference between the group included in this study and the entire NIDDM population at CHMC in terms of age, sex, ethnic distribution, or BMI.

Details of the 12 African-American patients who presented with ketosis are shown in Table 2. Seven of these patients (25% African-American patients) met the criteria for DKA at presentation, and four had an acute illness at presentation. Of the African-American patients presenting with ketosis, 75% had acanthosis nigricans, sug-

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CHMC, Children's Hospital Medical Center; DKA, diabetic ketoacidosis; ICA, islet cell antibody; MODY, maturity-onset diabetes of the young.

Table 1—*Race, sex, age, and BMI in NIDDM study populations at CHMC*

	NIDDM population at CHMC	NIDDM negative ICA	NIDDM negative ICA DKA
n	70	42	12
Race			
African-American	47 (67)	29 (69)	12
White	31 (22)	12 (28)	0
Asian	1 (1.4)	1 (2)	0
Sex			
Girls	44 (62)	28 (67)	7 (58)
Boys	26 (37)	14 (33)	5 (42)
Age (years)	13.8 ± 1.9	14.6 ± 1.9	14 ± 0.7
BMI (kg/m²)	37.7 ± 9.6	39.9 ± 9.56	40.7 ± 1.2

Data are *n*, *n* (%), or means ± SD.

gesting the presence of long-standing insulin resistance. On the other hand, none of the 12 white patients had ketones at presentation or during the subsequent course. The single Asian patient presented with mild ketonuria without acidosis. Mean follow-up time for patients with ketosis was 24 months (range 10–57 months).

There was no statistical difference between the age or BMI of NIDDM patients with or without ketosis (data not shown). The sex distribution of the patients with ketosis closely reflected the sex distribution of the NIDDM population as a whole. On the other hand, previously diagnosed hypertension was present in 42% of NIDDM patients presenting with ketosis, compared with 17% of the general NIDDM population at CHMC.

CONCLUSIONS — This report documents a group of obese African-American adolescent patients with NIDDM who presented with various degrees of ketosis, including DKA. All patients included in this study were ICA negative, and 75% had acanthosis nigricans. Follow-up (10–57 months; mean 24 months) indicated that these adolescents were not insulin dependent (i.e., requiring insulin for short-term survival) under basal conditions. Furthermore, these patients do not fit the diagnosis of maturity-onset diabetes of the young (MODY), as they are strikingly obese and lack evidence of autosomal dominant inheritance (5). These observations indicate that ketosis may occur in adolescent African-Americans with NIDDM and that the presence of ketosis in obese young African-American patients does not necessarily imply IDDM.

Our observation that ketosis occurs among African-American adolescents with NIDDM agrees with recent reports of ketosis and DKA in obese African-American adult patients subsequently diagnosed with NIDDM (1). These adult patients have decreased insulin secretion and sensitivity at presentation. However, after recovery from the acute phase, the abnormalities resolve and the patients exhibit a clinical course typical of NIDDM. Antibodies to GAD and ICA were absent (6). Additional reports of patients with NIDDM and DKA have been reported among adults in the Japanese and Danish literature (7,8). However, the occurrence of DKA in association with NIDDM has not previously been reported in the pediatric population.

Winter et al. (9) reported an atypical form of diabetes in 12 African-American youths that the authors classified as MODY. The diabetes in these subjects was characterized by a lack of insulin dependence, an autosomal dominant pattern of inheritance, and negative ICA. Ten of these individuals had a history of ketosis, and six were obese. The degree of obesity was not reported, and it is unclear whether all obese subjects were ketotic. In contrast, the patients in our study did not have an autosomal dominant pattern of inheritance and had marked obesity as a universal finding. The two groups share the lack of insulin dependence and absence of ICA. The similarities and contrasts between our population and that described by Winter et al. (9) suggest that there may be two distinct populations of African-American adolescents with transitory ketosis or DKA. Lean African-American adolescents who are not insulin dependent and have an autosomal dominant inheritance pattern fulfill the criteria for the distinct genetic abnormality known as MODY.

Table 2—*Clinical details of African-American adolescents with NIDDM and DKA*

Name	Sex	Age (years)	Weight (kg)	BMI (kg/m²)	Urine ketones (mg/dl)	pH	Serum HCO_3 (mmol/l)	Follow-up (months)	Acute illness	PMH
FJ	F	11	99	46	>15	ND	26	22	No	HT
BB	M	14	144	45	>15	7.37	23	8	No	HT
MJ	F	16	111	44	>15	7.37	19	17	No	—
HC	F	13	120	42	>40	7.3	18	17	No	HT
RJ	M	15	102	36	>40	7.24	13	29	Asthma exacerbation	—
HC	F	16	104	42	>40	7.22	9	17	No	HT
ST	M	10	113	44	>80	7.42	21	29	No	—
MS	F	12	74	38	>80	7.24	10	53	No	—
L	F	12	109	39	>80	7.28	5	6	Osteomyelitis	—
MB	M	17	105	40	>80	7.16	6	15	Gluteal abscess	—
KS	F	15	82	34	>80	7.00	7	14	Severe pharyngitis	HC
MD	M	17	100	35	>80	7.15	9	10	No	HT

HC, hydrocephalus; HT, hypertension; PMH, past medical history.

On the other hand, obese African-American adolescents who are not insulin dependent may, in fact, have the abnormalities recognized as NIDDM among adults. We suggest that this latter group consists of adolescents at high risk for the development of NIDDM due to ethnic and familial predisposition who are presenting early in life as a consequence of morbid obesity.

The distinction between NIDDM and IDDM may have implications for the design of an appropriate treatment regimen. Hyperinsulinemia has been implicated as a pathogenic factor in the development of atherosclerosis, ischemic heart disease, and hypertension in patients with diabetes (11). Therefore, the use of long-term insulin therapy as the mainstay of treatment in patients who are not insulin dependent may have unintended negative consequences including additional weight gain, increased burdens on the family, and an increase in the incidence of diabetic complications. On the other hand, the maintenance of good control, even at the expense of hyperinsulinemia, may be preferable to the alternative of poor control in patients unresponsive to other therapies. However, whereas the optimal therapy for NIDDM, in either adults or adolescents, remains controversial, potential treatment options available are broader than for IDDM and include diet/exercise, oral hypoglycemic agents, and insulin, alone and in combination. Therefore, attention to the diagnosis of NIDDM versus IDDM in obese adolescents may permit appropriate individualization of therapy to the physiology of the underlying disorder (12).

In summary, we have reported that obese African-American adolescents with NIDDM may have ketosis at the time of presentation. Therefore, the presence of ketosis among obese African-American patients does not necessarily imply insulin dependence, and the diagnosis of NIDDM needs to be considered. It is important for the clinician to take into account multiple features of the presentation in making a provisional diagnosis in these patients and in designing an appropriate initial treatment regimen. Furthermore, the initial diagnosis should be reevaluated based on the subsequent course. Clinicians should also consider screening for diabetes among at-risk obese black adolescents, especially those from families with strong histories of NIDDM, to prevent the occurrence of potentially life-threatening metabolic deterioration.

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