

Familial Partial Lipodystrophy

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Familial partial lipodystrophy is a rare condition characterized by an abnormal distribution of fatty (adipose) tissue. Adipose tissue is normally found in many parts of the body, including beneath the skin and surrounding the internal organs. It stores fat as a source of energy and also provides cushioning. In people with familial partial lipodystrophy, adipose tissue is lost from the arms, legs, and hips, giving these parts of the body a very muscular appearance. The fat that cannot be stored in the limbs builds up around the face and neck, and inside the abdomen. Excess fat in these areas gives individuals an appearance described as "cushingoid," because it resembles the physical features associated with a hormonal disorder called Cushing disease. This abnormal fat distribution can begin anytime from childhood to adulthood.

Keywords: genetic conditions

1. Introduction

Abnormal storage of fat in the body can lead to health problems in adulthood. Many people with familial partial lipodystrophy develop insulin resistance, a condition in which the body's tissues cannot adequately respond to insulin, which is a hormone that normally helps to regulate blood sugar levels. Insulin resistance may worsen to become a more serious disease called diabetes mellitus. Some people with familial partial lipodystrophy develop acanthosis nigricans, a skin condition related to high levels of insulin in the bloodstream. Acanthosis nigricans causes the skin in body folds and creases to become thick, dark, and velvety.

Most people with familial partial lipodystrophy also have high levels of fats called triglycerides circulating in the bloodstream (hypertriglyceridemia), which can lead to inflammation of the pancreas (pancreatitis). Familial partial lipodystrophy can also cause an abnormal buildup of fats in the liver (hepatic steatosis), which can result in an enlarged liver (hepatomegaly) and abnormal liver function. After puberty, some affected females develop multiple cysts on the ovaries, an increased amount of body hair (hirsutism), and an inability to conceive (infertility), which are likely related to hormonal changes.

Researchers have described at least six forms of familial partial lipodystrophy, which are distinguished by their genetic cause. The most common form of familial partial lipodystrophy is type 2, also called Dunnigan disease. In addition to the signs and symptoms described above, some people with this type of the disorder develop muscle weakness (myopathy), abnormalities of the heart muscle (cardiomyopathy), a form of heart disease called coronary artery disease, and problems with the electrical system that coordinates the heartbeat (the conduction system).

2. Frequency

Familial partial lipodystrophy is a rare disease, affecting an estimated 1 in 1 million people overall. Type 2 is the most common form, with more than 500 cases reported in the medical literature. Women tend to be diagnosed with familial partial lipodystrophy more often than men, probably because a loss of fat from the hips and limbs is more easily recognized in women, and complications such as diabetes and hypertriglyceridemia occur more commonly in women.

3. Causes

Familial partial lipodystrophy can be caused by mutations in several genes. Type 2 results from mutations in the *LMNA* gene. The other, less common forms of the disorder are caused by mutations in different genes.

LMNA and the other genes associated with familial partial lipodystrophy provide instructions for making proteins with a variety of functions, including important roles in fat storage. In particular, these proteins play important roles in the development and function of adipocytes, which are the fat-storing cells in adipose tissue. Mutations in any of the genes associated with familial partial lipodystrophy reduce or eliminate the function of their respective proteins, which impairs the

development, structure, or function of adipocytes and makes the body unable to store and use fats properly. These abnormalities of adipose tissue alter hormone production and affect many of the body's organs. However, it is unclear why the changes cause fat to be lost in some parts of the body and stored abnormally in others.

In some people with familial partial lipodystrophy, no gene mutations have been found. Researchers are looking for additional genetic changes that can cause this disorder.

3.1. The Gene Associated with Familial Partial Lipodystrophy

- LMNA

4. Inheritance

Most cases of familial partial lipodystrophy, including type 2, are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Rare cases of familial partial lipodystrophy appear to be inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- Dunnigan-Kobberling syndrome
- FPL
- Kobberling-Dunnigan syndrome
- lipodystrophy, familial partial

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