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Ketosis-prone atypical diabetes mellitus or "African diabetes": what is special? About seven cases

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Abstract
Ketosis-prone diabetes -KPD is characterized by episodes of ketosis or ketoacidosis requiring insulin therapy, most often transient. It mainly occurs in subjects from sub-Saharan Africa and its pathophysiology is not known. In recent years, the presence of "atypical" diabetes in black people has been described in several studies. The molecular mechanisms behind the transient alteration of insulin secretion are still unknown, but may involve mechanisms of gluco- and lipotoxicity. The association with HLA alleles brings this type of diabetes closer to type1 diabetes, but the presence of a strong diabetic inheritance and the absence of markers of autoimmunity bring it closer to type 2 diabetes.
We discuss in our article, through seven cases of African diabetes, the specific diagnostic, metabolic, pathophysiological and management burden of this type of atypical diabetes.

Keys words: Ketosis-prone ; atypical diabetes mellitus

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I. Introduction:

For the past 20 years, diabetes has gained ground in Africa more rapidly than elsewhere in the world, its incidence having risen to more than 10% today [1].

But what surprises most is the existence of a form called African diabetes "DA" or ketonuric diabetes (ketosis-prone diabetes -KPD) which is characterized by episodes of ketosis or ketoacidosis requiring insulin therapy. most often transient. It mainly occurs in people from sub-Saharan Africa and its pathophysiology is not known.

The aim of this article is to try, through our series, to explain the specificities of "African" diabetes in order to establish an appropriate management strategy.

II. Patients and methods:

We emphasize the particularity of the clinical presentation, the course and the treatment of patients with African diabetes or also called type 2 ketotic diabetes.

	1	2	3	4	5	6	7
Age	36	43	39	28	44	30	45
Ethnicity	South Morocco	Africain	South Morocco	South Morocco	Africain	South Morocco	Africain
Sexe	F	M	M	F	M	M	F
diabetic Heredity	Yes	Yes	Yes	Yes	No	No	Yes
Ketosis / Ketoacidosis	Ketosis +++	Ketosis	Ketosis	Ketosis +++	Ketosis	Ketosis	Ketosis
IMC moyen KG/m²	24	22	29	27	27	23	25
Initial mean HbaA1c (%)	11,2	9,7	9,4	10,1	11,5	11,9	9,4
Long-term insulin dependence (wk)	40	26	12	18	48	35	21
Peptide C (µg/l)	1,8	2,3	3,6	2,8	3,8	2,1	3,4
Anti Beta cell antibodies (%)	Négatif	Négatif	Négatif	-	Négatif	Négatif	-

Table I: Summary of epidemiological and clinical data and evolution of patients with African diabetes.

III. Discussion

"African" diabetes or atypical diabetes mellitus with a tendency to ketosis is characterized by an onset of type 1 diabetes with severe hyperglycemia and ketosis and a subsequent progression to type 2 diabetes. Description of this type of diabetes has been made in black Americans from North America, Africans from Africa, Asians and Caucasians. Although the pathophysiological mechanisms are not yet well understood, the available clinical, metabolic and immunological data allow certain hypotheses to be drawn up.

ADA describes this diabetes as idiopathic type 1 diabetes or type 1b diabetes characterized by an initial acute presentation with severe hyperglycemia and ketosis as in type 1 diabetes, which progresses in a non-insulin-dependent type and which is distinguished from true type 1 diabetes by the absence of β-cell autoimmunity [2].

African diabetes has just been characterized and recognized as a separate entity, its true prevalence is still unknown. It was first described in 1987 by Winter et al. [3] who identified in a black population in Florida comprising 129 patients with diabetes declared in childhood or adolescence, 12 patients (9.3%) who presented with African diabetes whose clinical expression is identical to that of type 1 diabetes at the onset of the disease, but characterized by the presence of remission in several months to several years and by the absence of signs of autoimmunity. This type of diabetes was subsequently described in 1990 and 1994 in black American adults with a minority of patients with marked obesity [4,5]. More recently, publications have reported similar cases in Asian, Hispanic and Caucasian ethnic groups and among Africans (Table 2).

In fact, diabetologists in Africa have long known about this type of diabetes, as it can be found in Nigerian newsletters dating back to 1978 and 1981 cases of atypical diabetes with a noisy onset characterized by insulinopenia and a secondary course in the form of type 2 diabetes [5]. The clinical profile of patients with African diabetes is characterized by an average age between 35 and 46 years (our patients had an age between 28 and 45 years), a male predominance with an M / F sex ratio of 1.5 to 3 according to the series [6,7,8,9,10,11] (in our 4M / 3F series), a significant diabetic inheritance approaching 100% in certain publications (05 of our patients had a strong diabetic inheritance) and an average BMI of 26, 28–30, 37, 29 kg / m2 respectively in Paris, New York, Atlanta and in Asia [6,12,14]: it is 25.2 kg / m2 in our patients. The initial clinical expression is marked by ketosis with sometimes ketoacidosis (as is the case in two of our patients) associated with significant hyperglycemia [8,15]. Ketosis is often preceded by polyuropolydipsic syndrome and weightloss. It is often quickly controlled by intravenous insulin therapy and correction of fluid and electrolyte disturbances (it was resolved in less than 24 hours in five of our patients). There was no decompensating factor (infection, trauma or other intercurrent condition in five of our patients). Once the acute phase has passed, the progression is towards a correct glycemic balance under a basic regimen by the subcutaneous injection: the frequency of hypoglycaemia prompts the attending physician to gradually reduce the doses of insulin [15,16]. In a few days to a few months, stopping insulin is obtained in most patients, in favor of hygienic diet (RHD) and oral hypoglycemic agents (OH). In all of our patients, the switch to OH was done in a few weeks (without a recurrence of ketosis. Glycemic control during this period of "remission of insulin therapy" which can last several years (up to more than ten years), is maintained by HDRs and OHs. This period is to be distinguished from the “honeymoon” of type 1 diabetes which is much shorter duration.

Immunologically, several studies have shown that subjects with "African" diabetes had characteristics of type 1 diabetes and type 2 diabetes [2]. The presence of HLA-DR3, DR4 is found in 65% of patients, while this frequency is 30% in control subjects, which brings them closer to type 1 diabetes [17]. Likewise, an increased frequency of DQw8 was noted. In contrast, a family history of diabetes and the absence of autoimmunity markers (anti-GAD antibodies and ICA) suggest that it has type 2 diabetes [18,19]. The study of insulin secretion by glucose and glucagon stimulation tests reveals in subjects with "African" diabetes a basal level of C peptide higher than that of patients with type 1 diabetes but lower than those with type 2 diabetes.

At the same time, there is no acute insulin response in patients with atypical diabetes to intravenous glucose administration.

However, intravenous administration of glucagon in these same patients results in a significant elevation of basal C peptide levels. The acute insulin response to glucagon is greater in these patients compared to that seen in type 1 diabetics but weaker compared to that observed in type 2 diabetics [20].

Several physiopathological hypotheses have been raised. First, the phenomenon of glucotoxicity on insulin secretion and insulin resistance [2,17]: thus, the rapid improvement in glycemic control could be at the origin of a recovery of a correct insulin secretion and improvement in insulin sensitivity allowing prolonged remission in a large number of cases.

Furthermore, the phenomenon of lipotoxicity could also participate in metabolic alterations. Black women have been shown to have higher circulating levels of unesterified fatty acids and to show a decrease in the antilipolytic action of insulin on adipose tissue.

In 2004, Mauvais-Jarvis et al. have demonstrated in populations of African origin mutations in the PAXA4 gene: a transcription factor essential for the production of insulin by pancreatic β cells. These mutations seem to predispose to "African" diabetes [21].

More recently, a study by Sobngwi et al. suggests that the simultaneous existence of an alteration in the genes controlling the function of pancreatic β cells and those responsible for the expression of G6PD (an essential enzyme in the defense mechanisms against oxidative stress) predisposes to atypical diabetes [22].

The particularity of these patients is to present periods of absolute insulinopenia which can lead to ketoacidosis followed by periods of remission. We then observe a recovery of pancreatic functionality, sometimes total, allowing at least complete insulin withdrawal and sometimes even a suspension of all treatments for several months or years [37].

IV. Conclusion:

Although the prevalence of so-called "African" diabetes remains unknown, it appears to be significant among black populations of African origin. This form of atypical diabetes must be known in everyday practice, because it is not synonymous with lifelong insulin therapy, which is important to know, especially in the management of patients who may have difficulty accessing care, and therefore insulin. The molecular mechanisms behind this type of diabetes remain to be defined.

Table 2: summary of data from our series and literature

study	Patients (n)	Ethnicité (%)					Average age at	Male	Ketosis/acidoketosis	IMC moyen (kg/m	HbA1C	Need insulin to	Peptide C after	Antibody anticell β
		african	Hispanic	Asiatic	Caucasian	Afro-								
Yu et al.[11]	40		0	100	0	0	40,5	70	100	22,2	12,1	63	-	8
Sobngwi et al.[22]	21		0	0	0	0	42	86	100	26	11,9	52	3,7 ± 1,2	0
Mauvais Jarvis et al. [21]	111		0	0	0	0	39	76	100	25	–	24	–	0
Maldonado et al.[10]	62	29	15	1	55	0	39,1	58	100	30,3	13,6	50	18,7 ± 9	18
Ramos Romain et al. [15]	12	66	0	0	33	0	34,7	66	100	39,6	10,5	–	4,6 ± 3,4	–
Our study	7	0	0	0	0	100	37,8	57%	100	25,2	10,4	57	2,8±1,8	0

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No conflict of intersets

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