LYMPHEDEMA IN DERMATOLOGY: A MULTIDIMENSIONAL CLINICAL CHALLENGE

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Summary

Lymphedema is a chronic and progressive disease affecting the lymphatic system, characterized by underlying inflammation which further leads to various skin changes. With a significant impact on patients' quality of life, the management of this disease is challenging and requires a multidisciplinary team and early intervention to prevent disease progression. This paper aims to provide an overview of lymphedema with focus on the dermatologist's role in managing these patients.

Key words: *lymphedema, elephantiasis, Stemmer sign, elephantiasis nostras verrucosa.*

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Introduction

Lymphedema is a chronic disorder caused by impaired lymphatic drainage, leading to progressive swelling and tissue fibrosis due to the accumulation of lymph in the interstitial spaces. It is a relatively common condition, affecting an estimated 1.33 per 1,000 individuals, and is associated with a substantial negative impact on patients' quality of life [1–3].

Despite its high prevalence, only in recent years has the medical community shown interest in this pathology, unveiling the more complex mechanisms involved in lymphedema and innovative treatments for slowing the progression of the disease and minimizing the complications. The management of lymphedema requires a multidisciplinary team of medical professionals for early diagnosis and intervention to diminish the burden of this disease. This paper aims to provide an overview of lymphedema with focus on the dermatologists' role in treating these patients.

Classification and etiology

Lymphedema is classified into primary lymphedema and secondary lymphedema. Primary lymphedema is an inherited condition caused by abnormalities of the lymphatic system, most often due to genetic mutations. It is rare, affecting approximately 1 in 100,000 individuals,

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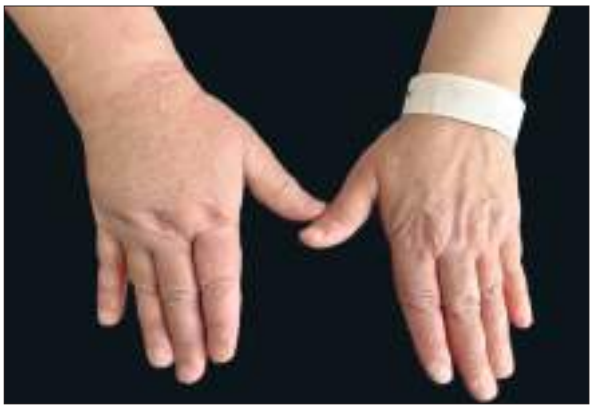

Figure 1 – Secondary lymphedema of the upper limb in a patient with a history of breast cancer treated by mastectomy and axillary lymph node dissection.

and can be categorized into three subtypes: congenital lymphedema, present at birth or within the first two years of life; lymphedema praecox, occurring around puberty or in early adulthood; and lymphedema tarda, which manifests after the age of 35 [4]. Secondary lymphedema is acquired, resulting from damage to previously normal lymphatic system [5].

Primary lymphedema encompasses all developmental lymphatic abnormalities that impair lymphatic drainage. It may occur at any age, in any part of the body, and may range from mild swelling to severe enlargement. Lymphedema may occur alone (non-syndromic primary lymphedema) or in association with other systemic features (syndromic primary lymphedema) [6]. Mutations in several genes involved in lymphangiogenesis have been identified in both syndromic and non-syndromic forms. Consequently, the prevailing hypothesis is that most cases of lymphedema have a genetic origin [7].

Genetic mutations may lead to lymphatic growth (hypoplasia, aplasia), increased lymphatic size (megalymphatic), increased vessel number (hyperplasia), lymphangiodysplasia, valvular dysfunction (resulting in lymphangiectatic dilatation, lymphatic reflux, lymphorrhea) [6]. These maldeveloped structures lack the capacity to adequately return interstitial fluid to the venous circulation, ultimately leading to lymphedema. To date, more than 20 genes have been implicated in primary lymphedema, including VEGFC, FLT4/VEGFR3, GJC2, CCBE1, FAT4, ADAMTS3, BRAF, FOXC2, and chromosomal abnormalities such as monosomy X [5].

Primary lymphedema may occur as an isolated condition or in association with syndromic features. For example, isolated lymphedema may occur in Milroy or Meige disease, while lymphedema in association with other distinct clinical features appear in syn-dromic types such as Turner syndrome, Noonan syndrome, lymphedema–distichiasis syndrome and others [5,8].

Secondary lymphedema is characterized by reduced lymphatic flow due to acquired or external factors. Reported causes include recurrent lymphangitis and cellulitis, filariasis, lymph node dissection (eg, in breast cancer) (Figure 1), malignant obstruction (eg, abdominal or pelvic tumors may compress the lymphatic vessels and veins, impairing drainage and contributing to edema), radiation injury, podoconiosis (from exposure to mineral microparticles in volcanic soils, most common in eastern Africa), granulomatous diseases (Crohn disease, granuloma inguinale, sarcoidosis), obesity, and trauma [9-11]. The most common cause of secondary lymphedema worldwide is filariasis, a parasitic infection due to Wuchereria bancrofti, whereas in Western countries the leading causes are cancer and cancer-related treatments [3].

Acute forms of lymphedema have been described in the literature, caused by temporary incompetence of lymphatic drainage as a result of a local inflammatory response. This leads to transient lymphedema due to lymphatic vessel dilation and impaired drainage. Such situations, observed in musculoskeletal trauma or burns, are referred to as post-traumatic edema (PTL) and are considered a physiological response. PTL usually resolves spontaneously, unless the lymphatic system is permanently damaged during the healing process [12,13].

Pathophysiology - from injury to skin changes

For many years, the pathophysiology of lymphedema was oversimplified, as it was commonly believed that impaired lymph drainage alone was responsible for the disease. However, recent studies suggest that lymphatic system

injury is only the initial step in a far more complex mechanism.

The lymphatic system plays a crucial role in regulating immune responses. When it is injured, this damage acts as a trigger event for a chronic inflammatory process that leads to lymphedema development. Damaged cells release damage-associated molecular patterns (DAMPs), which induce a local pro-inflammatory state and activate dendritic cells (DC). Once activated, DC migrate to the lymph nodes, influencing T-helper (Th) cell differentiation and promoting the production of inflammatory mediators such as interferon gamma (IFN-γ), interleukin-4 (IL-4), IL-13, and transforming growth factor β1 (TGF-β1) [14].

T-helper cells further differentiate into Th1 and Th2 subsets, each releasing a distinct subset of cytokines. Both Th1 and Th2 cells impair lymphangiogenesis and activate macrophages, but Th2 cells appear to play more important role in producing fibrosis [15].

Macrophages also play a pivotal role in the pathogenesis of lymphedema. They can differentiate into two main phenotypes – M1 and M2 – each with distinct cytokine profiles that either promote inflammation (M1) or support tissue repair and regeneration (M2) [15]. In the early stages of lymphedema, M2 macrophages secrete growth factors that stimulate lymphangiogenesis. However, in later stages, once fibrotic changes are established, the number of M2 macrophages declines [15-17]. In addition, macrophages produce interleukin-6 (IL-6), a key regulator of adipose tissue deposition [15,16,18]. This perpetuates a state of chronic inflammation, which further impairs lymphatic drainage, inhibits lymphangiogenesis, and promotes fibro-adipose tissue accumulation – ultimately driving the progression of lymphedema.

Stanging

According to the International Society of Lymphology (ISL) Consensus, lymphedema is classified into four stages based on severity [19]. Stage 0 (latent/subclinical) is characterized by altered lymph transport without visible swelling, which may remain undetected for months or years before clinical edema develops.

Stage 1 involves the early accumulation of protein-rich fluid with pitting edema that is reversible with limb elevation; increased cellular proliferation may also be observed. Stage 2 is marked by non-pitting edema, the onset of fibrosis, and the persistent accumulation of pathological solids such as fat and proteins; at this point, limb elevation rarely reduces swelling, and pitting may disappear as fibrosis and adipose deposition progress. Stage 3, or lymphostatic elephantiasis, presents severe swelling, skin thickening, papillomatosis, acanthosis, and further fibroadipose deposition – irreversible changes in skin structure [19]. The ISL Consensus notes that more than one stage of lymphedema may be present on the same limb, depending on the degree of alterations in different lymphatic areas [19].

Clinical examination

Lymphedema can affect any part of the body, the limbs being most commonly involved. Early changes usually begin distally, in the hand or foot, with progressive swelling. Less frequently, edema of the head and trunk is observed in primary generalized lymphedema, with swelling more prominent in the morning and decreasing during the day as upright posture favors lymphatic drainage [20,21].

In lower-limb lymphedema, the dorsum of the foot is typically affected first, producing a „buffalo hump" appearance, while the toes are involved as well, often referred to as „sausage toes" (Figure 2) [22, 23]. Pitting edema is characteristic in the early stages but tends to disappear as the disease progresses, due to increasing fibroadipose tissue deposition [20]. The foot and ankle lose definition as a result of edema filling the retromalleolar spaces and due to effacement of the natural transverse creases of the foot (Figure 2) [21].

Patients most commonly report a sensation of heaviness which may result in functional impairment, particularly the inability to carry out typical age-appropriate physical activities includind eating or writing (when the upper extremity is affected), crawling or walking (lower extremity), and playing sports [4,6].

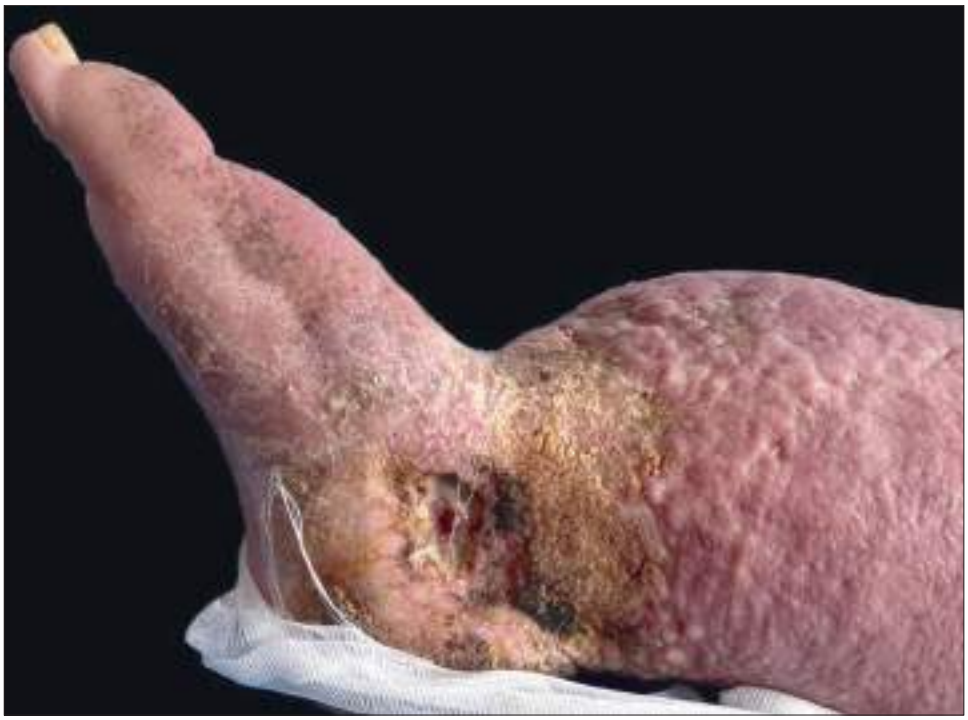

Figure 2 – Lower limb affected by elephantiasis, showing a characteristic "buffalo hump" deformity of the foot and "sausage toes", with loss of malleolar definition. The skin presents erythema and fibrosis, accompanied by varying degrees of papillomatosis (firm papules distally, nodules proximally) and hyperkeratosis. A well-defined ulcer with abundant yellow exudate is present in the medial malleolar region.

As the skin thickens, forming folds that cannot be pinched or lifted, proper hygiene becomes challenging, and the skin is predisposed to breaking and infections. Lymphorrhea may appear in some cases, manifesting as lymph fluid leaking through skin surface, either through a lymphocutaneous fistula or as transsudate [24].

Initially, skin texture changes consist of fine papillomatosis and hyperkeratosis, giving the surface a rough, sandpaper-like feel on palpation, progressing to firm papules and nodules [21,23]. Skin ulceration is unusual if the arterial and venous circulation is intact, however they can occur in severe cases of lymphedema, starting from minor skin breaking [20]. Lymphatic drainage impairment may also prevent wounds from healing [4].

Stemmer sign

The Stemmer sign is a useful tool, reflecting skin fibrosis. In early disease, the skin on the dorsal surface of the second toe can be pinched and lifted (negative Stemmer sign), while in advanced lymphedema, skin thickening prevents this maneuver (positive Stemmer sign) [21]. The Stemmer sign has a sensitivity of 92% but a specificity of only 57%. A positive Stemmer sign strongly suggests lymphedema, although false positives may occur in obese patients. A negative Stemmer sign does not exclude the diagnosis, as patients may be in the early stages of the disease; in such cases, further diagnostic methods, such as lymphoscintigraphy, should be considered [20,25].

Elephantiasis nostras verrucosa

A particular type of elephantiasis is represented by elephantiasis nostras verrucosa (ENV) and is usually described in lower limbs. In 1969, Castellani described four subtypes of elephantiasis: elephantiasis tropica (secondary to filariasis), ENV (caused by recurrent bacterial infections that impair lymphatic drainage), elephantiasis symptomatica (resulting from non-bacterial infections, cancer, or trauma), and elephantiasis congenita (inherited forms) [26]. ENV was originally defined as a condition arising from lymphatic obstruction caused by recurrent bacterial infections, with the term „nostras" used to distinguish lymphadenomatous changes observed in temperate regions from filarial lymphedema seen in tropical regions. Although the terminology has historically been inconsistent, recent literature defines ENV

more broadly as a manifestation of lymphatic obstruction caused by either infectious or noninfectious factors [26,27].

Clinically, ENV is characterized by a dramatic enlargement of the limb, with "woody" fibrosis and cutaneous changes. Papillomatosis with a cobblestone-like pattern may progress to nodular lesions, resulting in a verrucous, mossy appearance of the skin (Figure 3) [9,27]. Histo-logically, ENV shows pseudoepitheliomatous hyperplasia, dilated lymphatic vessels, loss of dermal papillae and sweat glands, and fibrosis of the dermis and subcutis [27]. Disease progression leads to severe complications, including recurrent infections and disability, with amputation sometimes required in advanced cases [27].

Papillomatosis cutis lymphostatica

Papillomatosis cutis lymphostatica is a rare manifestation of primary lymphedema. It presents as focal hyperkeratotic, verrucous lesions of the skin, with a wart-like appearance. Histologically, it is characterized by hyperkeratosis, verrucoid acanthosis of the epidermis, dilated lymphatic vessels, and dermal fibrosis [21,28,29].

Lymphedema rubra

Lymphedema rubra refers to the blanchable erythema that may appear in a lymphedematous limb and is often mistaken for cellulitis. Unlike true infection, it typically evolves in a stationary manner, without fever, and the erythema persists despite antibiotic treatment. These features should raise suspicion for this diagnosis. The condition is thought to result from local inflammation leading to hyperemia and warmth of the affected area, and it is considered an early sign of lipodermatosclerosis [23,24,30].

Bilateral lower extremity inflammatory lymphedema (BLEIL)

BLEIL is a recently described condition characterized by symmetric edema of the lower limbs, accompanied by erythema and pain, clinically resembling cellulitis. BLEIL is considered the result of prolonged orthostatism which leads to venous stasis, subsequent lymphedema, and associated vasculitis. This form of lymphedema has been reported in young adults ini-

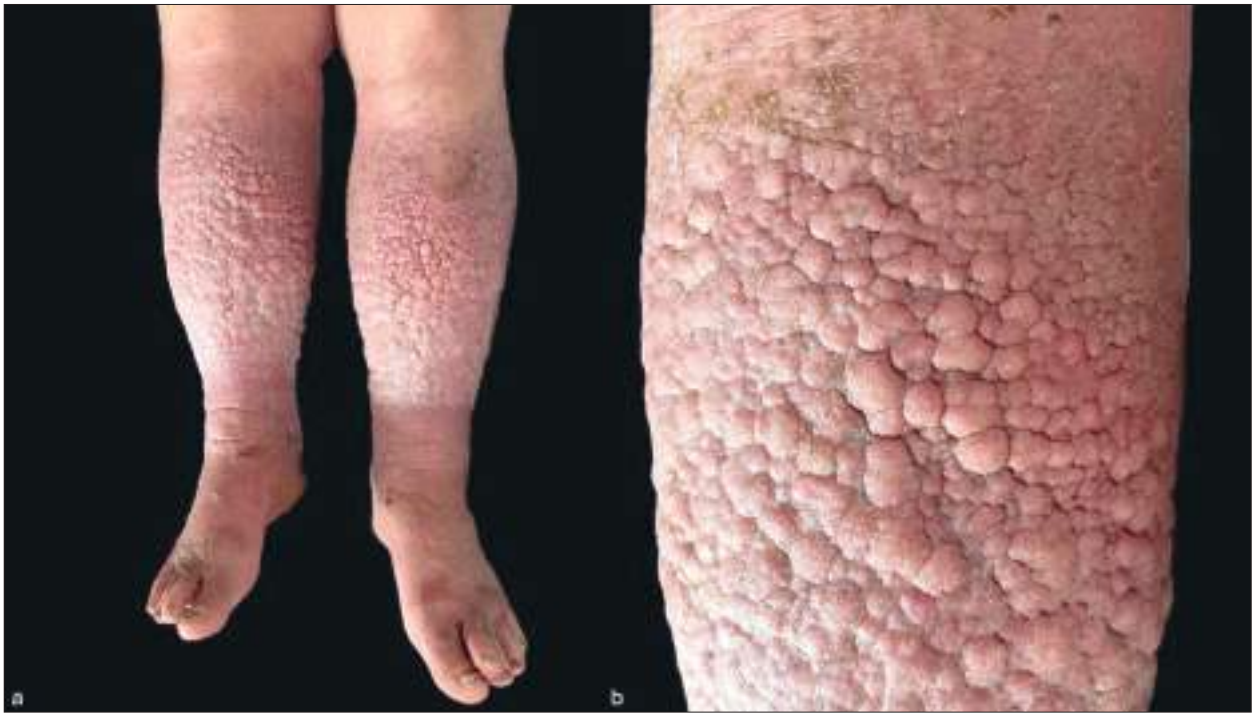

Figure 3 – Patient with ENV exhibiting characteristic verrucous, cobblestone-like papillomatosis.

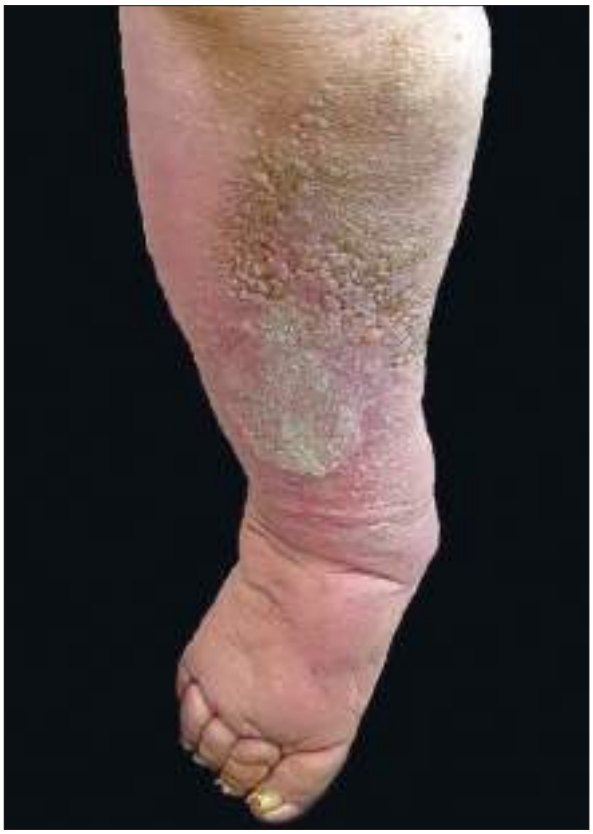

Figure 4 –Lower limb affected by lymphedema exhibiting papillomatosis, hyperkeratosis, characteristic deformities and koilonychia.

tiating military training and typically resolves spontaneously [31,32].

Phlebolymphedema and Lypodermatosclerosis

Phlebolymphedema is a form of lymphedema that develops secondary to chronic venous insufficiency (CVI). As CVI progresses, venous hypertension leads to increased interstitial fluid accumulation, exceeding the drainage capacity of the lymphatic system and resulting in secondary lymphedema [23,24].

Phlebolymphedema can be categorized into two types: dynamic insufficiency phlebolymphedema and lymphatic insufficiency phlebolymphedema. The first is characterized by interstitial fluid overload with normal lymphatic drainage, whereas the second results from permanent lymphatic damage [23,24]. Over time, the inflammation extends into the subcutaneous tissue, causing panniculitis, which in chronic stages evolves to lipodermatosclerosis. Clinically, the leg develops the characteristic "inverted bottle" shape due to extensive fibrosis and sclerosis, while the skin may show induration, hyperpigmentation, or atrophie blanche [30].

Nail changes

Koilonychia, described as hypoplastic, concave ("spoon-shaped") toenails, may also occur in primary lymphedema. These so-called "ski-jump nails" can represent an early sign of the disease (Figure 4) [22,28].

Yellow nail syndrome should be considered in patients with lymphedema and recurrent respiratory symptoms. Slowly growing, thickened yellow nails with subungual hyperkeratosis, onycholysis, cross-ridging, and abnormal cuticles should raise suspicion for Yellow Nail Syndrome in these patients. The absence of fungal infection and poor response to antifungal therapy further support the diagnosis [33].

Diagnosing lymphedema

The diagnosis of lymphedema is generally clinical, based on the appearance and symptomatology of the affected limb, correlated with the patient's history and associated comorbidities.

Regarding primary lymphedema, most patients can be diagnosed based on medical history and physical examination – mandatory steps when evaluating infants, children, or adolescents presenting with swollen extremities. Age of onset, pattern and progression of edema, aggravating or alleviating factors, history of infections, and associated symptoms should be assessed. In pediatric cases, a detailed perinatal history is essential [6].

Clinical examination should begin with precise localization of the swelling and assessment of its extent, followed by evaluation of pitting, presence of fibrotic tissue, and signs of infection. Examination should also include screening for features suggestive of secondary lymphedema (e.g., signs of external compression by a mass or systemic disease) as well as stigmata of syndromes associated with primary lymphedema (such as distichiasis, facial dysmorphism, or intellectual disability). A baseline laboratory panel – including complete blood count, renal

and hepatic function tests, thyroid function, and serum albumin – should be performed in all children with lymphedema to exclude systemic causes of edema. When history and physical examination are inconclusive, lymphoscintigraphy is recommended as the gold standard diagnostic tool, allowing functional assessment of lymphatic drainage [6].

Paraclinical investigations

Several non-invasive techniques are available for assessing lymphedema, including circumferential limb measurements, water displacement volumetry, bioimpedance spectroscopy (BIS), perometry, and tonometry. Despite their high availability and low cost, volumetry and tape measurements have sensitivity and practical limitations. BIS allows early detection of lymphedema by measuring extracellular fluid via electrical impedance, perometry uses infrared scanning to provide rapid and repeatable limb volume assessment, and tonometry estimates tissue compressibility to evaluate fibrosis and swelling, each with specific advantages and technical constraints [34,35].

Imaging techniques provide functional and anatomical information about the lymphatic system and surrounding tissues.

Contrast lymphography was the first used lymphatic imaging technique. It provides detailed anatomical visualization of lymphatic channels through direct cannulation and iodinated contrast injection but is invasive, technically demanding, and largely abandoned in routine practice due to complications [36].

Lymphoscintigraphy and SPECT-CT lymphoscintigraphy (Single-photon emission computed tomography combined with computed tomography) is considered the gold standard. Lymphoscintigraphy uses subcutaneous injection of a radiotracer, typically Tc-99m to assess lymphatic drainage function over time, while the SPECT-CT variant increases spatial resolution, provides precise anatomical correlation, being particularly useful for preoperative planning [37].

MR (magnetic resonance) lymphangiography performed with or without gadolinium contrast uses MRI (magnetic resonance imaging) sequences to visualise lymphatic vessels and surrounding tissues, offering excellent soft tissue contrast, whole-limb visualisation, and no radiation exposure [38].

Near-infrared fluorescence (NIRF) lymphangiography or indocyanine green fluorescence lymphangiography (ICG-FL) uses indocyanine green dye and near-infrared imaging to visualise superficial lymphatic vessels in real time, providing dynamic, high-resolution images with minimal invasiveness but limited tissue penetration of only 1-2 cm and may be considered more accurate than lymphoscintigraphy [39].

Ultrasound is a widely available, inexpensive, and radiation-free tool that can detect associated venous or soft tissue pathology, although it offers limited direct visualisation of lymphatic vessels and is operator-dependent [40].

CT lymphangiography involves contrast injection into lymphatic vessels or nodes, followed by CT imaging, to obtain high-resolution anatomical detail for surgical mapping. It is invasive and involves both radiation and contrast-related risks [40].

Photoacoustic imaging is an experimental method combining laser light excitation with ultrasound detection to produce high-resolution functional and structural images of lymphatic and vascular systems [40].

The challenge of differential diagnosis

The differential diagnosis of lymphedema includes a broad spectrum of conditions that may present with limb swelling. These range from systemic causes of edema – such as congestive heart failure, renal failure, nephrotic syndrome, and cirrhosis – to localized causes, including deep vein thrombosis (DVT), CVI, lipedema, pretibial myxedema, cellulitis, Baker cyst, idiopathic edema, drug-induced edema (antipsychotics, antidepressants, anti-Parkinsonian agents, bisphosphonates), and postoperative complications. In children, associated lower-limb swelling in the setting of arthritis should also be considered [41].

Systemic edema

Systemic edema (heart failure, renal failure, nephrotic syndrome, cirrhosis) is characterized by increased interstitial fluid compared to lymphedema which is caused by an accumulation of

lymph fluid [4]. Systemic edema is typically bilateral. Laboratory investigations and imaging modalities, such as echocardiography, liver ultrasound with function tests, renal ultrasound, and serum albumin levels are necessary in order to diagnose the cause [41].

DVT and CVI

DVT presents with acute onset of swelling, warmth, and calf tenderness; the diagnosis is confirmed with Doppler ultrasonography. One of its chronic sequelae is postphlebitic syndrome, in which venous reflux or insufficiency leads to chronic swelling, lipodermatosclerosis, varicose veins, or venous ulcers. In CVI, edema typically improves with limb elevation, a feature not observed in advanced lymphedema. Importantly, patients with venous disease have also been shown to develop impaired lymphatic drainage. In uncertain cases, lymphoscintigraphy is useful to differentiate between primary lymphedema and venous-origin edema [41].

Lipedema

Lipedema is a chronic disorder, usually affecting women, characterized by symmetrical, disproportionate adipose tissue deposition in the lower extremities. The lower limbs are affected symmetrically, from hips to the ankles, sparing the feet—a clinical feature referred to as the "cut-off sign". In addition to a negative Stemmer sign, the distinction between lymphedema and lipedema can be made through clinical examination and family history [22].

Complications of lymphedema

Infectious complications

In lymphedema, infectious complications such as cellulitis, erysipelas, and lymphangitis are common due to impaired lymphatic drainage and protein-rich fluid accumulation, which reduce local immune defences and facilitate infection.

Cellulitis and erysipelas usually present with a flu-like febrile prodrome, swelling, edema, redness, and pain in the affected limb, although some signs may be masked by the pre-existing lymphedema. The risk is particularly high in patients with chronic or poorly controlled lymphedema, especially those with tissue fibrosis or a positive Stemmer's sign. Furthermore, these infections can exacerbate lymphedema, thus creating a vicious cycle [42,43].

Lymphangitis, an inflammation of the lymphatic channels, is most often caused by bacterial infections but may also arise from parasitic infections such as filariasis or mycobacterial infections. It typically presents with rapidly spreading linear erythematous streaks accompanied by systemic symptoms like fever, chills, and malaise [44].

Fungal infections, particularly tinea pedis, are reported in approximately 40% of patients with lymphedema. The maceration and disruption of the skin barrier associated with these infections increase the risk of bacterial colonization, thereby predisposing patients to cellulitis [6].

Recurrent episodes of infection are common in lymphedema, significantly impairing quality of life and worsening clinical outcomes, highlighting the importance of prevention and effective management. Standard measures include compression therapy, manual lymphatic drainage, proper skin and nail care, and avoidance of trauma or excessive heat, while emerging interventions such as liposuction, lymphovenous anastomosis, and vascularized lymph node transfer are increasingly adopted to manage lymphedema and reduce the risk of infection [45].

Angiosarcoma and Stewart-Treves Syndrome

Angiosarcoma is a rare but highly aggressive complication of chronic lymphedema, with a reported risk of approximately 10% in lymphedema persisting for more than a decade [46]. It is most notably associated with Stewart-Treves syndrome, a condition that predominantly occurs in patients with post-radiotherapy lymphedema, affecting the upper limb in over 90% of cases [47]. The highest-risk group comprises middle-aged women with a history of mastectomy for breast cancer. Chronic lymphatic stasis and tissue hypoxia are thought to drive the malignant transformation of endothelial cells, with neoplastic changes potentially arising from newly formed lymphatic vessels in the affected tissue [47,48].

Clinically, angiosarcoma often presents as a bruise-like discoloration that gradually enlarges, infiltrates the overlying skin, and may progress to edema, ulceration and necrosis with associated pain. The condition is associated with comorbidities such as arterial hypertension and other cardiovascular diseases. It metastasizes early, most commonly to the lungs, thoracic cavity, liver, or bones. Management involves a combination of surgical resection and oncologic therapy, yet the prognosis remains poor due to the tumor's aggressive behavior [48,49].

Other malignancies

Other malignancies have also been reported in the setting of chronic lymphedema, including Kaposi's sarcoma, basal cell carcinoma, squamous cell carcinoma, melanoma and cutaneous lymphoma. Their occurrence is thought to be facilitated by chronic inflammation, persistent lymph stasis, and local immunosupression, which together create a permissive environment for malignant transformation. This risk of developing Kaposi sarcoma or melanoma is particularly notable in lymphedema secondary to filariasis caused by Wuchereria bancrofti, where aberrant and dilated lymphatic vessels develop, predisposing to neoplastic changes [46,50,51].

Lymphatic thrombosis

A rare but possible complication of lymphedema is the formation of lymphatic vessel thrombi. This phenomenon, although uncommon, has been documented in patients with secondary lymphedema following oncologic surgery with lymph node dissection. Histopathological analysis typically demonstrated organized thrombus and fibroblast proliferation within the lymphatic lumen. Awareness of this complication is important, as it may influence surgical planning and postoperative outcomes [52].

Management and treatment

Effective management of lymphedema begins with conservative, non-invasive strategies that reduce swelling, avoid complications and improve limb function. Central to this approach is complete decongestive therapy (CDT), a structured program that integrates several complementary techniques. Compression garments, such as sleeves or multilayer bandages use graduated pressure to promote lymphatic flow and prevent fluid accumulation. Manual lymphatic drainage (MLD) is a massage technique that improves drainage by encouraging the flow of lymph towards functional lymphatic pathways. Low-impact physical activities such as walking or swimming, stimulates the muscle pump, while weight loss reduces mechanical stress and inflammation in the affected tissues. Patients are also advised to avoid excessive heat, such as saunas or hot baths, which can exacerbate swelling. Proper skin and nail care, including moisturizing, cleaning, and treating minor injuries helps prevent infections, particularly cellulitis, which can worsen lymphatic dysfunction [53]. Additional supportive measures include sequential pneumatic compression devices to provide intermittent gradient pressure as an adjunct to therapy, kinesiotaping to gently lift the skin and improve lymph flow, and elevating the limb to promote fluid return. Also, it is important to avoid injections, blood draws, or blood pressure measurements in the affected limb to minimize trauma and infection risk [54].

Emollients and keratolytics, such as salicylic acid and urea, may be applied to improve the skin's appearance [24]. Oral retinoids can be prescribed for ENV to reduce papillomatosis and normalize keratinisation. Topical retinoids may serve as an alternative to minimize systemic side effects; however, their long-term efficacy remains to be confirmed [27].

When conservative measures are insufficient to control lymphedema, surgical interventions may be considered. Lymphaticovenous anastomosis (LVA) is a microsurgical technique that connects functioning lymphatic vessels directly to nearby veins, allowing lymph to bypass obstructed pathways and reduce fluid accumulation. Vascularized lymph node transfer (VLNT) involves transplanting lymph nodes, along with their blood supply, from a donor site to the affected area to restore lymphatic drainage. Liposuction may be indicated in patients with chronic lymphedema who have developed fibrotic or fatty deposits to remove the excessive subcutaneous tissue and improve limb shape. In

particular, liposuction-assisted protein lipectomy (SAPL) can target protein-rich lymphedematous tissue, reducing both volume and lymph stasis. In selected cases, surgical resection of severely fibrotic tissue can be performed to reduce limb volume and improve function. Both micro-surgical and excisional procedures are often integrated with ongoing conservative measures to maximize outcomes [54,19].

In addition to surgical approaches, emerging molecular therapies are showing promise in lymphedema management. Topical tacrolimus has been studied for its potential to modulate local immune activity, reduce inflammation, and support lymphatic function in the affected tissues [55]. In experimental models, doxycycline managed to reduce symptoms of lymphedema due to its anti-Th2 effect, reducing inflammation [56]. Growth factors such as VEGF-C are being explored for their ability to promote lymphangiogenesis, while stem cell–based therapies aim to repair and regenerate damaged lymphatic structures [57,58]. Homeopathic treatment options have been reported in the literature, including plant extracts that showed promising results when used in combination with diuretics, although evidence supporting their efficacy remains limited [59,60].

Conclusions

Lymphedema is a complex entity that requires early intervention and a multidisciplinary team for proper management of patients. Dermatologists have a central role in correctly identifying the lymphedema and preventing the complications of the disease.

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Conflict of interest
NONE DECLARED

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