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Overview on Acquired Partial Lipodystrophy: Review Article

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ABSTRACT

Background: Acquired partial lipodystrophy (APL), an uncommon form of the disease, is characterised by a gradual onset of bilaterally symmetrical subcutaneous fat loss from the face, neck, upper extremities, thorax, and abdomen while sparing the lower limbs. About 20% of those with APL also have autoimmune disorders, especially membranoproliferative glomerulonephritis (MPGN). Additionally, the majority of patients have low levels of serum complement 3 (C3), and some of them also have C3 nephritic factor. Metabolic issues are uncommon.

Objective: This review aimed to provide an overview of acquired partial lipodystrophy's prevalence, pathophysiology, diagnosis, and treatment.

Methods: We scoured medical journals and databases including PubMed, Google Scholar, and Science Direct for information on: Acquired partial lipodystrophy, Pathophysiology, Diagnosis and Treatment. Between 2003 and 2022, however, only the latest or most comprehensive study was considered. The authors also assessed the usefulness of references drawn from similar books. Documents written in languages other than English have been overlooked because of lack of funding to translate them. Unpublished articles, oral talks, conference abstracts, and dissertations were all generally agreed upon not to constitute valid scientific investigation.

Conclusion: Hyperglycemia and hypertriglyceridemia that do not improve with medication or excessively high insulin dosages may be important signs of lipodystrophy in the clinical environment. It is important to emphasise that these criteria have not been prospectively tested, despite the fact that efforts to introduce these criteria to various treatment contexts (private, academic, government, and others) may be significant for figuring out the true incidence of these diseases. By enhancing lipodystrophy identification and increasing public awareness of the ailment, it will be simpler to ensure that patients with the condition receive the proper care. Acquiring metabolic control and treating aesthetic issues brought on by fat loss are the main goals of therapeutic care for patients with acquired lipodystrophy.

Keywords: lipodystrophy, acquired, glomerulonephritis, metabolic disease.

INTRODUCTION

The term "lipodystrophy" is used to describe a variety of metabolic disorders marked by either a total or partial loss of fat (lipoatrophy), which may coexist with abnormal fat accumulation in other parts of the body [1]. Additionally, it was shown to be a group of uncommon heterogeneous illnesses that are all characterised by a lack of adipose tissue without signs of malnutrition or a catabolic condition [2]. These conditions can be thought of as lipid-partitioning disorders because their primary flaw is the destruction of functional adipocytes, which results in ectopic steatosis, severe dyslipidemia, and insulin resistance [3]. However, regardless the etiology, what disrupts insulin sensitivity and lipid metabolism is the selective absence of adipose tissue and the diminished capacity to store long-term energy [3].

Lipodystrophic patients frequently have metabolic issues, highlighting the significance of adipose tissue as an active endocrine organ. Diabetes mellitus, hypertriglyceridemia, and hepatic steatosis, which can progress to steatohepatitis, are only a few of the metabolic abnormalities that frequently accompany significant insulin resistance in lipodystrophy syndromes. Acanthosis nigricans, polycystic ovarian syndrome (PCOS), and eruptive xanthomas are further public symptoms (Due to severe hypertriglyceridemia) [2, 4]. Additionally, the loss of adipose tissue frequently causes a decline in leptin levels, which inhibits the transmission of hunger-satiety signals and frequently results in hyperphagia [5].

There are various subtypes of lipodystrophy, each with a unique pattern of fat loss and the potential to be either congenital or acquired. Although all acquired variants are generally uncommon, they have grown in popularity as a side effect of specific drugs and iatrogenic processes. However, depending on the subtype, decreases in overall adipose burden could lead to metabolic issues, which would increase morbidity and mortality in people with lipodystrophy [6, 7].

Based on the aetiology (genetic or acquired) and distribution of lost adipose tissue, which may affect the entire body (generalized) or only specific parts, lipodystrophies are categorised (partial). These results in the creation of four main categories: familial partial lipodystrophy (FPLD), acquired generalised lipodystrophy (AGL), and congenital partial lipodystrophy (CGL) [8]. All acquired variants are rare, although as a side effect of some pharmaceuticals as a result of iatrogenic causes, they have increased in popularity [9].

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One of the uncommon types of lipodystrophies is known as acquired partial lipodystrophy (APL), also known as Barraquer-Simons syndrome or cephalothoracic lipodystrophy. At a median age of 7 years, acquired partial lipodystrophy commonly begins in infancy [11]. It influences females and regularly follows an acute, febrile viral illness, most commonly measles [10]. A kind of acquired partial lipodystrophy characterised by symmetrical loss of adipose tissue on both sides of the upper torso [2]. APL is characterised by a distinctive, cephalocaudal pattern of fat loss. The face is where fat loss starts, and it then spreads to the neck, upper extremities, thorax, and abdomen. Instead of exhibiting lipoatrophy, the lower limbs, lower abdomen, and gluteal area accumulate more adipose tissue [11].

About 20% of those with APL also have autoimmune disorders, especially membranoproliferative glomerulonephritis (MPGN). Additionally, the majority of patients have low levels of serum complement 3 (C3), and some of them also have C3 nephritic factor. Metabolic issues are uncommon [11].

Prevalence

APL syndrome was first described in 1885 and was further classified by Barraquer and Simmons in the 20th century. Additionally, only about 250 cases have been reported in English-language literature since then [10]. About four as many women as men experience this. The majority of these cases have been of European ancestry. Although commencing as late as the fourth or fifth decade of life has also been reported, the typical age of lipodystrophy onset has been reported to be around 7 years [11].

Pathophysiology

APL's exact pathophysiology of fat loss is unknown. The metabolic alterations in lipodystrophies patients are due to a general decrease in the load of adipose tissue [9]. Patients with APL commonly have C3 hypocomplementemia, which is characterised by dysregulation of the alternative pathway (AP) of the complement system and is frequently brought on by the presence of C3 nephritic factor (C3NeF) [12]. The AP C3 convertase autoantibody C3NeF works by stabilising and lengthening the complex's half-life, which causes C3 consumption and chronic C3 hypocomplementemia [13].

The serum levels of C3 and polyclonal immunoglobulin C3 nephritic factor are typically low in patients with both APL. It has been hypothesised that C3 nephritic factor, a serine protease enzyme also known as adipsin, directs factor D, whose differential expression by a variety of bodily tissues determines the cephalocaudal pattern of fat loss that is characteristic of APL [11, 14]. Factor D (FD), as previously suggested by other authors [10, 11, 15], could be regarded as a key role in the pathophysiology of BSS given the association between adipose tissue and complement system activation. A recent investigation discovered an uncommon mutation in this gene to be more frequent in patients with APL than in control subjects, suggesting that changes in the LMNB2 gene may also contribute to the development of APL [16].

The metabolically active tissue known as adipose serves a variety of physiological purposes. Adipose tissue serves as insulation in addition to mediating inflammation and secreting a variety of hormones that are important for endocrine function. Certain hormones are lacking in people with lipodystrophies due to a decrease in adipose tissue [9]. The production and secretion of the adipokines leptin and adiponectin are drastically decreased in pathological conditions where adipose tissue function is severely compromised [2].

Adipose tissue releases the proinflammatory adipokine leptin. Because it regulates appetite mediators and energy expenditure mediators, it is frequently referred to as the "satiety hormone." Reduced leptin causes insulin resistance with a potential for developing into diabetes, hyperinsulinemia, hypertriglyceridemia, and hepatic steatosis, whether it occurs in the context of intrinsic leptin deficiency or lipodystrophy [17, 18, 19].

Symptoms

Loss of adipose tissue, which is a significant symptom of APL, first appears in the face and then gradually spreads to the upper extremities, thorax, and upper belly. Although it spares the lower extremities, it proceeds predictably in a cephalocaudal pattern. Fat accumulation in the lower belly, gluteal area, and lower extremities is possible [3]. There are several common metabolic problems linked to high insulin resistance that are present in lipodystrophy syndromes, including diabetes mellitus, hypertriglyceridemia, and hepatic steatosis, which can progress to steatohepatitis. Acanthosis nigricans, polycystic ovarian syndrome (PCOS), and eruptive xanthomas are other common symptoms [4].

Diagnosis

Due to the rarity of these disorders and inability of doctors to recognise this condition, the diagnosis of lipodystrophy is frequently delayed. The diagnosis is typically made clinically based on the patient's medical history, body fat distribution, physical exam, and metabolic profile [2]. Any person who has a partial or total lack of subcutaneous adipose tissue should be suspected of having it [2].

For a precise clinical diagnosis of lipodystrophy, a thorough physical examination is required. Clinicians should carefully examine determining how muscular and lean the extremities and gluteal region are. In addition, various bodily parts should be checked for the buildup of too much fat [20].

The absence of subcutaneous fat can be measured by conventional anthropometric measurements, dual energy x-ray absorptiometry (DXA) scanning, whole-body magnetic resonance imaging (MRI), and computed tomography (CT) scanning [4]. Anthropometric measurements of limb circumference and skinfold thickness are quick, easy, and inexpensive ways to track fat reduction and redistribution [21].

Doctors appreciate using laboratory tests as a tool to assist the diagnosis. Hyperglycemia and hypertriglyceridemia that are unchanged or unresponsive to conservative treatment may serve as additional signs to the doctor that a patient may have lipodystrophy when fat loss is not confirmed by the physical examination or by an imaging modality [3]. All patients should have their blood sugar levels, glycated haemoglobin (HbA1c), serum lipids (particularly triglyceride levels), and liver function tests checked both during the first evaluation and at subsequent appointments. Leptin levels may also be used to support the diagnosis in addition to these laboratory evaluations [4].

Treatment

Treatment for lipodystrophy aims to improve both pathological abnormalities in fat distribution and metabolic problems. Acquired partial lipodystrophy (APL) is typically treated with aesthetic, nutritional, or medicinal measures [1]. In order to avoid difficulties, it concentrated on managing metabolic imbalances as well as outward appearance. Despite the lack of clinical trial data, diet and exercise are essential components of the therapy approach [22].

For the majority of patients, a diet with a well-balanced macronutrient composition of roughly 50–60% carbs, 20–30% fat, and roughly 10–20% protein is acceptable [22]. Patients should be encouraged to engage in physical activity because, barring contraindications, exercise can assist the advancement of metabolic parameters [2].

The use of lipid-lowering drugs and diabetic medications is crucial for patients with severe metabolic imbalance. In this patient population, pioglitazone has been shown to be more effective than metformin at increasing insulin sensitivity [9]. APL's fat distribution may benefit from treatment with rosiglitazone or pioglitazone, according to a number of case reports [23, 24]. They attach to the gamma subunit of the peroxisome proliferator-activator receptor (PPAR-gamma), which promotes the transcription of adipocyte-specific genes that are necessary for adipocyte growth and differentiation [25].

The sole FDA-approved replacement medication for some individuals with lipodystrophy is metreleptin, a recombinant human leptin [9]. Currently, the only medication specifically approved for treating lipodystrophy is metreleptin therapy, which has been shown to reverse metabolic abnormalities in patients with the disease, including decreased blood triglyceride levels, increased insulin sensitivity, and decreased hepatic steatosis [26].

Cosmetic Treatment

Lipodystrophy-induced body shape changes can frequently result in emotional distress and occasionally even physical discomfort, such as from the absence of fat pads on the feet and buttocks [22]. Patients with lipodystrophy report an increase in their quality of life along with cosmetic improvement of lipoatrophy and fat excess. Data on cosmetic surgery, however, are scarce [26]. Dermal fillers, autologous fat transfer (in APL), or muscle transplants may be used to treat facial lipoatrophy [27, 28]. Extra fat from the head, neck, or vulva may be surgically reduced or refined utilising liposuction and breast implantations for better cosmetic results in women [20, 29]. Moreover, fillers such poly-L lactic acid and calcium hydroxyapatite may be used to treat patients with lipodystrophy in aesthetically delicate areas [9].

In order to develop diagnostic and management guidelines for lipodystrophies, more research generally has to be done in this area. Additional therapy options are anticipated to emerge for this patient population as we learn more about the specifics of metabolic control [30, 31, 32].

CONCLUSION

Hyperglycemia and hypertriglyceridemia that do not improve with medication or excessively high insulin dosages may be important signs of lipodystrophy in the clinical environment. As the body of information about lipodystrophy grows as a result of ongoing research activities, this consensus statement will likely be updated and improved. Its objective is to increase the detection of all lipodystrophies. It is important to emphasise that these criteria have not been prospectively tested, despite the fact that efforts to introduce these criteria to various treatment contexts (private, academic, government, and others) may be significant for figuring out the true incidence of these diseases. By enhancing lipodystrophy identification and increasing public awareness of the ailment, it will be simpler to ensure that patients with the condition receive the proper care. Acquiring metabolic control and treating aesthetic issues brought on by fat loss are the main goals of therapeutic care for patients with acquired lipodystrophy.

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