CASE REPORT

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Primary Lymphedema and Chronic Venous Insufficiency: Case Report and Review

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Primary lymphedema is characterized by swelling that is present at birth or that develops later in life, and is caused by genetically-mediated impairment of lymph vessels and lymph node development. The venous and lymphatic circulation systems are closely connected, and phlebolymphedema is the most common combined venous and lymphatic insufficiency disease. However, primary lymphedema is only rarely combined with chronic venous insufficiency. We describe a case in which the patient, who was diagnosed with primary lymphedema, developed chronic venous disease.

Key Words: Lymphedema · Venous insufficiency · Lymphatic system

INTRODUCTION

Leg swelling is a common symptom that can be caused by complications that include volume overload, venous and lymphatic pathology, lowered oncotic pressure and increased capillary permeability. Chronic venous insufficiency (CVI) and impaired lymphatic function are the primary pathologies related to leg swelling [1]. Chronic venous disease (CVD) conditions include varicose veins, superficial thrombophlebitis, CVI, venous leg ulcers, deep venous thrombosis, and venous thromboembolism [2-3]. In this paper, CVI is used to describe the full range of CVD symptoms [4]. CVI is commonly caused by insufficient valves and venous hypertension. CVI causes complications such as leg edema, leg pain, varicose veins, skin changes, and most severely, venous ulceration [5]. The venous and lymphatic circulation systems are closely connected; hence, out of all patients with advanced CVI, 20-30% also have associated lymphatic dysfunction, which is likely attributable to secondary damage from overload or recurrent lymphangitis.

Phlebolymphedema is widely used to designate lymphedema of venous origin [6-9]. The most common combined venous and lymphatic insufficiency disease is phlebolymphedema. However, in this study we describe a case in which the patient initially had primary lymphedema, and later developed skin ulceration due to CVI. We propose that a vicious cycle of primary lymphedema, compromised venous dynamics and worsening tissue edema and injury may result in repetitive inflammation, infection and skin ulceration.

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CASE REPORT

A 59-year-old female patient initially presented with edematous swelling in her left lower extremity, at birth. The swelling in her left lower extremity was occasionally aggravated by excessive exercise during adolescence, but improved through rest with leg elevation. The swelling was further aggravated during pregnancy, but improved after childbirth. The patient sustained a traumatic wound to the left tibia while working when she was 35, but did not receive appropriate treatment, and therefore experienced wound infection symptoms, including heat sensation, redness and swelling. She was diagnosed with lymphangitis and treated with antibiotics. However, the treatment was stopped before she had healed completely. The wound went through a cycle of repeated worsening and improvement. She experienced erythematous crusting and squamous ecchymosis changes. After that she visited medical center and diag-

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nosed with lymphangitis as well. The crust was removed without appropriate treatment for cosmetic reasons, and repeated infection and swelling aggravation were observed later.

The patient was hospitalized due to the continuous symptoms described above. Upon admission, swelling, heat sensation and diffuse redness were observed on the left lower extremity, and erythematous crusting, squamous ecchymosis, and ulceration were observed on the left tibia, toes, and sole of the foot (Fig. 1). The circumference of the left lower extremity was 5 cm greater than that of the right lower extremity.

The patient had no family history or past medical history of disease that might result in edema (i.e., thyroid disease, diabetes, heart disease). Physical examination did not reveal any signs of muscle weakness or sensory loss in either leg. In addition, her deep tendon reflexes were normal and pathologic reflexes were not observed. In laboratory findings, no abnormal signs, except for a slight increase in ESR (25 mm/hr (1-20 mm/hr))

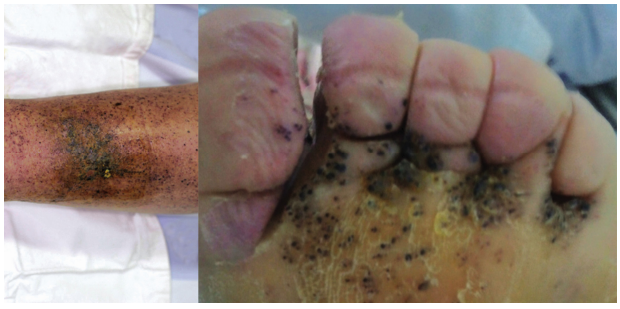


Fig. 1. Erythematous crusting, squamous ecchymosis and ulcer-like findings were observed on the left tibia, toes and sole of the foot.

were observed. On lymphoscintigraphy, dermal back flow and reflux flow appeared at the skin level on the left lower extremity, and left inguinal lymph node absorption was not identified (Fig. 2). On ultrasound, the deep veins of the left lower extremity from the common femoral to posterior tibial veins showed patent lumina with no evidence of thrombosis. On Doppler examination, bidirectional flow wave forms were detected by the Valsalva maneuver in the left common femoral and great saphenous veins, which indicated valvular insufficiency. Mildly engorged perforating veins were indistinct in the left posterior tibia (Fig. 3). On 3D angio CT of the lower extremity, no meaningful stenosis or occlusions were observed from the common iliac artery to the foot artery in either extremity. However, severe venous engorgement was observed along the subcutaneous area and the muscle of the left lower extremity. No signs of deep vein thrombosis or occlusion were observed.

We diagnosed the patient with venous ulcers and lymphangitis caused by chronic venous insufficiency combined with primary lymphedema. Drug therapy (Venitol, Kwang Dong Pharmaceutical, Seoul, Korea, Mucolase, Hanmi Pharm, Seoul, Korea, and several antibiotics) and sterile dressings were administered for 2 weeks. The heating sensation and diffuse redness improved. In addition, multilayer bandages and air pressure pneumatic compression were started. However, manual drainage was not performed because such treatment was likely to aggravate venous insufficiency. The therapy was maintained for 4 weeks. After 6 weeks of treatment, the circum ference of the left lower extremity was reduced by 3 cm. Erythematous crusting, squamous ecchymosis and ulceration were also mildly improved (Fig. 4).

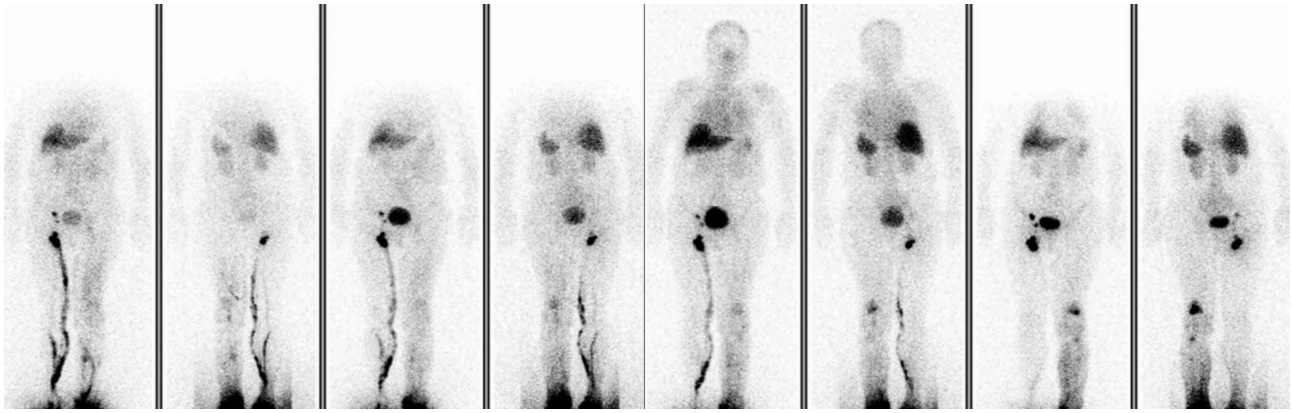


Fig. 2. Lymphoscintigraphy after an intradermal injection of 100 uCi/0.02 mL of filtered ^{99m}Tc phytate. Dermal back flow and reflux flow at skin level appeared on the left lower extremity. Left inguinal lymph node absorption was not apparent.

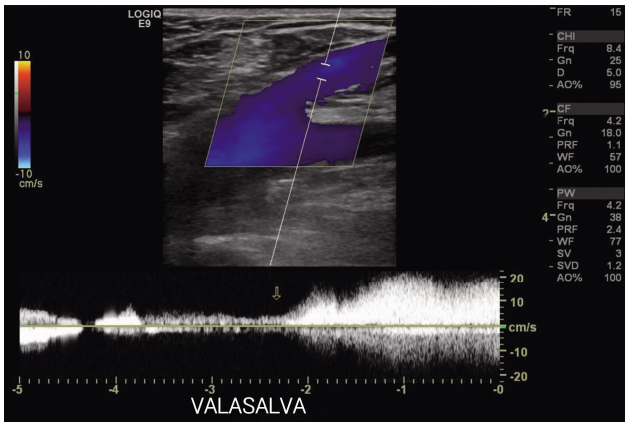


Fig. 3. On Doppler examination, there were bidirectional flow wave forms with the Valsalva maneuver in the left common femoral and great saphenous veins, which indicated valvular insufficiency. Mildly engorged perforating veins were indistinct in the left posterior tibia.



Fig. 4. After 6 weeks, the patient's erythematous crusting, squamous ecchymosis and ulcer-like lesions had improved.

DISCUSSION

Lymphedema is the chronic progressive swelling of a tissue caused by insufficient lymphatic function. The primary cause of lymphedema is anomalous lymphatic development, and the secondary cause of its occurrence is injury to the lymphatic vessels or the lymph nodes. When protein-rich fluid collects in a superficial interstitial space, the lymphedematous tissue enlarges due to adipose deposition and fibrosis [10]. Lymphedema is a pathological disease that may be complicated by in fection, cutaneous changes or rarely by malignant transformation. Patients with lymphedema may also experience a combination of psychological morbidity due to abnormal appearance of limbs or genitalia, have difficulty fitting into clothes, and experience deteriorated function of the affected area.

CVD includes a spectrum of overlapping diseases that result in venous disease abnormalities. The venous and lymphatic circulation systems are closely connected. For example, venous decompensation results in an extra work load on the lymphatic system due to the increased amount of lymph-transported water and protein. Inflammation of the venous system often accompanies lymphangitis and lymphadenitis and reduces lymphatic transport capacity. The lymphatic system is directly affected by venous insufficiencies. Insufficient venous return causes the blood capillary pressure to increase, resulting in net filtrate increases. An edema protective mechanism involves the reaction between the lymphatic system and safety factors. Among patients with advanced venous insufficiencies, 20-30% also have associated lymphatic dysfunction, which is likely due to secondary damage caused by overload or recurrent lymphangitis [7,8]. The term phlebolymphedema is commonly used to distinguish this form of lymphedema of venous origin [9].

The occurrence of secondary lymphedema due to venous origin is widely known. However, in this case, the patient did not conform to the diagnostic criteria of lymphedema of venous origin, such as phlebolymphedema. Edematous swelling was observed in the patient's left lower extremity since birth, and this swelling had fluctuated during childhood and adolescence. She had undergone several tests during development, but the exact cause for the swelling had never been identified. She had been told that the swelling might represent hypoplasia lymphedema, which is a form of primary lymphedema, but did not undergo any relevant tests or treatment. The patient eventually visited our hospital when she was 59. Signs of venous ulceration were observed in the left tibia, toes and sole of the foot. Venous ulceration is the most severe complication of CVI, but the results of ultrasound and 3D angio CT examination revealed only mild valvular insufficiency rather than severe CVI, which might cause venous ulceration. On lymphoscintigraphy, dermal back flow and reflux flow at the skin level appeared on the left lower extremity, and there was no indication of left inguinal lymph node absorption.

Our case was similar to phlebolymphedema in that it involved chronic venous-lymphatic insufficiency. However, our patient exhibited venous ulceration and lymphangitis caused by chronic venous insufficiency combined with primary lymphedema, which is very unusual. The cause of severe venous ulceration in patients with mild chronic venous insufficiency remains unclear. Based on research, we hypothesize the following scenarios: First, primary lymphedema progresses chronically in the venous and lymphatic circulatory systems, which may cause CVI

and eventually lead to venous ulceration. However, this is very unlikely when comparing the lymphatic system with its relatively small capacity and the venous system with its large transport capacity. Second, a patient with chronic primary lymphedema may have mild VI for unknown reasons, which causes the transport capacity of the lymphatic system to increase to compensate. However, primary lymphedema causes mechanical insufficiency, also known as low-volume insufficiency, to exist in the lymphatic system; thus, VI is not compensated. This situation progresses chronically and results in repetitive infection, which may consequently lead to dynamic insufficiency of the lymphatic system. Thus, the proposed cycle explains primary lymphedema, CVI, worsening tissue edema and CVI complications.

Complex decongestive therapy (CDT) including manual lymph drainage, bandage is current treatment of primary lymphedema of the extremity. Wearing graded compression stockings can be encouraged in CVI [11,12]. In this case, CDT was not selected because the patient had dynamic insufficiency and CDT was likely to cause reduced transport capacity of the lymphatic system. We report a rare case of primary lymphedema combined with CVI. As CVD may be occured secondarily in primary lymphedema patients, careful follow-up is necessary.

Acknowledgments

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