

Unilateral leg edema: Is it always vascular?

Tek taraflı bacak ödemi: Her zaman vasküler midir?

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Summary– Unilateral lower extremity edema below the knee commonly results from deep venous thrombosis, venous insufficiency, or lymphedema. The patient history, a physical examination, and lower extremity venous duplex ultrasound often reveal the underlying etiology, which is frequently of vascular origin. Presently described is the case of a 23-year-old patient who underwent a diagnostic work-up for unilateral leg swelling and was found to have a relatively uncommon cause of edema: lipedema. Lipedema is a disease characterized by subcutaneous adipose tissue deposition, and although diagnosed very rarely in general cardiology outpatient clinics, it has been demonstrated to be a cause of lower extremity edema in approximately one-fifth of cases in specialized clinics.

Lower extremity edema may have various causes. Heart failure, liver cirrhosis, nephrotic syndrome, and hypothyroidism are among the more common causes of bilateral lower extremity edema. Unilateral lower extremity edema below the knee commonly results from deep venous thrombosis (DVT), venous insufficiency, or lymphedema, although one-third of lymphedema cases may also be unilateral. Patient history, a physical examination, and a lower extremity venous duplex ultrasound (US) often reveal the underlying etiology, which is frequently of vascular origin. Lipedema is subcutaneous fat deposition with or without accompanying lymphedema and it is exclusively bilateral.^[1] This is a case of lipedema as the cause of unilateral lower extremity edema.

Abbreviations:

BMI	Body mass index
DD	Dercum's disease
DVT	Deep vein thrombosis
MLS	Multiple systemic lipomatosis
MRI	Magnetic resonance imaging
US	Ultrasound

Özet– Diz altındaki tek taraflı ekstremitte ödemi genellikle derin ven trombozu, venöz yetersizlik ya da lenfödem nedeniyle gelişir. Hastanın öyküsü, fizik muayene ve alt ekstremitte venöz dupleks ultrason çoğu zaman damar kaynaklı olan etiyolojisi ortaya koyar. Bu olgu sunumunda, 23 yaşındaki hastamız tek taraflı bacak şişliği nedeniyle tanınal değerlendirilmelerden geçmiş ve klinikçi ödemin göreceli olarak nadir bir nedenini ortaya çıkarmıştır: Lipoödem. Lipoödem subkütan yağ dokusu birikimiyle kendini gösteren bir hastalıktır ve her ne kadar genel kardiyoloji kliniklerinde nadiren tanısı konulsa da, özelleşmiş kliniklerde yaklaşık beş hastadan birinde alt ekstremitte ödeminin nedeni olarak gösterilmiştir.

CASE REPORT

A 23-year-old woman presented at the clinic with worsening swelling and tenderness and easy bruising in her left leg and ankle ongoing for 6 months. The symptoms worsened as the day progressed and improved at night. Her left leg had been larger than the right since birth. Her family history revealed that her aunt and her niece also had a history of leg swelling in the past. There was no history of medication use. The thigh circumference 10 cm proximal to the patella was 52 cm on the left side and 50 cm on the right. Measurement of the leg circumference 10 cm distal to the patella was 44 cm on the left side versus 36 cm on the right (Fig. 1). The cuff sign was positive. Her body mass index (BMI) was 22 kg/m² with no recent weight loss. The waist-to-hip ratio was 0.71. Non-pitting edema classified as 2+ was noted. The lower extremity pulses were equal and palpable bilaterally.

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Ankle or foot involvement was not present. There was pain on palpation.

Differentials included DVT, chronic venous insufficiency, and lymphedema. Blood count, chemistry, thyroid function tests, and lipid profile levels were within normal limits. A lower extremity duplex US was negative for DVT and venous insufficiency. Magnetic resonance imaging (MRI) was the next diagnostic step. A homogenous increase in subcutaneous fat with minimal subcutaneous edema and without fibrosis or skin thickening was reported (Fig. 2). The final diagnosis was lipedema. Complex decongestive physiotherapy and intermittent pneumatic compression

were prescribed. The patient demonstrated slight relief in her quality of life during follow-up.

DISCUSSION

This was a case of unilateral, nonpitting edema in a 23-year-old woman whose history, physical examination, and diagnostic work-up excluded the commonly observed etiologies and pointed to a relatively uncommon cause of this condition: lipedema.

Our patient was a young woman of normal weight who presented with unilateral, painful, nonpitting pretibial edema. The family history and nonpitting character of the edema without involvement of the feet (i.e., inverse shoddering) were features typical of lipedema.^[2] Kaposi- Stemmer's sign, which is pathognomonic for lymphedema was absent (a fold of skin could be pinched on the upper surface of the second toe). The clinical picture was compatible with type 5 (involving legs), stage 2 (uneven skin with indentations in the fat) lipedema (Table 1).^[3] Although a diagnosis is usually made based on the history and physical examination, MRI was the next diagnostic step after duplex US since it is a more sensitive method than computed tomography to differentiate lymphedema from lipedema and it is considered one of the diagnostic modalities in lipedema. MRI typically reveals fatty hypertrophy without skin abnormalities.^[2] The unilateral involvement and atypical features observed



Figure 1. (A, B) Photos demonstrating left-sided, unilateral, lower extremity edema below the knee, without involvement of the foot (A: Front; B: Back).



Figure 2. Lower extremity magnetic resonance images illustrating (A) a considerable increase in subcutaneous adipose tissue in the left leg, and to a lesser extent in the lower right leg, and (B) accompanying minimal edema (LL: Left leg; RL: Right leg).

Table 1. Adapted from lipedema classification&staging

Types of lipedema	
Type I	Between buttocks and hips
Type II	Buttocks to knees
Type III	Buttocks to ankles
Type IV	Arms
Type V	Lower legs
Stages of lipedema	
Stage 1	Smoothness of the skin surface preserved with thickening in hypodermis
Stage 2	Skin indentations with encapsulated masses, lipomas, and angioliomas
Stage 3	Deformations on the thighs and around the knees
Stage 4	Lipedema with lymphedema

in this case could be due to presentation at an early stage. Mild involvement of the ipsilateral lower leg supports this theory.

Lipedema is aberrant subcutaneous fat deposition in the lower limbs. It is characterized by gradual, bilateral lower leg swelling sparing the feet. It is an important, under-recognized cause of bilateral lower extremity edema in up to 18.8% of cases with lower extremity edema at specialized centers.^[1] Unilateral involvement has not previously been reported. The condition is often misdiagnosed as lymphedema, but a detailed history and physical examination will usually discriminate between these diseases. Autosomal or X-linked dominant genetic inheritance has been proposed as a potential etiology, and several candidate genes have been named. The condition is sometimes accompanied by obesity.^[2] Lymphedema has also been shown to accompany lipedema in varying degrees. Advanced stages of lipedema cause considerable disability.

Differential diagnoses include DVT, cellulitis, venous insufficiency, malignancy, lymphedema, lipohypertrophy, phlebedema, and lipoedema, as well as rare adipose disorders. In this case, the nonpitting character of the edema, the tenderness over the area, and a negative Stemmer sign were physical examination findings that led us to exclude lymphedema. Lipohypertrophy was not considered a primary differential diagnosis since there was no involvement of the trunk; the patient demonstrated tenderness, which wouldn't be expected in lipohypertrophy; and the BMI wasn't as elevated as would be expected in lipohypertrophy (>30 kg/m²). The presence of edema is a strong indicator to exclude lipohypertrophy as well.

Among rare adipose disorders, we mainly focused on multiple systemic lipomatosis (MLS) and Dercum's disease (DD). The differential diagnosis is made using the patient history and physical examination. While MLS involves mainly the neck, arms, and upper trunk, DD involves various localizations in a symmetrical manner with painful, nodular, subcutaneous adipose tumors.^[4,5] These findings led us to exclude these rare adipose disorders.

Assessments of hormonal markers, such as estrogen, oxidative markers, tissue biopsy, and MRI-lymphangiography, can be ordered for investigational purposes, but it is without clear benefit in the diagnosis

or management of the disease. MRI and US have been shown to be effective in the diagnosis of lipedema and lymphedema in the absence of lymphoscintigraphy.^[6] MRI has also been proven to be safe and effective in the definitive diagnosis and demonstration of the extent of lipedema accompanying lymphedema.^[7] Nonetheless, although usually painful, MR-lymphangiography or lymphangioscintigraphy is usually recommended as confirmatory modalities. Our patient declined to undergo these tests due to the expected discomfort.

Treatment options are limited. Exercise, diet control, and treatment of the associated symptoms are needed; liposuction is an option if these conservative measurements fail. Low-level compression therapy is suggested to halt progression, since it can prevent the advance to lymphedema.^[8] Our patient responded reasonably well to this treatment. Psychological support and counseling may also be beneficial in selected patients.^[9] Large-scale, controlled trials are needed to develop more evidence-based and effective treatments for this rare disease.

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