An Imaging Study of Body Composition Including Lipodeposition Pattern in a Patient of Familial Partial Lipodystrophy (Dunnigan Type)


Abstract

Familial Partial Lipodystrophy, Dunnigan type (FPLD), is characterised by loss of subcutaneous fat from the limbs and an excessive accumulation of fat on the neck, shoulder girdle and face. Affected individuals have insulin resistance, dyslipidaemia and early cardiovascular events. Body composition (BC) with details of adipose tissue distribution were studied by Dual-Energy X-ray Absorptiometry (DEXA) and Magnetic Resonance Imaging (MRI) in an heterozygote for the FPLD mutation LMNA R482W, and in an age, sex and body mass index (BMI) matched normal control. DEXA revealed a marked decrease in total as well as regional fat percentage in the patient compared to a normal control. Marked reductions in subcutaneous fat in the extremities with substantial lipodeposition in the nape of the neck were confirmed with MRI. The importance of increased perinephric, retroperitoneal and intermuscular fat in the thighs found in this patient, needs to be explored vis-à-vis the pathogenesis of insulin resistance found in FPLD.

INTRODUCTION

Familial Partial Lipodystrophy of the Dunnigan type (FPLD) is a rare autosomal dominant genetic disorder. It is phenotypically characterised by the loss of subcutaneous fat from the extremities and trunk with a selective lipodeposition viscerally and around the shoulders, neck, chin and face.1-3 These patients have hyperinsulinaemia, dyslipidaemia and a high risk of cardiovascular disease, which is similar to that described for visceral or abdominal adiposity.2 Obesity-induced insulin resistance is associated with development of the metabolic syndrome. However, regional fat distribution, particularly truncal adiposity is more highly correlated with the pathogenesis of hyperinsulinaemic dysmetabolic syndrome and associated increased risks of cardiovascular morbidity and mortality.4 Detailed studies of patterns of adipose tissue distribution are thus important for FPLD patients. Anthropometric methods are limited in their ability to detect sites and extent of fat deposition in various body areas. Newer imaging methods like DEXA and MRI are providing to be better tools to precisely measure fat deposits in various regions of the body.5 A few MRI studies done in patients of FPLD report differing results.6,7 The present communication reports a detailed MRI and DEXA study of an affected female, 26 years of age, belonging to an extended Gujarati family with FPLD. We have previously studied the pedigree, phenotypic presentations, endocrine and metabolic profiles including serum leptin in a large number of this extended family.2,3 These studies confirmed the autosomal dominant nature of FPLD, marked insulin resistance and advanced metabolic disorder, including cardiac events, in a number of affected family members. Some of the family members studied for leptin showed hypoleptinemia inspite of normal body mass index (BMI).3 Genetic studies done in 22 members of the extended family have shown that 16 are heterozygous for the R482W missense mutation in LMNA,8 which encodes the nuclear envelope structural proteins, lamins A & C.9

The patient (Ms. JD), currently 26 years of age, was first evaluated at 15 years of age as a part of family screening, since both her sisters had a typical FPLD phenotype. At her initial visit, physical examination had revealed a marked reduction of subcutaneous fat from extremities with prominent veins (Fig.1). Concentration of blood sugar was normal and serum triglyceride was...
mildly elevated. She had developed progressive lipodeposition in the neck, for which she had undergone a submental lipectomy at 22 years of age. She also developed progressive insulin resistance and hypertriglyceridaemia (Table 1). Her weight was 55 kg and BMI 21.0 kg/m². Body composition (BC) analysis was performed using DEXA and MRI in the patient and in an age (23 years), sex and BMI (BMI 21.5 kg/m²) matched normal healthy control.

**METHODS**

Whole body fat assessment by DEXA was performed using DPX–IQ, Lunar (GE Medical Systems, Milwaukee, WI) using pencil–beam technology.

MRI studies were performed on a 1.5 T Echospeed scanner (GE Medical Systems, Milwaukee, WI) using a quadrature body coil, 128 x 256 matrix and 2-fold excitation. The entire body was scanned using contiguous axial 10 mm T₁ weighted spin echo sequence, with a TR of 500 ms and TE of 30 ms slices from the nape of the neck up to the ankles. Additionally, coronal T₂W images of the thorax were also obtained as fat appears hyperintense on this sequence and is easily identifiable.

**RESULTS**

Results of DEXA in both the patient and the control subject are shown in Table 2. Though the total tissue mass was similar in both, the patient’s fat mass was considerably reduced in the extremities and trunk compared to the control subject. The patient’s lean body mass was increased compared to the control subject. Despite similar BMI, the patient’s percent body fat was only 16.7% compared to 44.4% in the control subject. Bone mineral content was normal in both subjects.

On MRI the patient’s supraclavicular fat pad and the fat in the posterior triangle of the neck were markedly prominent as was the fat layer at the nape of the neck, in spite of prior liposuction (Fig. 2). Decreased subcutaneous fat was confirmed on MRI with marked reduction of the subcutaneous fat mainly in the limbs but also in the trunk. Fig. 3 shows an axial section through the chest, which shows predominantly glandular breasts without the normal fatty component, and also marked reduction of the subcutaneous fat in the anterior chest wall fat. A coronal image of the chest wall showed fat under the pectoralis major and in the axilla in an unusually symmetrical wingshaped appearance (Fig. 4). The normal dual layering of the anterior abdominal fat was not seen in Ms JD due to loss of the superficial fat layer. However, the fat layer deeper to the posterior abdominal muscles was normal. In

<table>
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<th>Date (Year)</th>
<th>Age (Year)</th>
<th>Wt. (Kg.)</th>
<th>Blood Sugar (mg%)</th>
<th>Insulin (µU/mL)</th>
<th>Lipids</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>F 1 hr 2 hr</td>
<td>F 1 hr 2 hr</td>
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<td>70 156 170</td>
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TC = total cholesterol; TG = triglycerides

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<th>Fat (gm)</th>
<th>Fat (%)</th>
<th>Lean (gm)</th>
<th>BMC (gm)</th>
<th>Fat (gm)</th>
<th>Lean (gm)</th>
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<td>11.7</td>
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<td>20.9</td>
<td>19799</td>
<td>657</td>
<td>24803</td>
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<tr>
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<td>8871</td>
<td>16.7</td>
<td>42072</td>
<td>2086</td>
<td>52575</td>
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BMC: Bone mineral content
normal individuals the subcutaneous abdominal fat constitutes the larger mass as seen in the control. However, in the patient the intra-abdominal visceral fat was abundant especially in the perinephric areas (Fig. 5). At the level of the liver there was an increased deposition of fat in the posterior aspect of the abdominal wall compared to the uniform distribution in the control subject (Fig. 6). Sections obtained through the patient’s thigh revealed reduced subcutaneous fat but an increase in the intermuscular fat compared to the control (Fig. 7). The muscle mass also appeared bulky.

**DISCUSSION**

The present study reveals that adipose tissue though completely absent in the subcutaneous areas of the
extremities, is selectively deposited in excess in the other areas of the body in FPLD patients.

The important observation of an unusually large amount of fat deposition in perinephric areas needs further exploration. Classical books of Ayurveda describe the kidneys as a root part of the adipose system (Meda Dhatu). It may be worthwhile to investigate the role of the perinephric fat and kidneys in lipid metabolism.

Understanding of adipose tissue mediated regional control and regulation of metabolic hormones like insulin and leptin is emerging through body composition studies. The presence of hypoleptinemia in spite of selective lipodeposition in FPLD in our earlier study suggests that leptin production may vary as per the adipose tissue from different sites in the body.  

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