Metabolic Syndrome in adults with congenital adrenal hyperplasia due to 21-hydroxylase deficiency

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Introduction :

21-Hydroxylase deficiency is the most frequent form of congenital adrenal hyperplasia (CAH) which is a common autosomal recessive disorder characterized by impaired adrenocortical and adrenomedullary function, and adrenal hyperandrogenism.

There are two classic forms, the saltwasting form (SW) manifested neonatally by severe salt loss, and the simple virilizing form (SV) where salt loss is mild or absent. The nonclassic (NC) variant is usually diagnosed with hyperandrogenism later in childhood or adulthood with most males being identified in the course of family investigations Chronic glucocorticoid therapy and excess androgen exposure in patients with CAH may predispose them to developing a metabolic syndrome in adulthood.

Our objective is to evaluate the metabolic syndrome in adulthood in a Tunisian cohort.

Patients and methods :

We underwent a prospective study of 26 patients over 16 years of old with CAH.

Results 1 :

The cases included 26 patients including 11 males and 15 females, with CAH due to 21-hydroxylase deficiency with a mean age of 27.4 years (16.5-48 years). Eighteen patients had the classical CAH form and the remaining 8 patients had the non-classical form. The mean body mass index was 26,9 ± 4,27 kg/m2 (20,3-34,8 kg/m2). The most commonly used drug was hydrocortisone which was used by 21 cases. Five cases had been managed on dexamethasone alone. The mean body fat mass was 17,88 ± 9,8 kg (6-39,3kg) 24,8 ± 10,65 % of body mass (10,9 - 41,6 %). Eight patients suffered from obesity. Mean fasting serum glycaemia was 4,82 ± 0,52 mmol/l (3,85-5,54 mmol/l). Eighteen patients (78.2%) had a normal glucose tolerance, whereas 4 patients (17.4%) had impaired glucose tolerance and only one patient had diabetes. A hypercholesterolemia was observed in one patient, a combined hyperlipidaemia in another one and finally a low HDL-cholesterol in 5 patients.

Only 23 patients underwent the assessment of fasting insulinemia to calculate the HOMA-IR (homeostasis model of assessment of insulin resistance) and leptin plasma (table I).

Hepatic cytolysis was noticed in one patient with a hepatic steatosis in abdominal ultrasound. Hypertension was confirmed in two patients.

Table I: confrontation betwwen metabolic features and CAH phenotypes

	(N= 23 cas)	SW (N= 9 cas)	SV (N= 7 cas)	NC (N= 7 cas)
Weight (kg)	68,18 ± 12,7	68,3 ± 13	72 ± 16,2	**64,14 8,07**
BMI (kg/m2)	26,9 ± 4,27	25,5 ± 4,54	27,9 ± 3,8	**27,81 ± 4,92**
Waist Circumference (cm)	85,54 ± 12	84,6 ± 15,21	84,85 ± 12,2	**85,7 ± 12,17**
MG corporelle (%)	24,8 ± 10,65	21,6 ± 10,32	25,7 ± 8,36	**27,89 ± 12,5**
Fasting blood glucose (mmol/l)	4,82 ± 0,52	4,49 ± 0,3	4,62 ± 0,6	**5,46 ± 2,5**
Blood glucose after oral (mmol/l)	6,39 ± 1,41	5,94 ± 0,9	6,22 ± 1,56	**7,14 ± 1,56**
Cholesterol (g/l)	1,66 ± 0,26	1,54 ± 0,08	1,64 ± 0,15	**1,87 ± 0,38**
Triglyceride (g/l)	0,91 ± 0,27	0,89 ± 0,28	0,93 ± 0,24	**0,98 ± 0,3**
HDLc (g/l)	0,46 ± 0,06	0,47 ± 0,06	0,43 ± 0,06	**0,47 ± 0,07**
LDLc (g/l)	1,01 ± 0,27	0,89 ± 0,1	1,02 ± 0,13	**1,2 ± 0,3**
Aspartate aminotransferase (U/l)	25,86 ± 17,3	22,5 ± 3,8	35,57	**20,4 ± 3,9**
ALAT (UI/l)	27,7 ± 16,1	17,3 ± 4,58	49,7	**19,14 ± 8,35**
Alanine aminotransferase (U/l)	24,47 ± 7,57	27,2 ± 6,24	26 ± 9	**19,42 ± 5,76**
Fasting insulin (µUI/ml)	9,6 ± 4,35	8,8 ± 0,9	11,2 ± 7,2	**9,05 ± 3,2**
HOMA-IR	2,1 ± 1,12	1,77 ± 0,62	2,43 ± 1,6	**2,29 ± 1,2**
Leptin plasma level (ng/ml)	**7,51 ± 4,73**	**6,34 ± 5,41**	**8,57 ± 2,23**	**7,41 ± 5, 66**

SW: salt waisting form; SV: simple virilising form; NC: non-classic form

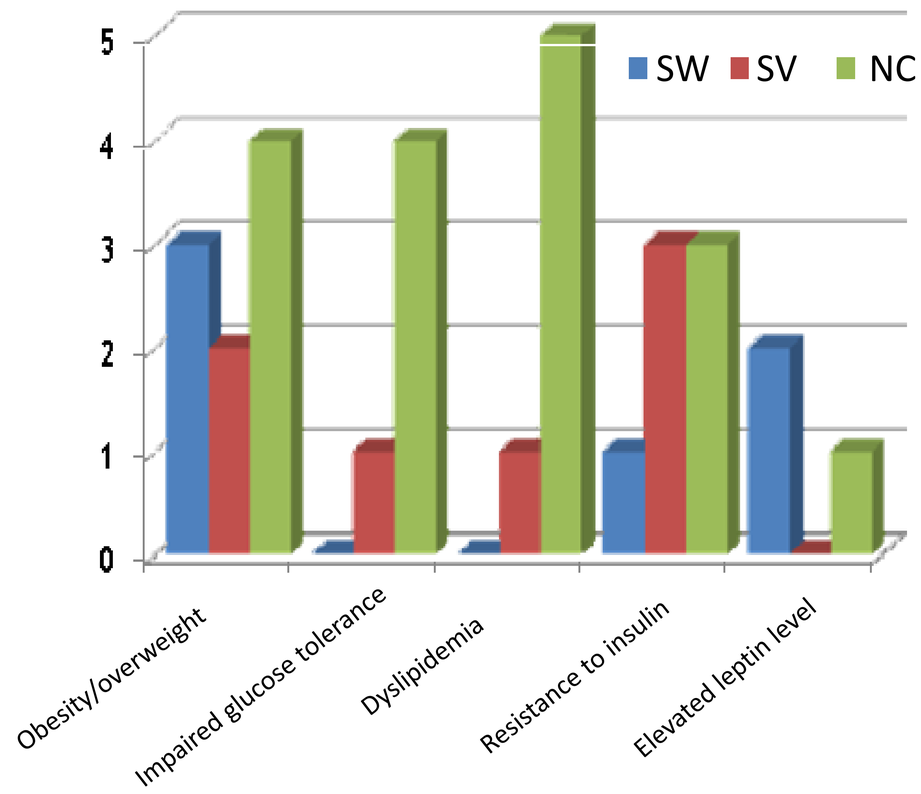

Figure I: confrontation betwwen metabolic features and CAH phenotypes

At the end of this metabolic assessment and according to the criteria of theNCEP-ATPIII, the metabolic syndrome was confirmed in a single patient associating android obesity, diabetes and hypoHDLemia.

Discussion et conclusion:

The risk of developing a metabolic syndrome appears to be considerably increased in case of CAH.

Several studies demonstrated that CAH have increased levels of visceral and abdominal adipose tissue mainly beacause of the lifelong glucocorticoid replacement.

Several clinical studies have shown that increased androgen levels are associated with decreased leptin concentrations.

Longstanding undertreatment with elevation of adrenal androgens may also reduce insulin sensitivity and induce hypogonadism with low testosterone values by gonadotropin suppression. Hypogonadotropic hypogonadism has been shown to be a risk factor for the metabolic syndrome and T2DM and to increase cardiovascular mortality .

All the compounds of metabolic syndrome have been identified during 21-OH deficiency, such as obesity, hyperleptinemia, dyslipidemia, insulin resistance and increasing body fat requiring screening in this population to prevent the complications of those comorbidities.

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Fat, metabolism and obesity

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