Dual-Energy X-Ray Absorptiometry Study of Body Composition in Patients With Lipodystrophy

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Lipodystrophies are acquired or inherited disorders characterized by selective or generalized loss of adipose tissue. Affected patients are predisposed to insulin resistance and metabolic complications of insulin resistance (1). Noticeably, patients with acquired or hereditary generalized forms are extremely insulin resistant (2,3). On the other hand, in partial forms the ample phenotypic spectrum determines clinical presentations and metabolic profiles of variable degrees (4). Among diagnostic resources for fat distribution evaluation, dual-energy X-ray absorptiometry (DEXA) has been utilized because of its accuracy, reproducibility, and good correlation with computerized tomography (5,6). The purpose of this study was to evaluate body composition with DEXA in patients with different types of lipodystrophy and to determine the correlation between densitometric, clinical, and metabolic features.

RESEARCH DESIGN AND METHODS

— Five female patients with lipodystrophy phenotype had been studied, selected from an outpatient clinic. Three patients had diabetes (patients 1, 4, and 5). Laboratory evaluation was performed. Patients signed an informed consent, and the ethical committee of the institution approved this study. Whole-body DEXA scans were obtained at DENSSO laboratory with GE Lunar Prodigy Advance software, version 9.5, LNR 41569 model.

RESULTS

— The relevant results are depicted in Table 1. Plasma leptin was markedly diminished, consistent with body fat mass. All patients exhibited severe hepatic steatosis at ultrasound study.

Case reports

Patient 1. Patient 1 was a 42 year-old woman who first noticed fat redistribution after her first pregnancy. She was diagnosed for hypertension and type 2 diabetes at 39 years of age and had ischemic heart disease recently recognized. Physical examination revealed abnormal fat distribution showing lack of adipose tissue in members extending to the gluteus region and fat accumulation in the abdomen, face, and neck. DNA sequencing showed the R482Q mutation in lamin A/C gene (LMNA), leading to a diagnosis of familial partial lipodystrophy of Dunnigan variety (FPLD). Two older sisters (patients 2 and 3) with the same phenotype were invited and exhibited the same mutation.

Patient 2. Patient 2 was 45-year-old woman and was patient 1's sister. She noticed a lack of fat from extremities and abdominal fat deposition since puberty. Her appearance was similar to that of her sister.

Patient 3. Patient 3 was a 47-year-old woman, also patient 1's sister, who first noticed fat redistribution around puberty. Results of her physical examination were similar to those of her sisters, except for hirsutism and weight.

Patient 4. Patient 4 was a 54-year-old woman who had noticed fat redistribution and muscular arms since childhood. She presented poorly controlled type 2 diabetes, hypertension, and dyslipidemia. During physical examination, marked lack of adipose tissue in face, arms, and trunk and normal fat deposition in hip and legs were noted. Extensive investigation was undertaken for autoimmunity, and results were negative (except for thyroid antibodies). Clinical presentation pointed to Barraquer-Simons syndrome.

Patient 5. Patient 5 was a 30-year-old woman who presented congenital generalized lipodystrophy, diagnosed at birth. She started insulin therapy at 2 years of age. She presented a good response to rosiglitazone therapy, reducing insulin dosage from 2.74 units $\cdot$ kg^{-1} $\cdot$ day^{-1} to 1.5 units $\cdot$ kg^{-1} $\cdot$ day^{-1} within 3 months. However, the drug was withdrawn because of adverse effects. She exhibited a complete absence of subcutaneous fat, with fat preservation in palms, soles, and scalp.

DEXA analysis of body composition

Remarkably, fat mass differs between partial (patients 1–4) and generalized (patient 5) lipodystrophies. In the same way, the ratio between the fat percentage in trunk and inferior members, defined as fat mass ratio (FMR) to characterize lipodystrophies (7), was markedly different in partial lipodystrophies subtypes. Interestingly, patients with fat accumulation in the upper-body compartment demonstrate an FMR >1.0, while a low FMR (<1.0) was present in patient 4, with lower body fat accumulation. Patient 5, with the generalized form, exhibited a normal value (around 1.0) once she presented an extremely low fat percentage in both compartments.

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Received for publication 9 January 2007 and accepted in revised form 14 March 2007.

Published ahead of print at http://care.diabetesjournals.org on 23 March 2007. DOI: 10.2337/dc07-0025.

Abbreviations: DEXA, dual-energy X-ray absorptiometry; FMR, fat mass ratio; FPLD, familial partial lipodystrophy of Dunnigan variety.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Laboratory tests/DEXA*

Test	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Fasting glucose (70–100 mg/dl)	96	102	81	153	111
2-h glucose (<140 mg/dl)	—	108	122	—	—
Insulin (6- 27 μU/ml)	7.5	12.3	6.3	23.3	—
AlC (%)	7.1	6.1	6	10.9	7.2
Cholesterol (mg/dl)					
Total (<200)	202	244	224	158	179
LDL (<130)	126	157	153	72	105
HDL (>45)	35	39	40	35	31
Triglycerides (<150 mg/dl)	204	125	154	253	217
AST (10–37 mg/dl)	44	28	15	20	21
ALT (10–37 mg/dl)	84	37	11	19	27
Uric acid (2.4–5.7 mg/dl)	4.2	3	3.7	4.4	6.2
Leptin (<17 ng/ml)	7.1	7.3	2.7	5.6	0.2
Fibrinogen (180–350 mg/dl)	381	407	283.5	210.4	350.5
Lipoprotein (<30 ng/dl)	46.5	39.8	21.13	<11.5	19.3
RCP (mg/dl)	<0.08	0.17	0.04	—	—
ApoA (125–215 mg/dl)	135	145	117	88	110
ApoB (55–125 mg/dl)	110	121	126	57	103
DEXA					
Height (cm)	164.00	165.00	161.00	166.00	165.00
Weight (kg)	60.91	61.40	60.40	73.62	59.10
BMI (kg/m²)	22.64	22.60	23.10	26.70	21.50
Fat (%)					
Total	22.70	27.60	16.60	23.10	5.10
Trunk	30.90	34.40	21.40	23.40	5.40
Upper-body limbs	15.80	22.10	12.50	9.70	4.20
Lower-body limbs	13.00	19.10	11.20	27.70	4.40
Android	36.70	39.00	26.00	22.80	4.70
Gynoid	24.60	32.20	19.40	30.20	6.10
Fat mass (g)	13.39	16.33	9.68	16.43	2.86
Lean mass (g)	45.46	42.94	48.64	54.77	53.64
FMR	2.38	1.80	1.91	0.84	1.23

ALT, alanine aminotransferase; AST, aspartate aminotransferase; apo, apolipoprotein; RCP, reactive C protein.

CONCLUSIONS — The phenotypic characterization of five patients with different forms of lipodystrophy was performed, and body composition evaluated by DEXA is presented. Patients 1, 2, and 3 were diagnosed with FPLD. LMNA sequencing showed an R482Q mutation. As pointed out by Garg et al. (4), this type of lipodystrophy can show some clinical heterogeneity at presentation. This was clearly demonstrated by DEXA; patient 3, with lower total and troncular fat percentage, presented a less aggressive metabolic profile. She had a greater BMI than her diabetic sister but less fat mass and greater lean mass. Accordingly, she presented lower levels of plasma leptin, fasting insulin, and homeostasis model assessment of insulin resistance (1.26 × 3.09 compared with patient 2, who was also nondiabetic). This finding suggests that her body composition has provided some metabolic protection.

Patient 4 had a phenotype suggestive of an acquired partial form (Barraquer-Simons). In DEXA analyses, she was the only one with a greater percentage of gynoid fat instead of android fat. This accumulation of peripheral fat, however, did not confer a less aggressive metabolic profile, as could be expected. Patients with Barraquer-Simons syndrome usually present gradual onset and cephalocaudal progression for fat loss. They also exhibit evidence for autoimmune disease (8,9) but seldom present metabolic disarrangement (10). This patient has some coincidental findings for Barraquer-Simons, but she presented a severe metabolic disarrangement. An alternative hypothesis is that the case reported here is a hereditary form with an unknown genetic basis. Indeed, Misra et al. (11) studied nine cases of acquired partial lipodystrophy with techniques of molecular biology, in four of whom were mutations in the LMNB2 gene. Clearly, further studies are necessary to clarify the genetic basis of the syndrome.

Only recently, DEXA has been used for body composition estimation. There are few studies describing its use in lipodystrophic patients (12,13). To our knowledge, most were performed in acquired lipodystrophies, as HIV treatment–related lipodystrophy. Bonnet et al. (7) showed body composition reference values for fat distribution evaluation. In this study, 162 HIV-infected men and 241 control subjects were evaluated, and FMR was suggested as helpful for defining lipodystrophy diagnosis. Comparing the group using antiretroviral therapy with control subjects, they found a cutoff of 1.3 ± 0.2 for distinction between them. In the present study, the patients with FPLD have FMRs well above this cutoff point (2.38, 1.8, and 1.91, respectively, for patients 1, 2, and 3). By contrast, pa-

tient 4, with a partial lipodystrophy that spares fat from lower extremities, had an FMR of 0.84.

In conclusion, in this study DEXA measurements of fat distribution helped to better characterize diverse forms of lipodystrophy. Utilization of FMR could be helpful in precocious identification of partial forms, where this ratio could be > or <1.0. Further studies with larger series are necessary to improve strategies in the diagnosis of lipodystrophies.

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