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Review Article

Lipedema and lipedematous scalp: An overview

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ABSTRACT

Lipedema is a chronic, progressive disease marked by abnormal fat distribution in the limbs, resulting in disproportionately sized and painful limbs. It primarily affects women and causes significant disability, functional impairment, and psychological distress. Despite its clinical significance in women's health, lipedema is largely unknown, underdiagnosed, and misdiagnosed with other diseases with similar symptoms including obesity. It is difficult to distinguish between obesity and lipedema since these two conditions often coexist. Since the precise etiology of lipedema is yet to be determined, there is no treatment that targets the underlying cause. The most basic conservative treatment is decongestive physical therapy, which is normally needed life-long. In some cases, surgical procedures such as liposuction and excisional lipectomy are the therapeutic alternatives. Lipedematous scalp is a rare, dermatological condition with no known cause, characterized by increased subcutaneous tissue thickness and a smooth and boggy scalp. When it occurs in conjunction with alopecia, it is known as lipedematous alopecia, often mistaken as androgenetic alopecia. The goals of this article are to explain the etiology, clinical features, and treatment options for lipedema and lipedematous scalp (two relatively less known conditions), as well as to highlight their diagnostic features.

Keywords: Lipedema, Lymphedema, Obesity, Lipedematous scalp, Lipedematous alopecia

INTRODUCTION

In 1940's Allen and Hines described lipedema for the 1st time as a syndrome characterized by "large legs due to the subcutaneous deposition of fat."[1]

The abnormal deposition of subcutaneous adipose tissue, results in bilateral, disproportionate, swelling of extremities that typically spares the hands and feet.[2] The disease affects women, typically manifests at puberty and may worsen during periods of pregnancy or menopause.[3] It is a chronic, painful and progressive disease that can lead to significant disability, impairment of function, and psychological distress.[4] In contrast to obesity, the adipocyte hypertrophy and swelling in lipedema are resistant to dietary modifications and exercise or bariatric surgery.[5]

Patients often complain about increased pressure sensitivity, pain, easy bruising, and ankle edema.

INCIDENCE AND PREVALENCE

Exact incidence and prevalence remain unknown.[2] Lipedema almost exclusively affects females.[6] The approximate prevalence documented is around 10% of female population.[7] The low prevalence could partly be due to misdiagnosing the condition as obesity or lymphedema.[8] There are a few case reports of lipedema in males. The affected males tend to have disorders

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associated with higher estrogen and decreased testosterone levels.[9]

In majority of the cases lipedema manifests during or soon after puberty.[10]

PATHOGENESIS

The exact etiology of the disease is unknown.[1] The various hypotheses put forth explain the role of hormonal influences, genetics, defects in adipogenesis, vascular factors, inflammatory mechanisms, and lymphatic defects in the development of the disease.[2,11-14]

Almost 60% of the affected had a first degree relative with similar features. Analyses of familial clusters suggest an autosomal dominant inheritance pattern with incomplete penetrance.[12]

The disease typically manifests during the periods of hormonal change such as puberty, pregnancy, or menopause. It is speculated to be estrogen driven, since it results from polygenically mediated changes in the distribution of alpha and beta estrogen receptors (ER) in the white adipose tissue of the affected areas. This modulates the lipid metabolism which, in turn, leads to increased lipogenesis and decreased lipolysis in the affected areas.[11,13,15] Further researches showed decreased ER-α and increased ER-β expression in the gluteal region in comparison to the abdominal region.[11]

Cytological and protein expression studies conducted on lipoaspirates from lipedema patients found changes in the initial steps of cell differentiation in adipogenesis.[2] It is believed that the massive adipose tissue enlargement classically found in lipedema is due to the enhanced proliferation of adipose stem cells in these patients.[14]

Many studies have demonstrated a reduction in capillaries in the subcutaneous fat tissue of patients with lipedema. The resultant hypoxia and altered cytokine secretion cause inflammation of the adipose tissue that ultimately affects the adipogenesis.[2,16] The influx of inflammatory cells into the interstitium can play a role in the signaling pathways that lead to adipocyte hypertrophy.[9] Thus, the initial swelling in lipedema is due to adipocyte hyperplasia and hypertrophy.[13]

In addition, there is thickening of the interstitium and an increase in interstitial fluid as a result of increased hydrostatic pressure.[17] At least in the early stages, the lymphatic system functions normally, despite the elevated interstitial fluid.[17] However, as lipedema progresses, the lymphatic channels stretch and dilate, resulting in the formation of numerous "microaneurysms" that leak. These leaking microaneurysms and a rise in interstitial fluid cause the late-stage lipolymphedema.[13]

The subdermal vascular plexus undergoes conformational changes that are consistent with a microangiopathy that occurs in addition to adipocyte hypertrophy, interstitial thickening, and lymphatic changes.[17] This microangiopathy produces capillary fragility and leakage. This explains the telangiectasias and easy bruisability seen in patients with lipedema.[17] The other postulates put forth for the microvascular dysfunction in lipedema include increased angiogenesis and mechanical disruption of lymph drainage. It is suggested that the excessive adipose tissue expansion seen in lipedema may result in endothelial dysfunction. This serves as a hypoxic stimulus and induces angiogenesis.[2] Increased capillary permeability causes proteins to leak into the extracellular compartment ("capillary leak"), resulting in tissue edema.[2]

The enhanced pain sensitivity associated with lipedema has been linked to an inflammatory mechanism that disrupts the regulation of locoregional sensory nerve fibers.[7] Since lipedema is more common in women, hormonal factors can also play a role in increased perception of pain sensation. Ovarian sexual hormones modulate opioid system of neurotransmitters and serotonin.[11]

CLINICAL FEATURES

Initial symptoms often appear during periods of hormonal transition (puberty, pregnancy, and menopause).[2] Lipedema patients commonly experience pain (either random or pressure-induced), discomfort, tenderness, cold skin, and easy bruising.[18] The pain associated with lipedema is characterized as dull, hard, and pressing. The femoral and anterior tibial regions are the most frequently affected. Touch or slight pressure can cause discomfort. Prolonged standing or sitting (as at the end of the day) can also cause discomfort.[3] Exercise or warm weather can precipitate pain.[17]

The defining feature of lipedema is a disproportionate distribution of body fat on hips, buttocks, thighs, and lower legs, in a gynoid pattern, producing a disproportion between the upper and lower halves of body.[3] Hands and feet are typically spared. The appearance is also known as the "saddle bag phenomenon," because it mostly affects the hips and thighs while the rest of the body maintains normal proportions.[19] Lipedema is distinguished by a clear distinction between normal and abnormal tissues at the ankle (the "cuff sign") and a large disparity in circumference between the hips and waist.[3] Since the feet are usually spared, an "inverse shouldering" effect or "bracelet effect" occurs at the ankles.[20] Women with lipedema, unlike lymphedema patients, can easily pinch the skin on the dorsum of their feet and hands (the "negative" Kaposi-Stemmer sign).[2]

On palpation, the adiposity is granular, with a "sand grain" texture, but it can also be nodular, with a "beans in a bag" feel. Lipedema patients bruise quickly and may have

telangiectasias that correspond to delicate subdermal capillaries.[1]

Wold *et al*. first described the diagnostic criteria for lipedema in 1951, and Herbst has recently modified them [Table 1].[1,2]

Five types of lipedema have been identified based on distribution.[2,17]

Type I: Fat tissue accumulates around the hips and buttocks

Type II: Fat accumulation in the area extending from hips to knees

Type III: Fat accumulation from hip to ankle

Type IV: Approximately 80% of affected women have additional involvement of arms

Type V: Fat accumulates predominantly in the calf region alone.

Lipedema, like many illnesses, tends to worsen over time, so the severity of the disease can be classified into stages as followed.[1]

Stage 1: Even skin surface with an enlarged hypodermis

Stage 2: An uneven skin pattern with the development of a nodular or mass-like appearance of subcutaneous fat, lipomas, and/or angiolipomas

Stage 3: Large growths of nodular fat causing severe contour deformity of the thighs and around the knees

Stage 4: Presence of lipolymphedema

While lymphatic dysfunction and obesity are common findings in late-stage lipedema, lipedema, lymphedema, and obesity are distinguished by a number of characteristics [Table 2].[21,22]

In long standing cases, the consequences include gait disorders, joint damage, and immobility, secondary lymphedema, which raises the risk of cellulitis and sepsis, venous insufficiency (which can lead to venous leg ulcers), depression, weight gain, and maceration, and infection because of bulging tissue and deep skin folds.[17,18]

ASSOCIATED DISORDERS

Lymphedema, obesity, eating disorders, sleep apnea, hypertension, hypothyroidism, and venous insufficiency were the most commonly recorded associations in the previous studies.[2,21,23]

HISTOPATHOLOGY

Adipocyte hypertrophy and hyperplasia, increased numbers of macrophages, and blood vessels, and dilation of capillaries are the histopathology findings.[24]

Table 1: Diagnostic features of lipedema.

- Almost exclusively seen in females
- Fatty tissue hypertrophy on the limbs that is bilateral, symmetrical and disproportionate
- Hands and feet are spared (Cuff phenomenon)
- Arms involved in 30% of patients
- Negative Stemmer sign
- A feeling of heaviness and tension in the affected limb
- Pain on pressure and touch
- Increased tendency to form hematomas
- Limb circumference remains unchanged on weight reduction or caloric restriction
- Worsening of symptoms over the course of the day and in summer
- Telangiectases
- Hypothermia of the skin

Table 2: Differentiating features between lipedema, lymphedema, and obesity.

Clinical feature	Lipedema	Lymphedema	Obesity
Gender	Female	Both	Both
Family history	Common	Rare	Frequent
Symmetry	Present	Absent	Present
Involvement of feet	Feet spared	Involved	Involved
Pitting edema	None	Present	None
Effect of leg elevation	Little to none	Moderate improvement	No effect
History of cellulitis	None	Frequent	None
Pain on touch or pressure	Yes	No	No
Tissue consistency	Soft	Firm	Soft
Involvement of trunk	Absent	Absent	Present

DISEASE COURSE AND PROGNOSIS

Lipedema is a progressive, lifelong disorder.[21]

INVESTIGATIONS

Diagnostic evaluation includes detailed history, inspection, and palpation, with special attention paid to the manifestations described in Table 1 which are crucial in determining the correct diagnosis.[2]

Ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) help to verify whether the swelling is due to homogenous enlargement of the subcutaneous compartment.[8]

Lymphedema can be ruled out by indirect lymphography, fluorescence micro lymphography, functional lymphatic scintigraphy, and magnetic resonance lymphangiography which can assess the structural and functional states of the lymphatic system. Other tests such as dual energy-

ray absorptiometry and bio-impedance analysis provide information about quantification and distribution of total and regional fat and bone mass, making it a useful method for diagnosis, staging, and follow-up.[8]

For follow up assessment, Reich-Schupke et al. recommended clinical metrics such as daily activity index, weight, body mass index, waist-hip ratio, waist-height ratio, and measurements of limb circumference and volume.[25]

It is advised to evaluate the affected for renal and hepatic dysfunction, hypothyroidism (possibly subclinical), abnormal lipid profiles, and insulin resistance.[2]

DIFFERENTIAL DIAGNOSIS

Conditions presenting with swelling or excessive adiposity of the lower limbs, primarily lymphedema and obesity, are included in the differential diagnosis of lipedema. Lipedema is typically characterized by a high resistance to the reduction of lower limb volume by exercise, excessive dieting, or even bariatric surgery.[2]

Chronic venous disease is another common disorder that is mistaken for lipedema. Pitting edema, relief of symptoms and swelling with leg elevation, and skin changes such as brownish discoloration, white scars (atrophie blanche), and ulcers (in advanced stages) are the classic features of this condition.[2]

Dercum disease (adiposis dolorosa) is a clinical disorder that shares certain characteristics with lipedema, such as pain that occurs spontaneously or on palpation, and bruising. Dercum disease is characterized by numerous painful lipomas at first, with the possible progression to circumscribed or diffuse fatty deposition.[21,22]

Madelung's disease, also known as benign symmetrical lipomatosis, is a disorder of fat metabolism that causes an abnormal accumulation of fat deposits around the neck (type I), shoulder and upper arms (type II), or pelvic areas (type III).[6] Men are more likely to develop the disease, which is almost always linked to alcohol abuse and liver damage.[2,3,22]

Lipohypertrophy may resemble lipedema. Women have a symmetrical hip-and-thigh obesity due to a statutory disproportion in body form. Upper extremities are almost never affected. Lipohypertrophy, unlike lipedema, does not cause discomfort, edema, or bruising.[2,4]

Other classic causes such as idiopathic cyclic edema, edema due to cardiac, hepatic, or renal disease, myxedema, and orthostatic edema should be considered when patients present with more advanced edema.[2]

TREATMENT

Since the cause of lipedema is uncertain and there is no cure, the therapeutic approach focuses on resolving or alleviating the symptoms (particularly discomfort, bruising, and disproportion), improving the functional limitations and preventing the disease progression and the complications.[4,5]

Conservative therapies and surgical procedures are the two primary ways to treat lipedema.[2]

Conservative therapies include patient education, weight control and dietary counseling, physiotherapy and exercise therapy, psychosocial therapy, and compressive decongestive therapy (CDT).[2]

While conservative management results in only a small reduction in tissue volume, it does reduce the tenderness and limb tightness.[2]

Surgical therapies include liposuction and lipectomy.[2,4]

PATIENT EDUCATION

Patients should be fully informed about the evolution and progression of the disease. They should be informed of the chronicity of the condition, the therapeutic options and the measures to delay the disease progression.[2]

WEIGHT CONTROL AND DIETARY COUNSELING

Patients with lipedema are more likely to become morbidly obese.[2] Although the pathological subcutaneous fat in lipedema is thought to be immune to dietary restriction, weight loss may help to alleviate the symptoms.[5]

Since no randomized controlled trials on lipedema are available, there is no specific, evidence-based diet for patients with lipedema. Current dietary approaches are based on observational evidence and aim to reduce the body weight through hypocaloric feeding. Since insulin promotes lipogenesis and insulin resistance worsens edema, an isoglycemic diet can be beneficial.[1] Furthermore, a balanced diet that avoids the risk of obesity is crucial to avoid weight loss-weight gain cycles, which lead to the accumulation of lipomatous tissue.[13]

Anti-oxidative and anti-inflammatory agents may inhibit the systemic inflammation.[1]

PHYSIOTHERAPY AND EXERCISE THERAPY

While lipedema fat is resistant to lifestyle changes, there is evidence that exercise, and lifestyle changes may help to improve the accompanying lymphedema, lymph flow, and overall health.[1]

Exercise therapy should be customized to the patient's specific needs and stage of the disease. In general, sports that involve controlled, cyclical walking or running movements that stimulate the calf-muscle pump without causing unnecessary tissue trauma are beneficial.[17]

Swimming, aqua-jogging, and aqua-gymnastics are advised because the pressure gradient under water helps to reduce the edema; exercise under water often bring less stress on the joints of overweight patients, and lower the risk of potential orthopedic complications.[17]

PSYCHOSOCIAL THERAPY

Women suffering from lipedema often suffer from psychosocial disorders such as depression, anxiety, and eating disorders. Hence, psychological support is recommended whenever required.[1,17]

COMPLEX DECONGESTIVE THERAPY (CDT)

It is also known as complete decongestive therapy or complete physical therapy. Manual lymph drainage (MLD), multilayered and multicomponent compression bandaging, meticulous skin treatment, and physical activity are the pillars of CDT.[17] It is a two-phased, multi-step approach with an initial intensive reductive phase and a maintenance phase.[26]

The reductive phase entails a proper regimen of manual lymphatic drainage (MLD), muscle pumping exercises, and external compression therapy. The second phase should begin immediately after the first, with the aim of maintaining and improving the first phase's effects. Compression therapy, as well as optimal exercises and MLD, are continued as required. By halting the progression of lymphedema, they can minimize the increase in limb volume and provide long-term benefits.[26]

Skin care

Gentle but thorough washing of the infected areas should be done on a regular basis, and the surface, especially the toes, should be dried thoroughly after each wash to avoid fungal infection caused by retained moisture.[3,26] Mild emollients are used to avoid dryness of skin and secondary eczema. Keratolytics can slow the progression of secondary changes by reducing the epidermal thickening.[26]

MLD

MLD, a component of CDT, is a form of gentle skin massage that promotes lymph collector contraction and improves protein resorption.[18] Low-pressure (30–40 mm Hg), low-frequency, circular, or spiral massaging techniques are employed by a specially qualified physical therapist during MLD. When combined with compression bandaging methods, the results improve further. The lymphatics become more contractile as a result of the massage, and the flow is redirected through the affected cutaneous channels. To prevent re-accumulation of fluid in the region, non-elastic high-pressure (40–80 mm Hg) compressive bandages or undergarments are applied after each session of MLD and during exercise.[26]

Compression therapy

External compression is an important step in the treatment of lymphedema at any point, and it can reduce the limb volume by 60%. Compression can help to increase the lymphatic flow and the venous return, regulate the limb volume, minimize the accumulation of protein and debris, protect the limb from external damage, and maintain a structural framework for the limb's shape.[26]

Compression therapy can be achieved by (a) compression bandages and garments or (b) intermittent pneumatic compression (IPC) devices.

Compression bandages and garments

A multilayer compression bandage has a protective cotton bandage against the skin, a middle layer of soft foam or synthetic wool underpadding, and an outermost layer of at least two stretchable outer bandages.[18] During the intense phase, compression is applied to the affected area for 24 hours. During the maintenance phase, single layer bandages are applied during the day. Elastic garments with graduated compression from distal to proximal are preferred and recommended for all-day wear.[26] The affected area should be elevated once the garment has been removed. The garments' compression is determined by the severity of lymphedema; a minimum pressure of 40 mm Hg is required, and the maximum compression tolerated by the patient is the most beneficial. The garments must fit properly and comfortably without having a tourniquet effect, and they must be replaced when their elasticity wears out. Before prescribing these garments, it is necessary to rule out contraindications such as peripheral arterial insufficiency and occult neoplasia. Infection at the site or open wounds are not absolute contraindications.[26]

IPC

IPC, a technique that involves application of rhythmic air pressure to the limbs through inflatable sleeves, gloves, or boots, could be incorporated into CDT.[3] But in a randomized study conducted in an inpatient setting, 30 minutes of intermittent compression in addition to 30 minutes of MLD was found to have no persuasive, synergistic, beneficial impact on the symptoms of lipedema. As a result, IPC may be reserved for patients with a higher lymphedema component.[17]

MEDICAL MANAGEMENT

Pharmacological choices have also been suggested, including beta-adrenergic agonists, corticosteroids, diuretics, flavonoids,

and selenium, but their true effectiveness in this disorder is yet to be determined.[17]

SURGICAL THERAPY

For patients who have made little or no improvement with conservative therapies and whose quality of life has been compromised despite adequate conservative management, the following two surgical options may be considered: liposuction and lipectomy.[17]

Significant relief of symptoms was observed with liposuction in five retrospective trials (follow-up lasting up to 8 years).[17] Both subjective parameters (pain perception, tightness, propensity to develop hematomas, and quality of life) and objectively measured factors, such as leg circumference and the required duration and extent of conservative care, are improved after surgery.[15] The procedure makes use of instruments that extract fat more gently, such as the vibrating cannula used in power-assisted or water-assisted liposuction.[1] According to the guidelines, more than 4-6 liters of fat per session should not be removed because the risk of cardiopulmonary complications increases with increasing blood and fluid loss.[5] It is also necessary to keep lymphatic support measures such as compression and CDT before and after surgery.[1]

Microcannular tumescent liposuction was able to permanently minimize body disproportion and pain, halt disease progression, and enhance quality of life.[5]

To avoid damaging the lymphatic vessels, liposuction should be performed using a wet technique.[17] It is recommended that liposuction should be performed in multiple sittings, rather than in a single sitting.[11]

The precise mechanisms by which liposuction reduces pain are unknown, and further research is needed on this subject.[18]

Liposuction is the only treatment that will stop the disease from progressing.[18]

The involved tissue becomes fibrotic in advanced stages of the disease, with associated lymphedema so that liposuction fails to sufficiently reduce the limb volume. Open surgical debulking (lipectomy) may be necessary in such cases.[17]

LIPEDEMATOUS SCALP

Lipedematous scalp (a condition unrelated to lipedema) was first described by Cornbleet *et al*. in 1935 in a 44-year-old black female who complained of cotton – batting like feeling on her scalp.[27,28] It is a rare dermatological disorder of unknown etiology, characterized by increased thickness of subcutaneous tissue resulting in soft and boggy scalp. If it presents along with alopecia or shortened hair, it is known as lipedematous alopecia, which was described by Coskey *et al*. in 1961.[27]

It is more commonly seen in females.[29] Etiology of lipedematous scalp and lipedematous alopecia remains unknown.[30] Proposed mechanisms include impairment in lymphatic flow, role of leptin, degeneration and disruption of adipocytes,[28] and lymphangiectasia.[28,30-32] Mean thickness of normal scalp is 5–8 mm.[31] In the cases reported, mean thickness of lipedematous scalp varied from 10 mm to 16 mm.[30,31]

Onset of lipedematous scalp/ alopecia is insidious.[28] Most patients are asymptomatic, but some may complain of mild itch, painful sensation, paresthesia, headache, and cotton wool like feeling over scalp.[28] On palpation, the involved area can be easily compressed to underlying bone, and on removing the pressure, it bounces back to the initial form.[30] Yasar *et al*. in a retrospective study of 31 patients with lipedematous scalp/ alopecia, noted an association with obesity.[28]

Trichoscopic examination reveals multiple linear telangiectasia.[30] Other investigation modalities found useful are ultrasonography, MRI or CT of scalp and measurement of the thickness of the scalp using needles.[32]

A consistent feature noted in deep, scalp biopsy of lipedematous scalp is increased thickness of subcutaneous fat composed of mature fat cells without cellular anomalies.[28] Other less commonly reported features include dermal edema, lymphatic dilatation, fragmentation of elastic fibers, coarsening and fragmentation of collagen and deposition of mucin in the dermis.[28]

Differential diagnosis includes cutis verticis gyrata, encephalocraniocutaneous lipomatosis, myxedema of scalp, and pachydermoperiostosis.[28,30]

Lipedematous alopecia may cause a diagnostic dilemma with traction alopecia, androgenetic alopecia, or central centrifugal cicatricial alopecia, if proper palpation of scalp is not performed.[30]

Therapeutic modalities tried include topical or intralesional steroid, surgical debulking, and systemic therapy with mycophenolate mofetil.[27,29] Spontaneous resolution is also reported.[31] Response to treatment is often unsatisfactory.[30]

CONCLUSION

Lipedema and lipedematous scalp are two less commonly reported and discussed entities. Most of the available information is in foreign literature. The rarity of reports from the country could be due to a lack of familiarity with the conditions. Through this review, we have attempted to bring these less known entities to the attention of the readers.

Declaration of patient consent

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Conflicts of interest

There are no conflicts of interest.

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