

CLINICAL MANAGEMENT

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Lipedema: A Frequently Misdiagnosed and Misunderstood Fatty Deposition Syndrome



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Dr Fife has disclosed that she is/was a recipient of grant/research funding from KCI; was a recipient of grant/research funding from Organogenesis; is/was a member of the speaker's bureau for KCI; and is/was a shareholder of Intellicure, Inc. Drs Maus and Carter have disclosed that they have no significant relationships with or financial interest regarding this educational activity. All staff, including spouses/partners of staff and authors, in a position to control the content of this CME activity have disclosed that they have no financial relationships with, or financial interests in, any commercial companies pertaining to this educational activity.

This continuing education activity will expire for physicians on February 28, 2011.

PURPOSE:

To enhance the learner's competence in caring for patients with lipedema through understanding the differential diagnoses, pathophysiology, and treatment/management options.

TARGET AUDIENCE:

This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES:

After participating in this educational activity, the participant should be better able to:

1. Differentiate lipedema from other similar diagnoses.
2. Tell patients with lipedema and their caregivers about treatment of this condition.
3. Construct assessments, treatment plans, and management options for patients with lipedema.

ADV SKIN WOUND CARE 2010;23:81-92; quiz 93-4.

INTRODUCTION

Lipedema is a condition in which there is a pathological deposition of fatty tissue, usually below the waist, leading to progressive leg enlargement. The leg enlargement is frequently misdiagnosed as lymphedema even when no lymphatic malfunction is present. However, lipedema can eventually result

in secondary lymphatic dysfunction leading to *lipolymphedema*. The diagnosis of lipedema is a clinical one and may be challenging to determine among patients who are overweight or obese. Understanding the features of lipedema and lymphedema will enable the clinician to make the correct diagnosis. Because there are no diagnostic tests for lipedema, the

diagnosis is made clinically, that is, based on the examination and history. Therefore, it is important for clinicians to understand the morphology of lipedema and its unique features.

Fat has been estimated to constitute approximately 8% to 23% of body composition in men and 20% to 35% in women with a normal body mass index.¹ This range narrows somewhat for specific ethnicities and increases slightly with age. In addition, the normal distribution of fat between the sexes is different, with women more likely to deposit fat subcutaneously and on their legs in comparison to men who are more likely to experience fat deposition in the abdomen.²

Nonsymmetric fat accumulations are known as lipomas, which may be isolated or clustered and are described as soft, benign, fatty tissue tumors.³ Multiple symmetric lipomatosis (Madelung disease) is a rare disease distinguished by non-encapsulated adipose deposits in the neck, the superior part of the trunk, and, on occasion, the limbs.³⁻⁵ It is common in middle-aged, white, Mediterranean men who have a history of alcoholism.

The most common form of symmetrical fat distribution is obesity. Many diseases and syndromes, however, give rise to unusual fat deposition patterns. For example, polycystic ovary syndrome, Cushing syndrome, and growth hormone-deficiency states produce disturbances in fat mass with truncal increases in fat common in the former 2 conditions.⁶⁻⁸

Herpertz³ describes lipohypertrophy as a condition that involves localized symmetrical deposition of fat in buttocks, or the upper or lower thighs, or the lower calves in which the feet are spared. Hypertrophy and hyperplasia of the associated adipocytes are present. But because pain is not present, this syndrome is different from lipedema—although it might precede it. This article will focus on lipedema, a unique fatty deposition syndrome. Readers will learn the physical findings characteristic in lipedema and how they differ from edema due to venous disease, or lymphedema due to congenital lymphatic disorders. All of these disorders can cause leg enlargement, and it is important for the clinician to understand the various etiologies of leg enlargement in order to understand what treatments may be effective.

CLINICAL PRESENTATION OF LIPEDEMA

General Features

Lipedema was first described by Allen and Hines⁹ in 1940 as a syndrome of subcutaneous deposition of fat in the buttocks and lower extremities coupled with the presence of leg edema. A larger case series published shortly thereafter defined the condition as a “symmetrical bilateral enlargement of the buttocks and lower extremities, which begins almost impercept-

ibly and progresses gradually.” Lower limb enlargement is accentuated by orthostatic edema, especially in warm weather, and an inability to completely reduce the enlargement by prolonged bed rest. The failure of bed rest to reduce the size of the legs indicates that most of the leg enlargement is due to the fatty deposits, not the edema.¹⁰

The condition almost exclusively affects women, with only 2 cases reported for men in the literature.^{10,11} Indeed, over a 10-year period in the authors’ lymphedema clinic, only 1 male patient with lipedema has been observed (Figure 1). Although as many as half of lipedema patients may be overweight or obese,¹⁰⁻¹³ most have a normal appearance from the waist up, so their upper body and lower extremities “do not match.” However, despite vigorous attempts at losing weight, which may result in substantial loss of upper body fat, the size of the legs does not decrease. Thus, clinicians often refer to lipedema fatty deposits as being “diet resistant.” Although some view lipedema as a syndrome in which depositions are restricted to the legs,¹⁴ the authors are in agreement with most reports that the abnormal fat deposition extends to the thighs, the buttocks, and perhaps the hips in some instances.

Onset is typically noticed during teenage years or in the third decade of life, but the first visit to a clinic may not take place until decades later when the condition has progressed.¹³⁻²⁵

Figure 1.
48-YEAR-OLD HISPANIC MAN WITH LIPEDEMA

The patient has had recurrent bouts of cellulitis in the legs. He has hemosiderin deposits, which may be due to recurrent infection or venous insufficiency. Note the sparing of his feet. In the 10-year history of the authors’ clinic, this is the only male patient seen with lipedema.



Patients may report other female family members being affected, with the incidence of familial patterns in the literature varying from 16% to 45%.^{10,13,15} This assessment can be difficult to make as it includes asking the question, “Who has big legs in your family?” rather than asking about who is overweight.

Clinical Findings

The typical appearance of the lower extremities in lipedema is one of bilateral symmetrical enlargement of the legs with sparing of the feet. In the early stages of the disorder, the only sign may be the disappearance of the concave spaces on both sides of the Achilles tendon (ie, the filling of the retromalleolar sulcus).²⁴ However, as the condition progresses, the characteristic “stove-pipe” legs emerge (Figure 2), and a sharp demarcation between normal and abnormal tissue at the ankle can often be observed, giving the appearance of “pantaloons” (Figure 3). Fat pads also are consistently found just anterior to the lateral malleolus with additional fatty tissue present between the Achilles tendon and medial malleolus (Figure 4). The skin is usually normal in texture and appearance, without the dermal thickening or induration common in lymphedema.¹² Some authors have also described fat deposits in the upper extremities that abruptly end at the wrist, thus sparing the hand, in conjunction with fatty deposition on the legs.²⁶ In the authors’ experience, arm involvement is less common in lipedema, but many patients in the clinic have demonstrable enlarged arms; Figure 5 shows a dramatic deposition of fat on the arm, but the patient has a normal forearm and hands. In the best descriptive study to date, Herpertz³ reported that of 144

Figure 2.
LIPDEMA WITH SPARING OF FEET DESPITE ENLARGEMENT OF LEGS



Figure 3.
PANTALOOON DISTRIBUTION OF FAT WITH OVERLAPPING AT ANKLES BUT SPARING OF FEET



patients with lipedema, excessive fat deposition was restricted to the legs in two-thirds, but only 3% had lipedema solely in the arms. In contrast, whereas 97% of the patients had lipedema in the legs, it was also present in the arms of 31% of the patients, suggesting that arm involvement is probably common.

Figure 4.
BILATERAL FAT-PAD SIGN AT ANKLES



Figure 5.
LIPDEMA OF UPPER ARM, BUT FOREARM AND HAND ARE NORMAL



Other features of lipedema include a minimal or mild pitting edema in perhaps a quarter of patients, which is sometimes relieved by elevation, and a sensation of heaviness or discomfort in the legs that is sensitive to digital pressure. The aching pain and tenderness described by many patients also gave rise to the term *painful fat syndrome*.⁹ The results of a recent pain study in 50 patients with stage II lipedema conducted by Schmeller and Meier-Vollrath²⁷ also suggest that although average pain scores were similar to the levels

reported by patients with chronic pain, the specific verbiage used—"heavy, pulling, torturing, enervating, violent, unbearable, exhausting, and stabbing"—indicates that the level and type of pain may be far more distressing than is commonly assumed. Table 1 summarizes the clinical findings.

Psychological Aspects

Lipedema is frequently misdiagnosed as lymphedema or chronic venous insufficiency, or patients are told they are "just fat."^{10,13,15,26,28} Thus, many patients endure treatments that will not improve their condition or embark on aggressive dietary programs that fail to result in weight loss in the legs. Coupled with the embarrassment of their condition, it is not surprising that the typical lipedema patient is demoralized. Although no formal quality-of-life assessment has been conducted, in the authors' clinic, lipedema patients have been observed with a higher severity of depression than patients with paralysis. Földi and Földi²⁸ list anorexia nervosa, bulimia nervosa, and pseudo-Bartter syndrome, caused by frequent use of diuretics, among the many conditions that lipedema patients may develop in addition to depression, which results from self-esteem issues and numerous, futile attempts at dieting and exercise to remove the excess fat on the affected extremities. Patients also struggle to find appropriately fitted clothing. Many report being "a size 12 on top and a size 20 on the bottom" (Figure 6, although it is hard to see with her arms at her sides, the patient has a relatively small waist). Thus, in a few cases, psychological counseling may be necessary in addition to the reassurance that the clinician can provide.

Table 1.
DIFFERENTIAL DIAGNOSIS BETWEEN OBESITY, LIPDEMA, LYPHEDEMA, AND LIPOLYPHEDEMA

Characteristic	Obesity	Lipedema	Lymphedema	Lipolymphedema
Gender	Male or female	Almost exclusively female	Male or female	Almost exclusively female
Time at onset	Childhood onward	Typically at age 10–30 y	Childhood (primary); adult (secondary)	Typically at age 30 y onward
Family history positive	Common	Common	Only for primary lymphedema	Occasionally
Effect of dieting on condition	Positive	None	None	None
Effect of elevation	None	Minimal	None	Helpful until fibrosis occurs
Pitting edema	Absent	Minimal	Pitting may stop as fibrosis progresses	Usually present to some degree
Bruises easily	No	Yes	No	Yes
Pain	None	Present in legs	None in the early stages	Present in legs
Area affected	All parts of the body	Bilateral legs, thighs, buttocks (feet spared); arms sometimes (hands spared)	Feet affected first, then progressive leg involvement; unilateral more common than bilateral	Feet affected eventually with positive Stemmer's sign; usually lower extremities (bilateral)
Stemmer's sign	Absent	Absent	Present	Present

PREVALENCE, CLASSIFICATION, AND PROGRESSION OF LIPEDEMA

Prevalence

The prevalence of lipedema in women is not known for certainty. In 2 clinics specializing in lymphology and edema, 10% to 20% of patients were diagnosed with lipedema, which suggests that lipedema is far more common than originally thought and not a rare disease.^{29,30} For example, Herpertz²⁹ recently estimated that in Germany there might be approximately 120,000 patients with lymphedema and 25,000 patients with lipedema,²⁹ which would suggest a prevalence of 0.06% to 0.07%. In the authors' clinic, of a consecutive sample of 792 patients with lymphedema of the lower extremities, 22.7% had a localized type of obesity, meaning an involvement of lipedema with their lymphedema.³¹ This represents a skewed population of patients who had already developed lymphedema. However, in an unpublished epidemiological study conducted in 2001, Földi and Földi²⁸ claimed that lipedema is present in 11% of the female population. This seems to be a very high number. Moreover, diagnosis of lipedema in the

Figure 6.
STAGE III LIPEDEMA WITH LARGE DEFORMING FAT DEPOSITS; NOTE SIZE DIFFERENCE BETWEEN UPPER AND LOWER BODY



Figure 7.
STAGE I LIPEDEMA



early stages of the condition is difficult, and thus, it would be challenging to accurately assess its prevalence in any cross-sectional study. Nevertheless, its incidence to some degree in the female population is probably higher than what clinicians might suspect.

Staging

Meier-Vollrath and Schmeller³² have proposed a staging system to describe the severity of lipedema in which stage I is described as flat skin with enlarged subcutis, which, when palpated, feels like “Styrofoam balls in a plastic bag” (Figure 7); in stage II, walnut to apple-like indurations can develop, and overlying skin has an irregular appearance akin to a “mattress” (Figure 8); and in stage III, larger indurations and deforming fat deposits are apparent (Figure 6).²⁶ Staging may be helpful in knowing where the patient is in terms of condition evolution, although it does not indicate whether progression to lipolymphedema will occur.

Lipedema Phenotypes

A classification system has been suggested to describe the pattern of fat deposits. As many as 5 different patterns of fatty deposition may exist,³² but a classification like this does not aid in treatment. Földi and Földi³⁰ suggest 2 major types of lipedema phenotype: columnar and lobar. The columnar type seems to be predominant^{11,13,15,17,19,20,26} and can be described as enlargement of portions of the lower extremities as a series of varying conic sections (Figure 9). The less common lobar type is typified by the presence of large bulges or lobes

Figure 8.
STAGE II LIPEDEMA WITH IRREGULAR SKIN AND NODULAR FAT DEPOSITS



of fat that overlay enlarged lower extremities or hips^{20,26} or even upper arms (Figures 5 and 10). Some patients may present with a hybrid of both types. The authors have noted a “Michelin tire” presentation (Figure 11; a severe columnar form), as well as a “jodhpurs” appearance (Figure 12; a severe lobar pattern).

Progression to Lipolymphedema

Although it can take several decades for patients to progress from stage I to III lipedema, at any time the patient can develop secondary lymphedema, gradually or suddenly.³¹ Many kinds of trigger mechanisms may exist, and clinicians do not know precisely what risk factors can predispose a patient toward the development of secondary lymphedema, but it is likely that obesity plays a role. There may be a preexisting, subtle lymphatic dysfunction, or lymphedema may be caused by the accumulative damage to the lymphatic and capillary systems that result from decades of lipedema.

DIFFERENTIAL DIAGNOSIS

Many lipedema patients have a history of varicose veins or thrombophlebitis¹⁰ but typically do not have chronic ve-

Figure 9.
ENLARGEMENT MOSTLY ABOVE THE KNEE OF THE LEGS



nous insufficiency, although some minor impairment of venous function may be apparent.¹³ Distinguishing obesity from lipedema can be accomplished by noting (*a*) whether the fat

Figure 10.
STAGE III LIPEDEMA WITH BULGING FAT DEPOSITS

This patient is developing lymphedema on the left as shown in the photograph.



Figure 11.
ADVANCED COLUMNAR DISTRIBUTION OF FATTY DEPOSITS (“MICHELIN TIRE” APPEARANCE)



deposits in the arms and legs spare the feet and hands, (b) whether the adiposity is predominantly in the extremities or it exists in the extremities *and* the trunk, and (c) by whether diet

Figure 12.
UPPER THIGH LIPEDEMA LYMPHEDEMA IN A “JODHPUR” DISTRIBUTION



and/or physical activities reduce truncal adiposity but not extremity adiposity (Table 1).³³ Easy bruising is often noted. Pain upon pressure is universal in patients with lipedema and is commonly described an “aching dysesthesia.”^{10,34}

Lymphedema is a condition in which edema leads to inflammation and fibrosis as a result of reduced lymphatic return. Lipolymphedema is the condition in which lipedema acquires a lymphedema component and is thus differentiated from pure lipedema by the presence of Stemmer’s sign. The Stemmer’s sign is the inability to pinch a fold of dorsal skin at the base of the toes and will be positive in patients who have developed secondary lymphedema.³⁴ In patients with pure lipedema, the Stemmer’s sign is negative. In lipedema patients, edema is minimal and relieved by elevation. In lymphedema patients, the edema is persistent. At first, it may be pitting but as fibrosis worsens, legs may become “wooden” in texture and without pitting.³⁴

In many women, lipedema will remain relatively stable, but in a proportion of patients, a gradual progression is observed, and in some, an abrupt development of the condition and/or evolution to lipolymphedema can occur (Figures 13 and 14). Exacerbation can be caused by pregnancy or surgery^{35,36} or some trauma, reminiscent of the triggers for primary lymphedema.³¹ It can be quite difficult when the clinician is presented with an advanced case of lipolymphedema, particularly in an obese patient, to know what the course of development was—for example, whether obesity and obesity-related sequelae, such as recurrent cellulitis or heart failure, predisposed the patient toward lymphedema at some stage following a stable

Figure 13.
LIPEDEMA WITH SEVERE SECONDARY LYMPHEDEMA AND DRAINING WOUNDS; THE FEET ARE NOW AFFECTED



Figure 14.

LIPDEMA WITH SECONDARY LYMPHEDEMA; THE FEET ARE STILL LARGELY SPARED



lipedema condition, or whether primary lymphedema came first followed by obesity and/or lipedema.³⁴

Imaging techniques, such as lymphoscintigraphy, computed tomography, magnetic resonance, or ultrasound, are not routinely needed to establish a diagnosis for lipedema.²⁶ As discussed, the diagnosis of lipedema is a clinical one. In some cases of lipolymphedema, where the extent of the lymphedema component is not obvious from clinical examination, and delineation would be helpful in terms of treatment planning, magnetic resonance lymphangiography is the recommended imaging modality of choice as it is the least invasive procedure and provides both anatomical location and severity assessment of any dysfunctionality within the lymphatic system.²⁵

PATHOPHYSIOLOGY

Several theories have been postulated regarding the etiology of lipedema. Földi and Földi²⁸ have proposed that microangiopathy in the area of the affected adipose tissue sets off the condition leading to increased permeability to proteins and increased capillary fragility. The latter feature is a hallmark of lipedema, and it is interesting that complex decongestive physiotherapy, a standard therapy for lymphedema, has been found to reduce capillary fragility.²² This suggests that some biochemical factor present in the lymph or perhaps the

interstitial fluid may be associated with this condition, which when partially removed improves capillary fragility. It should be noted, however, that the diminished venoarterial reflex found in lipedema may also contribute to hematoma formation.^{22,28,37}

Clinicians know that hypoxia is a major induction factor for angiogenesis and that, in the eye, pathological angiogenesis in the retina leads to catastrophic loss of vision in a variety of diseases, including retinopathy of maturity, diabetic retinopathy, and age-related macular degeneration.³⁸ The major characteristic of these new capillary vessels in these disease states is one of fragility,³⁹ which is also a common finding in lipedema patients. Angiogenesis is controlled by several factors, one of which is vascular endothelial growth factor (VEGF), and thus, it is reasonable to conclude that if the capillary fragility in lipedema patients is the result of pathological angiogenesis, then the levels of VEGF ought to be abnormally high. In a study of the effects of shock-wave therapy in patients with lipedema or cellulite, Siems et al¹⁸ did indeed find high levels of plasma VEGF levels at baseline, with an average value of approximately 530 pg/mL. Normal values of plasma VEGF are in the range of 100 to 130 pg/mL,^{40,41} so this would represent at least a 4-fold increase. Extracorporeal shock-wave therapy, however, did not change the levels of VEGF or the protein carbonyl concentrations, whereas it increased plasma levels of malonyl dialdehyde (MDA), carbonyls and MDA both being markers of oxidative stress. The high baseline levels of both MDA and protein carbonyls are indicative of severe preexisting oxidative stress that one might find in long-standing adipocyte inflammatory processes and likely represent an accelerated lipid peroxidation in lipedematous tissue. Although VEGF levels did not change after therapy, this does not preclude the presence of localized high concentrations in lipedematous tissue as VEGF is a protein of about 45 kDa and might not be as mobile as a small molecule such as MDA.

Another theory relates to the immunohistochemical findings of Suga et al.²³ Using the case of a 74-year-old Pakistani woman who was diagnosed with lipedema, these investigators discovered a high number of adipocytes in the affected tissue larger than 150 μ m and other degenerative changes characterized by macrophage accumulation and the formation of crown-like structures. This is reminiscent of similar reported changes in the adipose tissue in obese humans and mice in which some adipocytes undergo necrosis and are scavenged by macrophages.^{42–44} Hypoxia induced by excessive adipose hypertrophy has been proposed to cause adipose metabolic dysfunction and the production of adipose tissue cytokines in obesity—essentially an inflammatory reaction^{45,46}—and such factors might be operative in lipedema. However, in addition, Suga et al²³ also observed an increase in cells that had Ki67 and

CD34 markers, which are associated with cell proliferation, and adipose stem/progenitor cells, respectively. Based on this information, the authors propose that proliferation of adipose stem/progenitor cells indicated a rapid increase in adipogenesis, which in turn led to localized hypoxia and adipocyte necrosis.

Given the familial association of the condition, one might expect some genetic involvement in lipedema, but, to date, no known data have been published on the subject. Fourteen gene candidates and 38 quantitative trait loci have been reported for metabolic syndrome alone, and this is just scratching the surface for genes related to obesity and its sequelae.⁴⁷ Abnormal fat deposition patterns and/or dysfunctional fat metabolism, however, may be only part of the story. A number of gene candidates have been proposed for primary lymphedema. It has been speculated that specific mutations or certain gene haplotypes may be involved in the development of secondary lymphedema in which subtle changes give rise to subclinical syndromes that develop into fulminant lymphedema when the lymphatic system is locally injured or stressed.³¹ Such factors cannot be ruled out in the development of lipedema because they have not been studied.

Many studies have investigated the lymphatic system using a variety of imaging techniques, and although the findings in lipedema patients are not anywhere as severe as observed in lymphedema patients, a number of interesting abnormalities have been detailed.

Using dynamic radionuclide lymphangiography of the lower limbs in 12 females with lipedema, Bilancini et al¹⁴ reported that, as a whole, the lymphatic systems in these patients were much slower compared with normal subjects. The findings were similar to those with lymphedema, but the degree of impairment was less. Considerable variation was observed between lipedema patients, yet most subjects showed asymmetric lymphatic impairment in contrast to the bilateral clinical presentation of the disease. Although the authors proposed that differences in the venous calf pump might account for this strange finding, which they might, the similarity to the pattern of primary lymphedema is striking. In a smaller series of 10 patients with lipedema, Harwood et al¹³ noted from their lymphoscintigraphy study that only 1 patient had moderately impaired lymphatic function in both legs, whereas the other 9 patients had slight impairment in 1 or both legs. In a more sophisticated investigation of 22 lipedema patients that used dynamic lymphoscintigraphy, van Geest et al¹⁷ reported that in most women, epifascial and subcutaneous lymph drainage was not greatly disturbed, and Boursier et al⁴⁸ observed similar results in their case series, describing their patients as having lymphatic insufficiency without the morphological abnormalities seen in lymphedema.

Amann-Vesti et al¹⁶ and Bollinger and Amann-Vesti⁴⁹ used fluorescence microlymphography to visualize the superficial lymphatic capillary system of the dorsum of the foot, the medial ankle, and the thigh in lipedema patients and noted many microaneurysms, defined as segments exceeding twice the minimal individual diameter of the lymphatic vessel. In patients with thigh involvement, microaneurysms were common in the region, whereas in the lower leg, multiple microaneurysms were confined to the ankle. Although the significance of these microaneurysms is not known—it could be a cause of lipedema or secondary to established lipedema—they do not appear to represent severe impediment to lymph flow.

Magnetic resonance imaging has been used since the 1990s to investigate both lipedema and lymphedema and is probably the least invasive of the imaging techniques when contrast material is used. The imaging process typically reveals an increase in the subcutaneous fatty tissue layer in lipedema patients when compared with healthy individuals; however, the skin may or may not be thickened.^{11,20,50} In a recent study of 26 lower extremities in 13 patients with lipedema⁵ and lipolymphedema,⁸ an increased layer of subcutaneous fat in the lower and upper legs was clearly revealed, varying in thickness from 4.4 to 7.7 cm.²⁵ The lipedema patients demonstrated enlarged lymphatic vessels with a diameter of up to 2 mm in 4 lower legs and 2 upper legs, whereas in the lipolymphedema patients, 8 lower legs and 3 upper legs had enlarged lymphatic vessels up to a diameter of 3 mm, and in 2 lower legs, an area of backflow was seen indicative of lymphatic outflow obstruction. Lymphedema was also apparent in an epifascial distribution in 6 lower extremities in the latter group in both the upper and lower legs, whereas it was confined to the lower leg in the remainder of the patients.

In lipedema, lymphangion motor activity disturbances are also likely to be present as early work that used oil contrast lymphangiography showed wavy corkscrew-like suprafascial lymph collectors.²⁸ As the elasticity of the skin is strongly reduced—that is, compliance is increased—the failure of skin in regard to its role as an “abutment” for the venous calf pumps leads to passive hyperemia, and because the venoarteriolar reflex is absent, passive systems that guard against the development of edema become dysfunctional. Warmth from hot summer days also leads to active hyperemia and increases the lymphatic water load, resulting in pitting late in a warm day.²⁸

To summarize, perhaps due to genetic traits that become effective at puberty, abnormal fat deposition slowly begins that might be associated with aberrant local fat metabolism and/or hormonal changes. For several years, the early stage of lipedema can be characterized as one of lipohypertrophy and no pain. In some cases, however, the localized presence of so

much fat causes a low-grade chronic inflammation to set in, resulting in excessive lipid peroxidation, further disturbances in adipocyte metabolism and cytokine production, and the initiation of local hypoxia. These changes initiate VEGF responses and pathological angiogenesis, resulting in fragile capillaries. Perturbations in the structure and operation of the lymphatic system seem to be due to extravasation of proteins from leaky capillaries into the interstitial spaces, mechanical pressure from the high fatty masses, or development of collagen fibrotic abnormalities. In a small percentage of lipedema patients, the condition progresses to lipolymphedema.

TREATMENT

In Europe, compression and complex decongestive therapy are considered standard therapy for lipedema.^{18,21,22,26,28} These are also standard techniques for the treatment of lymphedema, and their application to lipedema patients will produce variable results according to the involvement of the lymphatic system. In patients without edema, compression will not reduce the size of the legs because the leg enlargement is due to deposition of adipose tissue, which will not decrease in volume with external compression. In addition, compression may not be tolerated by lipedema patients because of pain. Compression is challenging in obese patients and requires expert bandaging or semirigid devices in the initial stages,³⁴ although sequential external pneumatic compression⁵¹ may also be helpful. Custom-tailored garments can be used in the maintenance stage, but pain may limit how long they can be worn.

In both Europe and North America, removal of the excess adipose tissue has been successfully accomplished in the last 10 years by liposuction; however, if present, lymphedema should be treated first.^{11,19,24} Some clinicians are still reluctant to recommend liposuction largely as a consequence of the poor results that were obtained before it was understood that “dry” techniques using large sharp cannulas accompanied by circumferential rather than longitudinal motion caused considerable tissue damage and often worsened lymphatic function.¹⁹ The newer “wet” techniques use tumescent local anesthesia in which large amounts of fluid (6–10 L) containing saline, lidocaine, sodium bicarbonate, and epinephrine are first infiltrated into the subcutaneous tissues, thus separating out the fat lobules, which can be removed with vibrating microcannulas.^{19,24,36,52,53} Water jet–assisted liposuction also has been reported, which uses a fan-shaped water jet directed at the subcutaneous space to separate out adipose cells and has the advantage of using less than a fifth of the fluid required for tumescent liposuction, both of which with appropriate technique are optimal for preserving the collagen-

Practice Pearls

Lipedema differs from lymphedema in several key ways.

Lipedema usually:

- involves bilaterally symmetrical leg enlargement (lymphedema is often unilateral or at least much worse on one side)
- initially spares the feet (lymphedema usually begins in the feet)
- involves aching dysesthesia of the legs (lymphedema is usually painless)
- involves easy bruising
- involves “fat pad sign” at the medial ankle
- has diet-resistant leg enlargement and disproportionate upper vs lower body size
- is almost universally in females
- involves edema that is orthostatic and resolves with rest until late

The best treatment options include gentle compression garments to manage the orthostatic component of edema, rigorous weight control, and exercise. There is limited benefit from aggressive compression bandaging and manual lymphatic drainage unless lymphedema has developed. Liposuction can remove fatty deposits, particularly on the upper leg, but some techniques may damage lymphatics.

fibrous septal connective tissue and lymphatic vessels.²⁴ Unfortunately, liposuction is considered a “cosmetic” intervention and is not likely to be covered by third-party payers.

Liposuction can remove existing fatty tissue, but further fat deposition must be prevented. Weight control is critical; although excess weight will be preferentially deposited in the legs, weight loss after dieting occurs in other body areas. In obese patients, bariatric surgery may also prove beneficial in avoiding further weight gain that will aggravate the affected areas. Research is needed in regard to diet composition, which might indicate the kind of diet likely to be most beneficial.

For lipedema patients with varicose veins, treatment is often contraindicated because symptoms, such as leg swelling, generally worsened or remained unchanged.³⁵ Newer techniques, such as endovenous laser ablation, endovenous radiofrequency ablation, and chemical sclerotherapy, hold promise of being far less invasive; however, there are no reports to date of their use in patients with lipedema and varicose veins.⁵⁴ The real issue in such cases may be that these patients are more likely to have their leg enlargement mistaken for vein problems. And, having the veins treated will not fix the patient’s lymphedema if it is caused by lipolymphedema.

CONCLUSIONS

Lipedema is a genetically mediated disorder of fat deposition. It results in a characteristic pattern of lower-extremity enlargement that is resistant to diet and thus very demoralizing. It can eventually lead to lymphedema but should not be mistaken for lymphedema in its early stages.

After completing this activity, clinicians should be better able to evaluate patients with enlarged legs and identify those who suffer from lipedema. This frustrating genetic disorder of fatty deposition is not particularly rare, but is rarely diagnosed because clinicians fail to recognize it. Lipedema responds less well to aggressive compression than venous disease or lymphedema, so proper diagnosis can prevent costly and futile interventions. However, it can progress to lymphedema if left completely untreated. Therefore, clinicians must be prepared to correctly diagnose lipedema and create a realistic plan of care.

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