Reduction of Abdominal Obesity in Lipodystrophy Associated with Human Immunodeficiency Virus Infection by Means of Diet and Exercise: Case Report and Proof of Principle

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Lipodystrophy associated with human immunodeficiency virus infection causes abdominal fat gain, peripheral subcutaneous fat atrophy, insulin resistance, low levels of high-density lipoprotein cholesterol, and hypertriglyceridemia. An exercise program combined with a moderate-fat, low-glycemic-index, high-fiber diet can reverse several aspects of lipodystrophy, and, until specific treatment is available, should be considered for treatment of lipodystrophy.

With the advent of highly active antiretroviral therapy (HAART) for HIV infection, a new problem has been recognized: lipodystrophy, which appears to be a complication of the disease, usually in patients who are receiving HAART [1]. Lipodystrophy may cause atrophy of peripheral fat (in the legs, arms, and face) and accumulation of abdominal—especially visceral—fat, along with deposition of fat in the dorsocervical fat pad ("buffalo hump"), breasts, or both. In all forms of lipodystrophy, it is common to find insulin resistance, low serum levels of high-density lipoprotein cholesterol, and hypertriglyceridemia, although each of these features may be present to a variable extent in any given patient.

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Both the causes of and treatment for lipodystrophy are unclear; switching between different HAART regimens and addition of growth hormone or testosterone to the regimen are being tested in various studies. However, each of these approaches is limited by its clinical utility, cost, and associated side effects. We tested a combination of exercise and a low-fat, high-fiber diet intervention as treatment for lipodystrophy. The first patient to complete the 4-month study showed such dramatic improvement that we report the results here to indicate the potential efficacy of diet and exercise, without pharmacological management, as treatment for lipodystrophy.

Patient and methods. A 44-year-old white man received the diagnosis of HIV infection in 1997 and was treated with a combination of stavudine, lamivudine, and nevirapine beginning in 1998. In January 1998, his blood HIV RNA level was 2583 copies/mL and subsequently, from January 1999 through the most recent test on 12 April 2001, was <400 copies/mL; all testing was performed in the same laboratory. The CD4 count was 430 cells/mm^3 in January 1998, 508 cells/mm^3 in June 2000, and 559 cells/mm^3 in June 2001. From January 1998 through September 2000, he gained 12 kg, but he noted loss of fat and bulging veins in his arms and legs, along with an increase in abdominal girth, which required an increase in his pants size, and an increase in breast size. At study entry, his antiretroviral regimen remained stavudine, lamivudine, and nevirapine. He was moderately active but did not exercise regularly. He took no androgen or growth hormone supplements during the study. There was no family history of diabetes or hyperlipidemia.

Body composition was assessed by means of dual-energy x-ray absorptiometry, which was used to measure whole-body and trunk fat and the mass of lean tissue and bone [2]. Abdominal visceral, subcutaneous, and total fat was assessed by use of a single sagittal CT scan, done at the level of the midpoint of the L4–L5 interspace; the resulting images were analyzed with a computerized image analysis system. The maximum dynamic strength was measured with a 1-repetition maximum (i.e., the maximum weight that can be lifted, 1 time only, through a full range of motion) for 5 different muscle groups with use of Keiser pneumatic exercise equipment [2]. Insulin resistance was estimated by use of the homeostatic model assessment [3]. Fasting serum cholesterol, high-density lipoprotein cholesterol, triglyceride, free testosterone, and HIV RNA levels and CD4 cell counts were measured by use of standard methods.

The exercise prescription consisted of 4 months of progressive cardiovascular and resistance training at a local fitness

Table 1. Values determined at baseline and after 4 months of treatment for a patient with lipodystrophy.

	Measured value		Change in value	
Variable	At baseline	At month 4	Absolute	Percent
Body-mass index, kg/m^2	29.90	27.03	−2.87	−10
Resting energy expenditure, kcal/d	2379	2262	−117	−5
Waist-to-hip ratio	0.98	0.88	−0.10	−10
Body composition				
Fat, kg	25.9	17.3	−8.6	−33
Lean tissue, kg	59.4	61.5	2.1	4
Total, kg	87.9	81.4	−6.5	−7
Fat, %	29.4	21.2	−8.2	−28
Trunk fat, %	14.8	9.1	−5.7	−39
Abdominal CT findings				
Total abdominal fat area, cm^2	387.36	222.38	−164.98	−43
Subcutaneous abdominal fat area, cm^2	268.06	165.65	−102.41	−38
Visceral fat area, cm^2	119.3	56.73	−62.57	−52
Abdominal circumference, cm	106.82	97.43	−9.39	−9
Sagittal diameter, cm	26.41	23.63	−2.78	−11
Metabolic parameter values				
LDL cholesterol, mg/dL	189	159	−30	−16
HDL cholesterol, mg/dL	70	47	−23	−33
Total cholesterol, mg/dL	288	236	−52	−18
Triglycerides, mg/dL	147	149	2	1
Fasting insulin, μU/mL	7.925	4.375	−3.55	−45
Fasting glucose, mg/dL	83	72.25	−10.75	−13
Insulin resistance[a]	29.23	14.05	−15.18	−52
HIV clinical parameters				
CD4 count, cells/mm^3	508	479	−29	−6
Virus load, $\log_{10}$RNA	Undetectable	Undetectable	NA	NA
Fitness outcome: VO_2max, mL/kg/min[b]	29.7	34.7	5	16.8

NOTE. HDL, high-density lipoprotein; LDL, low-density lipoprotein; max., maximum.

[a] As determined by use of homeostatic model assessment [3].

[b] Maximum oxygen consumption.

center. Exercise was done 3 times each week on nonconsecutive days. Each session included a general warm-up, 20 min of cardiovascular exercise, 10 min of stretching and core exercises for the low back and abdominal muscles, 40 min of strength training, and 5 min of general cool-down. Cardiovascular exercise was performed on an elliptical training machine at an intensity of 80%–85% of the maximum heart rate, as determined by aerobic capacity testing. A heart rate monitor was worn during all sessions to ensure that proper training intensity was maintained. Three sets of 8 repetitions were performed for all core and strength training exercises. Five resistance training exercises targeting the large muscle groups of the body (leg press, chest press, leg extension, seated row, and knee flexion) were performed on weight-stack machines that were "selectorized" (i.e., the weight could be selected using a lever system). Approximately one-third of the exercise sessions were supervised by a trainer; the remaining exercise sessions were performed without supervision.

The dietary goals established for the study were as follows: energy intake, 1.3 times the resting energy expenditure, as measured by indirect calorimetry; protein intake, 15% of total calorie intake or 1.3–1.5 g/kg; total fat intake, 30% of total calories; saturated fat intake, $\leqslant$10% of total calories; fiber intake, $\geqslant$25 g per day; and simple sugars, $\leqslant$10% of total calories. Carbohydrates were from foods with a low glycemic index. The patient was seen weekly for nutrition counseling sessions during the 16-week study period.

The study was approved by the Human Investigations Review Committee of Tufts University and New England Medical Center, and the patient gave written informed consent.

Results. Patients are eligible for this study protocol if they report body shape changes consistent with lipodystrophy that

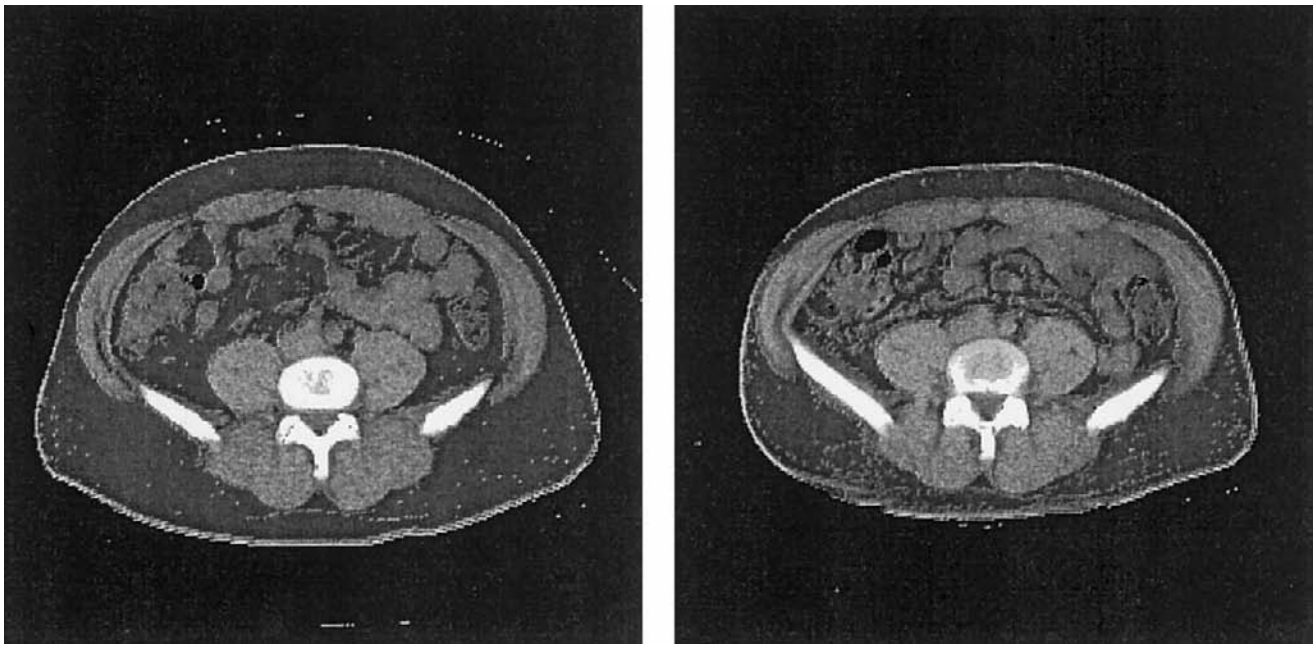

Figure 1. CT scans of the abdomen (at L4–L5 level) of a patient with lipodystrophy: at baseline *(left)* and after 4 months of controlled diet and exercise *(right)*. Note the reduction in fat area at follow-up. Fat shows as dark gray areas; lean tissue shows as light gray; bone shows as white.

are verified by objective measurement in our ongoing Nutrition for Healthy Living cohort study at Tufts University. The patient described here, the first to enter the study, was compliant with the exercise program and completed 90% of all required exercise sessions. His maximal dynamic strength increased by 54% (average value for 5 exercise machines). Results are shown in table 1. At baseline, the patient was overweight according to body-mass index criteria (body-mass index, 26–30 kg/m^2) and according to standards for percentage of body fat (for men, body fat >25%). He had severe abdominal obesity, with a waist-to-hip ratio of 0.98 (a desirable ratio is <0.90) [4]. Total calorie intake increased as his physical activity increased with the exercise regimen, from 2341 to 2733 kcal per day. His dietary intake of protein increased from 15% to 22% of total calories, and his intake of saturated fat decreased from 18% to 11% of total calories. His intake of dietary fiber more than doubled. His serum free testosterone level was in the normal range. No change in leg or arm subcutaneous fat was seen. Abdominal fat reduction is shown in figure 1.

Discussion. Lipodystrophy is a psychologically catastrophic and physiologically dangerous complication of treated HIV infection. It is associated with insulin resistance and hyperlipidemia, which puts patients at increased risk for atherosclerosis, diabetes, and hypertension [5]. Many patients are so distressed by lipodystrophy that they discontinue or become noncompliant with their HAART regimen, which puts them at risk for developing drug-resistant HIV disease.

To date, no therapy for lipodystrophy is recognized as safe or effective, despite intensive research. Most of this research evaluated alterations of HAART regimens or administration of metabolically active substances, such as recombinant growth hormone, testosterone, or hypoglycemic agents, such as metformin or the thioglitazones. However, these treatments are complex and expensive, and they are associated with many side effects.

To our knowledge, this report is the first to show that diet and exercise are capable of reversing much of the metabolic and body composition change seen in lipodystrophy. This patient was typical of men who develop abdominal obesity with peripheral subcutaneous fat atrophy, in that the changes occurred during the 2 years after he started HAART. On the other hand, he did not have other risk factors for lipodystrophy, such as prolonged duration of HIV infection or treatment, sharp changes in CD4 count or HIV RNA, or a family history of lipid- or glucose-metabolism disorders.

We recognize that this patient may well have had a greater response than will be seen in the majority of patients. Indeed, his response is more impressive than that seen in many patients without HIV or lipodystrophy who begin an intensive exercise program. However, we present these data to alert clinicians and patients to the potential benefit of diet and exercise modification as treatment for lipodystrophy while our study and others continue. Although the effect of this regimen on abdominal obesity, insulin resistance, and hyperlipidemia was profound,

no effect on peripheral fat atrophy was seen. However, if the metabolic dangers of lipodystrophy can be ameliorated with diet and exercise, patients can at least be reassured that the residual effects represent a cosmetic problem rather than a threat to their health. Diet and exercise should be considered part of the treatment for lipodystrophy, just as they are for treatment of hypertension, diabetes, and other chronic diseases. Further study of the optimal diet and exercise strategy for lipodystrophy is warranted.

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