Lipodystrophy

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Congenital lipodystrophy is an uncommon autosomal recessive disorder that occurs mainly in females and is characterized by loss of subcutaneous fat, insulin-dependent diabetes mellitus, and masculinization due to defective metabolism of fat. Acquired lipodystrophy is now most commonly encountered in patients infected with HIV who take protease inhibitors. We present an illustrative case of lipodystrophy and review the presenting signs allowing for an accurate clinical diagnosis.

Congenital lipodystrophy often is not diagnosed in a timely manner because the constellation of symptoms may be subtle and not immediately apparent to clinicians unfamiliar with it. Features of congenital lipodystrophy include loss of body fat, phlebomegaly, hepatosplenomegaly, diabetes, and lipemia.[1] Patients may have acanthosis nigricans and coarse curly hair. Hypermetabolism and excessive bone growth occur, and precocious enlargement of the genitalia may be evident. Mental deficiency, epilepsy, and renal anomalies may be seen in some individuals.

Case Report

A 55-year-old woman with a history of diabetes mellitus, coronary artery disease, and hypertriglyceridemia presented with unstable angina. She underwent coronary artery bypass grafting without complications but was noted to have marked hypertriglyceridemia. Laboratory studies revealed a triglyceride level of 1762 mg/dL, total serum cholesterol level of 301 mg/dL, and high-density lipoprotein level of 18 mg/dL.

Physical examination revealed a woman in no acute distress with masculine appearance, increased body hair, and curly scalp hair (Figure 1). She had prominent definition of muscles and veins and acanthosis nigricans of the nape of the neck and axilla (Figure 2). Biopsy from the axilla revealed papillomatosis and an increased stromal component consistent with acanthosis nigricans (Figure 3).

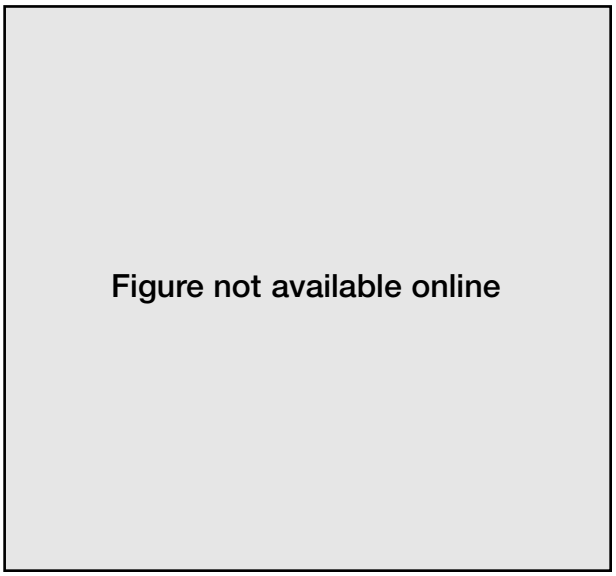

Figure 1. A 55-year-old woman with curly scalp hair and loss of subcutaneous fat.

Treatment for her hypertriglyceridemia included an insulin drip and thermofiltration. She was later placed on a regimen of self-administered subcutaneous insulin twice daily with good effect. Her C-peptide level was elevated at 6.3 ng/mL (normal, 0–3.0 ng/mL). C3 levels were normal, as were liver function tests, androstenedione levels, and a determination of insulin antibodies.

Comment

Lipodystrophy occurs in either an uncommon generalized form or as a localized response to injury or inflammatory disease. Congenital lipodystrophy has several synonyms including total lipodystrophy, lipotrophic diabetes mellitus, and Lawrence-Seip syndrome. Congenital generalized lipodystrophy typically presents in the first 2 years of life with loss of subcutaneous fat, muscular hypertrophy, hirsutism,

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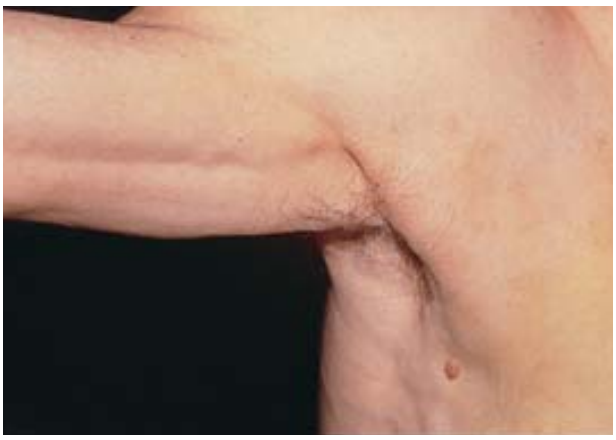

Figure 2. Prominent muscle definition and phlebomegaly.

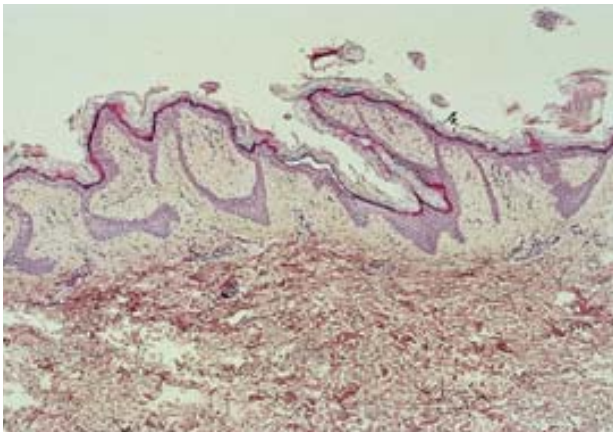

Figure 3. An axillary biopsy demonstrating papillomatosis consistent with acanthosis nigricans (H&E, orginal magnification ×20).

hepatosplenomegaly, and hypertriglyceridemia.[1-3] Diabetes mellitus often does not become pronounced until 10 years of age, with patients being extremely insulin resistant. Defective fat metabolism in these patients may lead to fatty infiltration of the liver causing portal cirrhosis. Lipodystrophy causes an accelerated growth rate and high basal metabolic rate, which lead to many of the outward manifestations of the condition. Also, this metabolic abnormality may be related to an abnormal somatotropin gene cluster as was reported in one patient.[4] Some researchers suspect that lipodystrophy may be caused by increased levels of hypothalamic releasing factors. In support of this theory, pimozide has been effective in reducing triglyceride levels in some patients, presumably by influencing the concentration of hypothalamic releasing factors.[5]

Acquired lipodystrophy is increasingly common in patients with HIV infection who take protease inhibitors. The protease inhibitors ritonavir and saquinavir are most closely linked with this form of acquired lipodystrophy.[6] Protease inhibitors have homology with cellular retinoic-acid binding protein and lipoprotein-related protein,[7] which both regulate lipid metabolism. Protease inhibitors binding to cellular retinoic-acid binding protein and related proteins may affect fat cell differentiation and apoptosis. Drugs binding to lipoprotein-related protein may impair chylomicron uptake, resulting in lipemia. Understanding the mechanisms of acquired lipodystrophy should lead to useful treatments. At present, treatment is primarily symptomatic and directed at controlling diabetes and hypertriglyceridemia by conventional means. Dietary fish oil supplementation[8] and substitution of medium-chain fatty acids for long-chain fatty acids have been effective treatments in isolated cases.[9] Early diagnosis allows for prompt treatment, which may include genetic counseling.

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