Lipodystrophy Syndromes

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KEYWORDS

• Lipodystrophy • Congenital generalized lipodystrophy
• Familial partial lipodystrophy • Acquired generalized lipodystrophy
• Acquired partial lipodystrophy • Metreleptin

KEY POINTS

- Lipodystrophies are a group of heterogeneous disorders characterized by varying degrees of body fat loss and predisposition to insulin resistance–related metabolic complications.
- They are classified as generalized, partial or localized by extent of fat loss; and genetic and acquired by etiology.
- Highly active antiretroviral therapy–induced lipodystrophy in HIV-infected patients and drug-induced localized lipodystrophy are more prevalent subtypes, followed by genetic and acquired autoimmune lipodystrophies.
- Common metabolic abnormalities and complications include insulin resistance and diabetes mellitus, hypertriglyceridemia, and hepatic steatosis.
- Management options include diet and exercise; conventional antihyperglycemic agents and lipid-lowering therapy; and metreleptin therapy, which is the only drug approved specifically for generalized lipodystrophy.

INTRODUCTION

Lipodystrophies are a group of rare disorders of diverse cause characterized by variable loss of body fat. The loss of body fat may affect nearly the entire body (generalized), only certain body regions (partial), or small areas under the skin (localized). Depending on the severity and extent of body fat loss, patients may be predisposed

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to metabolic complications associated with insulin resistance.[1,2] These metabolic complications include early onset of diabetes mellitus, hypertriglyceridemia, and hepatic steatosis.[1–3] In some patients, these metabolic complications are challenging to manage and can lead to complications including diabetic nephropathy and retinopathy, acute pancreatitis (from extreme hypertriglyceridemia and chylomicronemia), hepatic cirrhosis, and premature cardiovascular disease. Other common clinical manifestations include polycystic ovarian syndrome (PCOS), acanthosis nigricans as a result of severe insulin resistance, and eruptive xanthomas caused by extreme hypertriglyceridemia.[1–3]

The loss of body fat can result from underlying genetic defects (genetic lipodystrophies including autosomal-recessive or autosomal-dominant subtypes) or from autoimmune mechanisms (acquired lipodystrophies including generalized or partial subtypes) or drugs (eg, highly active antiretroviral therapy [HAART]-induced partial lipodystrophy in human immunodeficiency virus [HIV]-infected patients or localized lipodystrophies from insulin and other injected drugs).[1–3] The localized lipodystrophies and lipodystrophy in HIV-infected patients are the most prevalent subtype of lipodystrophies, whereas the other genetic and acquired lipodystrophies are rare.[2] Localized lipodystrophies do not predispose to metabolic complications because the loss of fat is trivial; however, other partial or generalized lipodystrophies cause variable predisposition to metabolic complications.

The major subtypes of lipodystrophy are described in **Table 1** and shown in **Fig. 1**. However, given the heterogeneity of manifestations, variable patterns of fat loss, and genetic basis that have yet to be identified, all lipodystrophy syndromes cannot be classified into these categories.[4] Regardless of the cause, patients with generalized lipodystrophy have extremely low serum levels of adipocytokines, such as leptin and adiponectin,[5,6] whereas serum leptin and adiponectin levels in those with partial lipodystrophies can range from low to high. Marked hypoleptinemia may induce excessive appetite and can exacerbate metabolic complications of insulin resistance.[3] This article covers the major types of lipodystrophy syndromes.

Table 1
General classification of major lipodystrophy subtypes

Lipodystrophy Subtype	Main Characteristics
Congenital generalized lipodystrophy	Presents with near total loss of body fat at birth or during infancy. Autosomal-recessive inheritance.
Familial partial lipodystrophy	Presents with variable loss of subcutaneous fat from the upper and lower extremities and the truncal region at puberty or later. Autosomal-dominant inheritance.
Acquired generalized lipodystrophy	Characterized by gradual loss of subcutaneous fat from nearly all over the body. Associated with autoimmune diseases.
Acquired partial lipodystrophy	Characterized by gradual loss of fat from the upper body, including head, neck, upper extremities, and truncal region during childhood. Associated with autoantibodies called complement 3 nephritic factor and in ~20% of patients with membranoproliferative glomerulonephritis.
HAART-induced lipodystrophy in HIV patients	Associated with therapy including HIV protease inhibitors or nucleoside analogues.
Localized lipodystrophy	Usually caused by insulin injections or other injectables, such as steroids.