ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA DOI: 10.31609/jpmrs.2024-107308

Differential Diagnosis of Lower Extremity Edema: A Retrospective Analysis

Alt Ekstremite Ödeminin Ayırıcı Tanısı: Retrospektif Analiz

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ABSTRACT Objective: Differential diagnosis of lower extremity edema is a diagnostic challenge for clinicians in busy outpatient clinics. A wide range of diseases must be considered in the differential diagnosis. Differential diagnosis is primarily based on the medical history, physical examination, and clinical presentation of edema. We aimed to present the demographic and clinical characteristics of the patients referred to the lymphedema outpatient clinic with swollen legs and to provide a diagnostic guide in the differential diagnosis of leg edema for clinicians. **Material and Methods:** Ninety-five patients referred to a physical and rehabilitation medicine lymphedema outpatient clinic with leg swelling between 2014 and 2016 were evaluated retrospectively. Demographic characteristics, medical history, physical examination, laboratory tests, lower extremity venous Doppler US, and if necessary, the other imaging tests were assessed. **Results:** Forty-seven percent three percent of patients were diagnosed as having lymphedema, 40% as having chronic venous insufficiency, 5.3% as having lipedema, 3.2% as having edema associated with calcium channel blockers usage, 3.2% as having idiopathic edema and 1% as having lipo-lymphedema. **Conclusion:** Lower extremity edema is a diagnostic challenge. A wide range of diseases must be considered in the differential diagnosis. This article provides a guide to the differential diagnosis of leg edema for clinicians.

Keywords: Leg edema; differential diagnosis; guide

ÖZET Amaç: Alt ekstremite ödemi yoğun poliklinik koşullarında fiziyatristler için tanısal zorluk oluşturmaktadır. Ayırıcı tanı primer olarak medikal öykü, fizik muayene ve ödem klinik özelliklerine dayanır. Klinisyenlere lenfödem polikliniğine bacak şişliği nedeniyle başvuran hastaların demografik ve klinik özelliklerini sunmayı ve bacak ödemi ayırıcı tanısı için bir rehber oluşturmayı amaçladık. **Gereç ve Yöntemler:** Fiziksel tıp ve rehabilitasyon lenfödem polikliniğine 2014 ve 2016 yılları arasında bacak şişliği nedeniyle başvuran 95 hasta retrospektif olarak değerlendirildi. Hastaların demografik özellikleri, medikal öyküleri, fizik muayeneleri, laboratuar testleri ve gerekliyse görüntüleme tetkikleri incelendi. **Bulgular:** Hastalarin %47,3'une lenfodem, %40'ina kronik venoz yetmezlik, %5,3'une lipodem, %3,2'sine kalsiyum kanal blokoru kullanimina bagli odem, %3,2'sine idiopatik odem ve %1'ine lipo-lenfodem tanisi kondu. **Sonuç:** Alt ekstremitre ödemi tanısal zorluk oluşturmaktadır. Ayırıcı tanı oldukça geniş bir yelpazede medikal hastalık içermektedir. Bu makale bacak ödemi ayırıcı tanısı için bir rehber oluşturacaktır.

Anahtar Kelimeler: Bacak ödemi; ayırıcı tanı; rehber

Edema is an abnormal accumulation of fluid within the interstitial spaces.[1] There are 3 types of leg edema: venous edema, lymphedema, and lipedema.[2] Venous edema is the accumulation of protein-poor, low-viscosity interstitial fluid. Causes of venous edema are chronic venous insufficiency (CVI), thrombosis, systemic illness (heart, renal, kidney, endocrine), drugs [calcium channel blockers (CCB), beta blockers, steroids etc.)] and hypoalbuminemia. Venous edema is usually pitting except in hypothyroidism. Hypothyroidism causes non-pitting edema. Lymphedema is the accumulation of protein-rich in-

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 06 Dec 2024 ***Received in revised form:*** 11 Mar 2025 ***Accepted:*** 18 Mar 2025 ***Available online:*** 25 Mar 2025

terstitial fluid within the skin and subcutaneous tissue. It is due to lymphatic dysfunction and is characterized by persistent, non-pitting edema. Lipedema is a bilateral, symmetrical deposited of adipose tissue in the legs. It is a form of fat maldistribution rather than true edema.[3]

Lower extremity edema is a diagnostic challenge. A wide range of diseases must be considered in the differential diagnosis. Differential diagnosis is primarily based on the medical history, physical examination, and clinical presentation of edema. If necessary, laboratory and imaging techniques can be performed. The most important imaging technique is venous Doppler ultrasonography (US).

In medical history, the onset of leg edema (acute or chronic), systemic illnesses (heart, liver, kidney, endocrine), cancer/cancer surgery/radiation therapy (abdominal, gynecologic, genitourinary, melanom), recently started medication, malabsorption syndromes, travel to tropical countries, and response to elevation should be evaluated. Physical examination should identify whether the leg edema is unilateral or bilateral, symmetrical or asymmetrical, pitting or non-pitting, or painful or not painful. Foot involvement, cellulitis/erysipelas, varicose veins, skin changes (lipodermatosclerosis, hemosiderin pigmentation, atrophy) and obesity (it can be related with lipedema and venous insufficiency) should also be assessed.[2]

We aimed to present the demographic and clinical characteristics of the patients referred to the lymphedema outpatient clinic with swollen legs and to provide a diagnostic guide in the differential diagnosis of leg edema.

MATERIAL AND METHODS

Ninety-five patients referred to a physical and rehabilitation medicine lymphedema outpatient clinic with leg swelling between 2014-2016 were evaluated retrospectively. The study was approved by the Ethics Committee of Dışkapı Yıldırım Beyazıt Research and Training Hospital in accordance with the ICMJE recommendations (date: April 17, 2017, no: 37/12). The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and all subsequent revisions.

In our lymphedema outpatient clinic, patients with leg swelling are evaluated according to the systematic guide developed by the authors (Figure 1 and Figure 2). We recorded the patients' demographic characteristics and medical histories (cancer/cancer related surgery, radiotherapy, systemic diseases, CVI, trauma, recurrent cellulitis/erysipelas, varricose vein surgery, prolonged immobilization, family history for swollen leg, travel to tropical regions, medications, edema onset, edema duration, response to elevation, heaviness). In the physical examination, the range of motion and circumferential measurements of the lower extremities (metatarsophalangeal, 2 cm above the medial malleolus, 10 cm below the inferior pole of the patella and 10 cm above the superior pole of the patella), affected extremity and edema localization, foot involvement, Stemmer's sign (skin at the base of the second toe can not be lifted), pitting edema, skin changes (lipodermatosclerosis, hemosiderin pigmentation, ulceration, hyperkeratosis, papillomatosis), bruising, tenderness, reticular veins, varicose veins, active cellulitis and arterial pulses were recorded.

In all patients, we performed a hemogram, liver function tests, kidney function tests, total protein, albumin, electrolytes, thyroid stimulation hormone and urinalysis to exclude underlying systemic disease. We also performed venous Doppler US in all patients to exclude CVI and thrombosis.

If there is a circumferential difference of 2 cm or more at a single anatomic level measured and a typical medical history such as lymph node dissection, radiotherapy and recurrent cellulitis, we accept the patient as having lymphedema. Complex decongestive therapy (CDT) is used for treating lymphedema. If the physical examination is consistent with lymphedema but there is no typical medical history, we prefer lymphoscintigraphy. If lymphoscintigraphy is normal or proximal painful edema without an obvious cause is detected, abdominopelvic chemotheraphy (APCT) is recommended. If the arterial pulses are diminished or absent, arterial Doppler US is recommended.

Chest X-ray and echocardiogram should be performed in patients with soft, deeply pitting acute

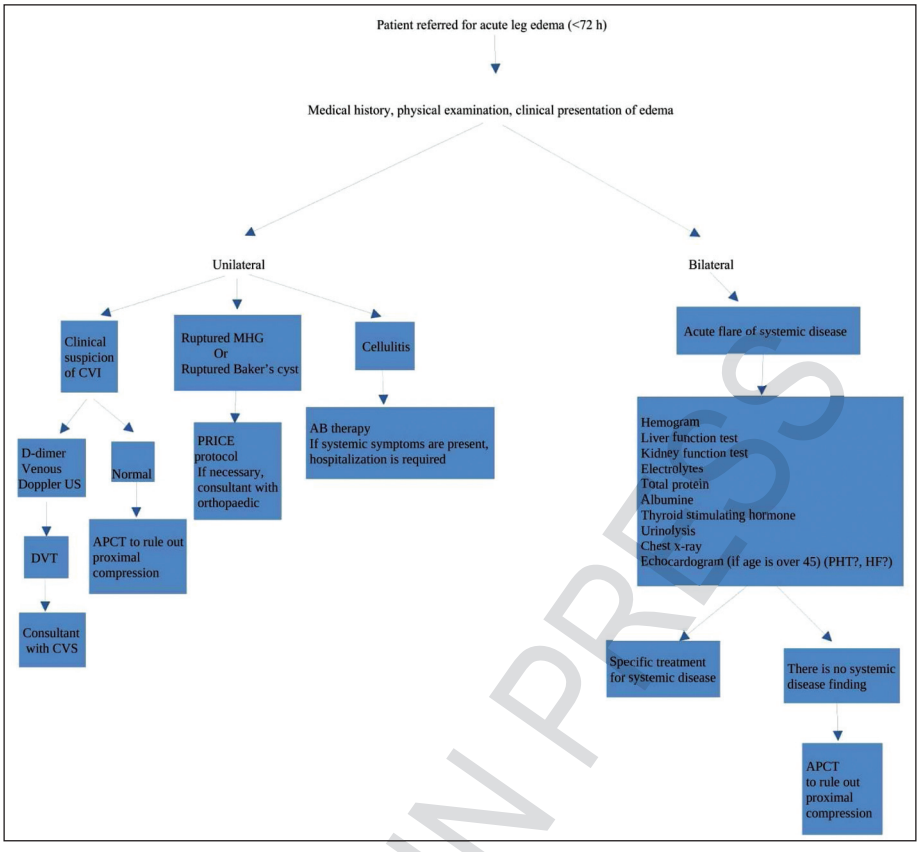

FIGURE 1: Systemic evaluation of acute leg edema

CVI: Chronic venous insufficiency; MHG: Medial head of gastronomies; US: Ultrasonography; DVT: Deep venous thrombosis; CVS: Cardiovascular surgery; APCT: Abdominopelvic chemotherapy; PRICE: Protect, rest, ice, compression, elevation; PHT: Pulmonary hypertension; HF: Heart failure AB: Antibiotic

edema. We also performed an echocardiogram in patients over the age of 45 years with edema of unclear etiology to rule out pulmonary hypertension and heart failure.

If the accurate diagnosis is lymphedema, the stage of lymphedema according to the International Society of Lymphology is recorded. In this system, the stages of lymphedema are assessed in 4 stages; Stage 0: subclinical stage; Stage 1: pitting edema that subsides with limb elevation; Stage 2: tissue fibrosis is more evident and edema is non-pitting; Stage 3: skin changes such as thickening and hyperpigmentation develop.[4]

If the accurate diagnosis is CVI, we use the Clinical manifestations, Etiological factors, Anatomical distribution of disease, Pathophysiological findings (CEAP) system to classify the clinical classification of the patients. In this system, clinical signs are evaluated in 7 classes: C0: no clinical signs; C1: telangiectasia or reticular veins; C2: varicose veins; C3: edema; C4: skin changes without ulceration (a: pigmentation or ekzema; b: lipodermatosclerosis or atrophy); C5: skin changes with healed ulceration; C6: skin changes with active ulceration.[5]

STATISTICS

Descriptive statistics were performed for the demographic and clinical characteristics of the patients. Continuous variables are presented as means±standard deviation. Categorical variables are presented as frequencies. The SPSS 17 software package (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

RESULTS

Eighty-seven of 95 patients (91.6%) were female and the mean age of the patients was 55.9±14.1. Descriptive characteristics, medical histories, and physical

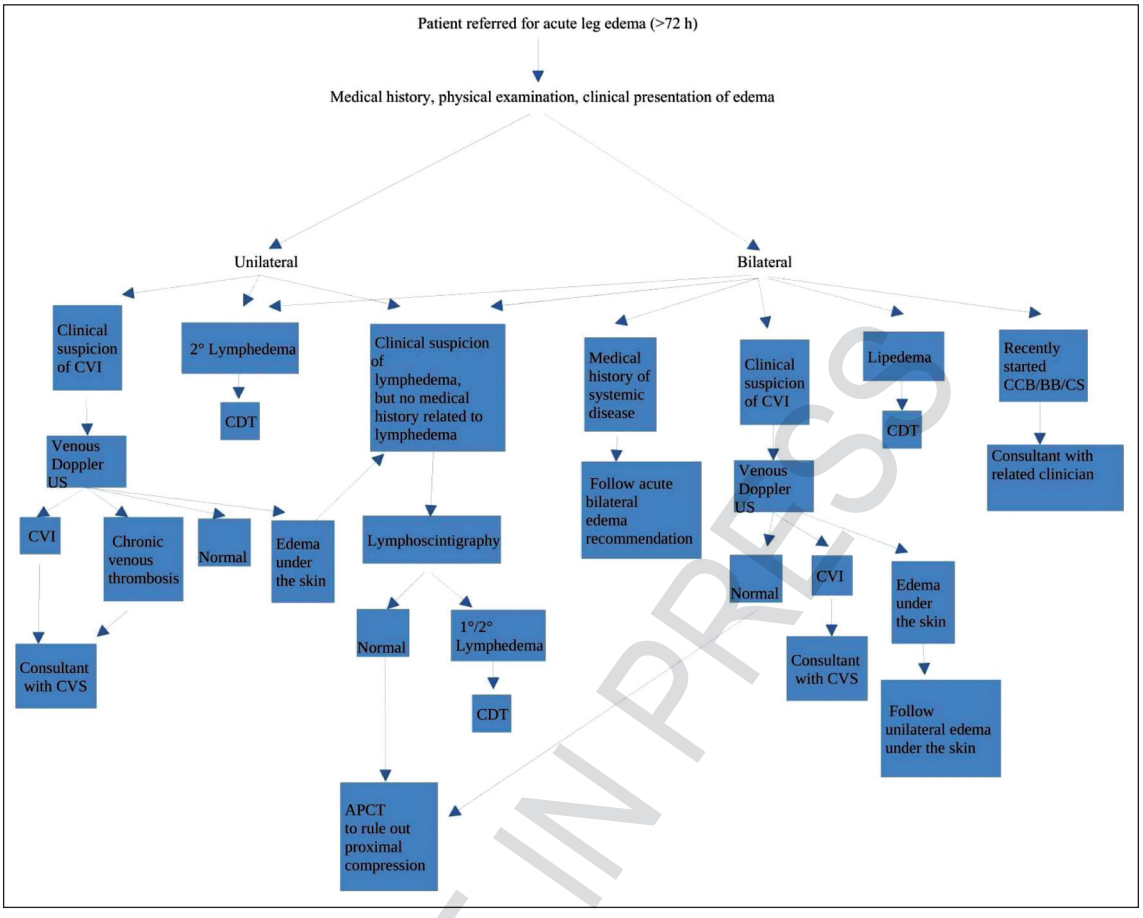

FIGURE 2: Systemic evaluation of chronic leg edema

CVI: Chronic venous insufficiency; US: Ultrasonography; CDT: Complex decongestive therapy; CCB: Calcium channel blocker; BB: Beta blocker; CS: Corticosteroid; CVS: Cardiovascular surgery; APCT: Abdominopelvic chemotherapy

TABLE 1: Descriptive characteristics of the patients with leg swelling

	All patients (n=95)	LE (n=45)	CVI (n=38)	LipE (n=5)	CCB usage (n=3)	IE (n=3)	LLE (n=1)
Gender (n)							
Male	8	6	3	0	0	0	0
Female	87	39	35	5	3	3	1
Age (years) ($\bar{X}$±SD,range)	55.9±14.1	51.7±15.8 (15-81)	59.8±12.6 (33-81)	54.8±14.6 (38-73)	59.5±9.6 (48-64)	50.7±8.9 (45-61)	46
Education (years) ($\bar{X}$±SD,range)	5.4±4.3	6.6±4.5	4.5±4.2	6.4±2.6	7±0.1	3.3±2.8	11
BMI (kg/m^2) ($\bar{X}$±SD,range)	35.3±8.4	32.5±8.2	36.5±7	42.4±8.8	40.2±2.9	47.3±20.9	36
Marital status (n)							
Not married	5	4	1	0	0	0	0
Married	72	34	28	5	2	2	1
Divorced	18	7	9	0	1	1	0

LE: Lymphedema; CVI: Chronic venous insufficiency; LipE: Lipedema; CCB: Calcium channel blocker; IE: Idiopathic edema; LLE: Lipo-lymphedema; SD: Standard deviation; BMI: Body mass index

examinations of the patients are shown in Table 1, Table 2.

We did not detect any severe abnormality in the laboratory tests and chest x-rays. While 44 patients (46.4%) had normal Doppler US, deep and superfi-

TABLE 2: Medical history of the patients with leg swelling

	LE (n=45)	CVI (n=38)	LipE (n=5)	CCB usage (n=3)	IE (n=3)	LLE (n=1)
Duration of swelling (months) ()	37.4±46.9 (1-180)	29.8±35.1 (1-120)	211±170 (94-480)	61.5±80 (3-120)	29.6±27.9 (5-60)	24
Onset of swelling (n)						
Acute (<72 h)	0	0	0	0	0	0
Chronic	45	38	5	3	3	1
Affected leg (n)						
Unilateral	33	18	0	0	0	1
Bilateral	12	20	5	3	3	0
Edema localization (n)						
Below knee	19	27	0	3	1	0
Leg	26	11	5	0	2	1
Foot involvement (n)	45	13	0	1	2	1
Response to elevation (n)	32	27	0	3	3	0
Heaviness (n)	41	28	5	3	3	1
Cancer (n)	27					
Ovarian	7					
Endometrial	10					
Cervix	6					
Vulva	1					
Bladder	1					
Melanoma	1					
Ewing sarcoma	1	0	0	0	0	0
LN dissection (n)	26	0	0	0	0	0
Inguinal LN Bx (n)	1	0	0	0	0	0
Adjuvant RT (n)	17	0	0	0	0	0
Adjuvant CT (n)	17	0	0	0	0	0
HF (n)						
Controlled	1	1	0	0	0	0
Uncontrolled	1	1	0	0	0	0
CKD (n)	1	1	0	0	0	0
Liver Disease (n)	0	0	0	0	0	0
Thyroid disease (n)						
Controlled	8	0	0	0	0	0
Uncontrolled	0	1	1	1	0	0
CVI history (n)	7	12	0	0	1	1
Venous insufficiency surgery (n)	2	4	0	0	0	0
DVT history (n)	1	2	0	0	0	0
Cellulitis history (n)	10	0	0	0	0	0
Orthopaedic surgery (n)						
Hip arthroplasty	0	2	0	0	0	0
Knee arthroplasty	0	8	1	0	0	0
Prolonged immobilization (n)	0	0	0	0	0	0
Major trauma (n)	0	0	0	0	0	0
Travel to tropic regions (n)	0	0	0	0	0	0
Family history of leg swelling (n)	1	2	0	0	0	0
Drugs usage (n)						
CCB	1	2	0	3	0	0
Others*	1	0	0	0	0	0
HT (n)	14	19	3	3	1	0
Diabetes (n)	10	10	1	1	0	0
RA (n)	3	1	0	0	0	0

*Beta blocker, steroid. LE: Lymphedema; CVI: Chronic venous insufficiency; LipE: Lipedema; CCB: Calcium channel blocker; IE: Idiopathic edema; LLE: Lipo-lymphedema; SD: Standard deviation; LN: Lymph node; Bx: Biopsy; RT: Radiotherapy; CT: Chemotherapy; HF: Heart failure; CKD: Chronic kidney disease; DVT: Deep venous thrombosis; HT: Hypertension; RA: Rheumatoid arthritis

cial reflux were detected in 51 patients (53.6%). Thirteen of the 51 patients had a diagnosis of lymphedema and the others had CVI. Lymphoscintigraphy was performed in 25 patients (26.3%). While 10 patients had normal lymphoscintigraphy, 15 patients had decreased lymphatic drainage or partial/total lymphatic obstruction. Echocardiogram was performed in 22 patients (23.1%) and detected normal. In 7 patients (7.4%), abdominopelvic CT was ordered. While it was normal in 6 patients, we detected a parailiac and pararectal metastatic mass in 1 patient with a diagnosis of melanoma.

Because of these findings, 45 patients (47.3%) have been diagnosed as having lymphedema, 38 (40%) as having CVI, 5 (5.3%) as having lipedema, 3 (3.2%) as having edema associated with CCB usage, 3 (3.2%) as having idiopathic edema and 1 (1%) as having lipo-lymphedema.

Cancer surgery-related lymphedema was detected in 26 patients (57.8%). The other causes of lymphedema were recurrent cellulitis in 10 patients (22.3%), active cellulitis in 4 patients (8.9%), inguinal lymph node biopsy in 1 patient (2.2%), Ewing sarcoma-related radiotherapy in 1 patient (2.2%), recurrence of melanom in 1 patient (2.2%), rheumatoid arthritis in 1 patient (2.2%) and 3x8 cm popliteal cyst in 1 patient (2.2%). Thirty-three patients (73%) had unilateral and 12 patients (%27) had bilateral lymphedema. Six patients (13%) had stage-1 and 39 patients (87%) had stage-2 lymphedema. Thirty-six of the patients (80%) had a new diagnosis of lymphedema.

Although superficial venous insufficiency was noted in all patients with CVI, deep venous insufficiency due to posterior tibial chronic thrombosis was detected in only 1 patient. Twenty patients (54%) with CVI had bilateral involvement. Isolated Greater Saphenous Vein (GSV) incompetence was found in 30 patients (78.9%), combined Saphenofemoral Junction reflux and GSV reflux was noted in 4 patients (10.5%), and combined small saphenous vein reflux and GSV reflux were noted in 3 patients (8%). In 1 patient (2.6%), combined GSV incompetence and posterior tibial chronic thrombosis was detected. Nineteen patients (51.3%) were classified as CEAP C2, 13 patients (35.2%) as CEAP C3, 4 patients (10.8%) as CEAP C4a and 1 patient (2.7%) as CEAP C4b.

DISCUSSION

The differential diagnosis of leg swelling is a diagnostic challenge. The clinician should consider several causes of lower extremity edema. A detailed medical history and a careful physical examination are required for the diagnosis. Laboratory tests (hemogram, liver function tests, kidney function tests, total protein, albumin, electrolytes, thyroid stimulation test, urinalysis) and doppler venous US are the most important medical examinations to confirm the diagnosis. The differential diagnosis of leg edema is shown in Table 3.

The most common cause of leg edema in patients aged >50 years is CVI. It affects up to 30% of population.[2] Older age, female gender, obesity and hypertension are risk factors. CVI is characterized by chronic, unilateral or bilateral pitting edema. It usually occurs in the lower leg and ankles. Venous Doppler US confirms the diagnosis.[6] In this study, 40% of the patients refered for leg edema were diagnosed with CVI. Similar to previous studies, most of the patients were female, older than 50 years old and obese [Body mass index (BMI>30 kg/m^2)]. The mean duration of swelling was 30 months. Half of the patients had bilateral pitting edema and the other half had unilateral pitting edema. Most of the patients had edema below the knee, reticular veins and varicose veins. Only 4 patients had brown hemosiderin pigmentation. All of the patients had superficial venous insufficiency detected by Doppler US. Only 1 patient had deep venous insufficiency due to tibialis posterior thrombosis. Cardiovascular surgery consultation was recommended for all patients.

Lymphedema is one of the most important causes of chronic progressive, unilateral or bilateral leg edema. It is a serious and debilitating condition.[7] It can be either primary or secondary. Primary lymphedema is a rare genetic disorder that may present at birth or begin in childhood, adolescence or after age 35.[8] Secondary lymphedema results from obstruction

TABLE 3: Differential diagnosis of leg edema

	CVI	IE	SD	10LE	20LE	Drugs	Hypot	Acute DVT	Lipedema
Type of edema	Venous	Venous	Venous	LE	LE	Venous	Venous	Venous	Fat
Acute/Chronic	C	C	A/C	C	C	A/C	C	A	C
Unilateral/Bilateral	U/B	B	B	U/B	U/B	B	B	U/rarely B	B
Foot involvement	+/-	+/-	+/-	+/-	+/-	+/-	+/-	-	-
Pitting	+	+	+*	_**	_**	+	-	+	-
Tenderness	+	+/-	+/-	-	-	+/-	+/-	+++	+++
Bruising	+/-	-	+/-	-	-	-	-	-	+++
Skin changes	Sclerosis brown pig stasis dermatitis ulcers	-	-	Hyperkeratosis papillomatosis	Hyperkeratosis papillomatosis	-	Plaque nodule	-	Lobulation
Stemmer's sign	-	-	-	+	+	-	-	-	-
Reticular vein	+	-	-	+/-	+/-	-	-	+/-	-
Varicose vein	+	-	-	+/-	+/-	-	-	+/-	-
Brawny enduration	-	-	-	+	+	-	-	-	-
Systemic findings	-	-	JVD (HF) Ascites and jaundice (LD)	-	-	-	+	+/-	-

*Highly soft and deeply pitting edema in cardiac diseases; **Pitting edema in early stage. CVI: Chronic venous insufficiency; IE: Idiopathic edema; SD: Systemic diseases (heart failure, pulmonary hypertension, renal failure, nephrotic syndrome, glomerulonephritis, chirrosis); LE: Lymphedema; Hypot: Hypothyroidsm; DVT: Deep venous thrombosis; JVD: Jugular venous distension; HF: Heart failure; Brown pig: Brown pigmentation; LD: Liver disease; A: Acute; C: Chronic; U: Unilateral; B: Bilateral; S: Symmetric; A: Asymmetric

or damage to the lymphatics. The most common causes in the world are filariasis (which occurs in tropical regions) and cancer surgery (lymph node dissection). The other causes are radiation therapy, tumor extension, cellulitis/erysipelas, varicose vein surgery, trauma, and advanced venous insufficiency. Lymphedema is typically diagnosed on the basis of medical history and physical examination.[9-11] Abdominal, gynecologic, prostate or melanoma cancer surgeries, radiation therapy, family history, and recurrent cellulitis should be included in the medical history. Unilateral or bilateral involvement, asymmetric involvement, positive Stemmer's sign, non-pitting edema due to subcutaneous fibrosis (except of early stage), and painless edema can be detected in the physical examination. In the late stage, skin changes such as hyperkeratosis and papillomatosis can be detected. If the diagnosis is doubtful, lymphoscintigraphy is the gold standard for assessing the lymphatics.[3] In the present study, 45 of 97 (46.4%) patients with leg swelling had lymphedema. Similar to previous studies, the most common cause of lymphedema was cancer-related lymphedema (especially ovarian and endometrial cancers). The diagnosis was based primarily on the clinical evaluation. We performed abdominopelvic CT (in 7 patients) and lymphoscintigraphy (in 14 patients) in suspected patients who had no medical history related to lymphedema or who had proximal painful edema. We detected lymphedema associated with rheumatoid arthritidis in 1 patient and lymphedema associated with melanoma recurrence in 1 patient. Lymphedema patients were hospitalized and treated with CDT.

A relationship exists between venous insufficiency and lymphedema. Venous insufficiency can lead to lymphedema due to the increased lymphatic load. This condition is called veno-lymphedema. On the other hand, untreated lymphedema can lead to secondary venous insufficiency due to compression and increased venous pressure.[12] In this study, 13 (~30%) lymphedema patients had venous insufficiency detected by venous Doppler US. CDT was applied to these patients.

Drug-induced leg edema may be caused by CCB, beta blockers, hydralazine, corticosteroids, and hormones.[2] Edema is a chronic bilateral edema that occurs more commonly in women. Recently started drug history should be questioned.[9] In this study, CCB-induced leg edema was detected in 3 patients. According to previous studies, all of the patients were women and all of them had bilateral symmetrical pitting edema below the knee. Venous Doppler US and echocardiogram were normal. In these patients, edema began to develop soon after the onset of CCB. The drug was switched to an angiotensin-converting enzyme inhibitor and a diuretic in 1 patient. Diuretics were added to CCB in other 2 patients. The edema regressed completely at follow-up.

The most common cause of leg edema in women under the age of 50 years is idiopathic edema.[2] Idiopathic edema is the term for fluid retention of unknown cause. It affects primarily middle aged women.[1] We detected idiopathic leg edema in 3 female patients after exclusion of other edema causes by medical history, physical examination, venous Doppler US and echocardiogram. Leg elevation, low sodium and carbohydrate diet, and exercises for calf muscle pump were recommended.

Lipedema is a bilateral symmetrical swelling that occurs due to the chronic accumulation of fat in the subcutaneous tissue. It is triggered at puberty, after pregnancy, or after surgery. It is a progressive disease and primarily affects women. The feet are not affected and the Stemmers' sign is negative. It is often tender and can bruise easily. There is no diagnostic test for lipedema. It is diagnosed based on the medical history and physical examination and must be distinguished from lymphedema.[13] We established lipedema in 5 patients according to the history and physical examination. All of them were morbidly obese women (BMI>40 kg/m^2) and had bilateral symmetrical non-pitting leg edema (no feet). We did not perform any diagnostic imaging test in these 5 patients. Lipedema may cause secondary lymphatic dysfunction leading to lipolymphedema.[13] In this study, we determined unilateral lymphedema by lymphoscintigraphy in 1 patient with lipedema. All patients with lipedema were treated with CDT.

The other most common cause of chronic bilateral leg edema is systemic diseases. Systemic diseases associated with leg edema include cardiac diseases (heart failure and pulmonary hypertension), renal diseases (renal failure, nephrotic syndrome, glomerulonephritis), liver diseases (chirrosis), and myxedema-related thyroid diseases (hypothroidism or hyperthyroidism). Edema is a bilateral, acute or chronic and symmetrical pitting edema (only myxedema is a non-pitting edema). The first line of evaluation is medical history, physical examination, and laboratory tests. Detailed investigation (e.g., chest x-ray, echocardiogram, abdominal US) for suspected diagnosis must be performed.[2,9-11] In the present study, we ruled out systemic diseases in all patients with bilateral leg edema. We did not detect any leg edema associated with systemic diseases. It is not necessary to rule out systemic causes when edema is unilateral.

Increased plasma estrogen concentration during the premenstrual syndrome may be associated with bilateral leg edema. It is sometimes called as cyclic edema. It is a periodic pitting edema that affects the face, hands, feet, and legs.[9] We did not observe cyclic edema in our outpatient clinic.

Hypoalbuminemia is associated with chronic bilateral leg edema. If the serum albumin level is below 2 g/dL, edema develops clinically. It can be caused by nephrotic syndrome, liver diseases and protein-losing enteropathies.[2] In this study, the albumin levels of all patients were normal. We did not observe edema related to hypoalbuminemia.

Chronic unilateral leg edema is usually due to venous insufficiency and secondary lymphedema. The other causes are tumor causing external pressure

and primary lymphedema. If there is a proximal leg edema, the clinician should suspect an external pressure of the tumoral mass. Abdominopelvic CT is the preferred screening examination for this condition. It must be kept in mind that chronic venous thrombosis may be responsible for unilateral chronic edema. Venous doppler US is the most useful imaging technique for unilateral or bilateral leg edema.[2] We detected a chronic posterior tibial venous thrombosis in 1 patient and a parailiac metastatic mass in 1 patient who was referred for unilateral proximal leg edema.

If the patient has an acute unilateral leg edema (<72 hours), deep venous thrombosis (DVT) should be considered first.[2] Advanced age, prolonged immobilization, recent major trauma or surgery, history of cancer, pregnancy, inherited diseases such as antithrombin III deficiency, and protein C and S deficiencies are risk factors for DVT. The physician should keep in mind the DVT in patients with these risk factors. In the physical examination, erythema, tenderness, warmth, pitting edema and positive Homans' sign (pain in calf with passive dorsiflexion of the ankle) were detected. D-dimer and venous Doppler US should be performed in these patients as a first-line laboratory and imaging technique.[14] In our outpatient clinic, we did not report any patient with acute DVT. The other differential diagnoses of acute unilateral leg edema are ruptured Baker's cyst, ruptured medial head of the gastrocnemius, and compartment syndrome.[2] We detected a 3X8 cm Baker's cyst by venous doppler US in a patient with acute onset, unilateral leg edema below the knee. Orthopedic surgery consultation was recommended.

Acute bilateral leg edema is usually due to the acute flare of systemic diseases and pulmonary hypertension. The systemic disease history and related laboratory tests should be assessed. An echocardiogram should be performed to rule out pulmonary hypertension in patients over the age of 45 years with bilateral leg edema of unclear etiology.[2] There was no patient referred to our outpatient clinic for acute bilateral leg edema.

CONCLUSION

The differential diagnosis of patients presenting to an outpatient clinic with leg edema is a diagnostic challenge. The differential diagnosis includes a wide variety of medical disorders. The most common causes in patients with leg edema should be considered, and the diagnosis must be established primarily by a detailed medical history and careful physical examination. This article provides a guide to the differential diagnosis of leg edema.

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