

Diffuse Large B Cell Lymphoma, Bilateral Lower Extremity Lymphedema, and Ulcerated Inguinal Lymph Node

NATA PRATAMA HARDJO LUGITO, ANDREE KURNIAWAN, THEO AUDI YANTO, MARGARET MERLYN, RESA SETIADINATA, INDRA WIJAYA

Faculty of Medicine Pelita Harapan University, Siloam General Hospital Karawaci, Tangerang Banten

Diterima 22 Januari 2014; Direview 27 Januari 2014; Disetujui 2 Maret 2014

ABSTRACT

Lymphedema (LE) is a chronic medical condition characterized by lymphatic fluid retention, resulting in tissue swelling. There are two general classifications of LE; primary and secondary which are based on two mechanisms; lymphatic obstruction and lymphatic interruption. The most common cause of LE in the developing world is secondary to an infection known as filariasis. Cancer including Hodgkin and non-Hodgkin lymphomas; and its treatment are some causes of secondary LE. LE also could maintain the persistence of an occult localization of lymphoma. This case illustration describes a female, 57 year-old with stage II lymphedema of both legs, bilateral inguinal lymphadenopathies that were biopsied. The filarial blood examination was negative. Biopsies showed diffuse large B-cell lymphoma.

Keyword: lymphedema, lymphoma.

ABSTRAK

Limfedema (LE) adalah kondisi kronik berupa pembengkakan jaringan yang disebabkan retensi cairan limfatik. Ada dua klasifikasi umum LE, yaitu primer dan sekunder yang berdasarkan dua mekanisme; obstruksi limfatik dan gangguan limfatik. Penyebab LE paling umum di negara berkembang adalah sekunder, setelah infeksi filariasis. Berbagai jenis kanker, termasuk limfoma Hodgkin dan non-Hodgkin serta tata laksanaanya, juga merupakan penyebab LE sekunder. Limfedema juga dapat menjadi tempat persembunyian limfoma. Pada ilustrasi kasus ini, seorang perempuan berumur 57 tahun dengan limfedema tingkat II pada kedua tungkai dan limfadenopati inguinal bilateral menjalani biopsi. Pemeriksaan darah filarial negatif dan hasil biopsi menunjukkan limfoma sel B besar difus.

Kata Kunci: limfedema, limfoma.

INTRODUCTION

Lymphedema (LE) is a chronic medical condition characterized by lymphatic fluid retention, resulting in tissue swelling. It is estimated that between 3 and 5 million patients in the United States suffer from LE, with a significant proportion developing the disease as a consequence of cancer or its treatment. In oncology, the most common etiology for the development of LE is the impaired or disrupted flow of lymph fluid through the draining lymphatic vessels and lymph nodes, usually as a consequence of surgery and/or radiation therapy.

Cancer including Hodgkin and non-Hodgkin lymphomas; its treatment and other types of trauma are causes of secondary LE. Recurrent and metastatic malignancy; any treatments, whether surgical or irradiation; lymphadenectomy or surgical excision

KORESPONDENSI:

dr. Nata Pratama Hardjo
Lugito, SpPD
Faculty of Medicine Pelita
Harapan University, Siloam
General Hospital Karawaci,
Tangerang, Banten.
Email: nata.lugito@uph.edu

of the inguinal, iliac, or auxiliary lymph nodes; and the most common non-infectious cause worldwide, especially following breast cancer treatment; nonsurgical trauma, e.g. radiation therapy to lymph node groups, surgery of the prostate, uterus, or cervix. Besides that, LE also could maintain the persistence of an occult localization of lymphoma, despite routine investigations found an apparent complete remission of disease

CASE ILLUSTRATION

Female, 57 year-old came with a complaint of swollen both legs since one year ago. The swollen legs initially came and go, but later stayed. She had no other complaints such as pain, pallor, or erythema. Then she experienced enlargement of bilateral inguinal lymph node since 6 months ago, but with no pain, pallor, or erythema. Then the left inguinal lymph node became ulcerated. She had no decreased body weight, cough, palpitation, chest pain, nausea, vomit, or diarrhea. She had no history of diabetes, hypertension, cardiac disease, asthma or allergy.

Her physical examination revealed within normal limit vital signs. Her general physical examination was also normal. Her legs were swollen, with non pitting edema, hyperkeratosis and hyperpigmentation, no pain, pallor or erythema. The circumference of the left femur was 77 centimeters and right femur was 72 centimeters. She also had bilateral inguinal lymphadenopathies with an ulcer in the left lymph node. Her laboratory results including hemostasis profile were within normal limits except lactate dehydrogenase (LDH) of 348 mg/dL. The filarial blood examination was negative. Computed tomography (CT) scan of the pelvic showed no mass. Biopsy done to the inguinal lymph node revealed that squamous epithelial cells, pleomorphic and hyperchromatic nucleated with coarse chromatin spreading to fibrous and muscle tissues, concluded as large B cell non Hodgkin lymphoma.

The patient received a chemotherapy regimen of cyclophosphamide, vincristine and doxorubicin. The chemotherapy was done 6 cycles at an interval of 3 weeks. The patient tolerated the protocol well and no complications occurred, but the lymphedema persisted.



Picture 1. Lymphedema of left and right legs. The lymphedema affected the left leg to a greater extent compared to the right leg. There were non pitting edema, with skin changes such as hyperkeratosis and hyperpigmentation, no pain, pallor or erythema. There were bilateral inguinal lymphadenopathies with an ulcer in the left lymph node

DISCUSSION

The development of LE occurs when the lymphatic load exceeds the transport capacity. There are two general classifications of LE; primary and secondary.^{1,2} Primary LE develops as a consequence of a pathologic congenital and / or hereditary etiology. These various conditions include reduced numbers of lymphatic collectors and the decreased diameter of existing lymph vessels (hypoplasia); increased diameter of lymphatic collectors (hyperplasia); absence of lymphatic system components (aplasia); and inguinal lymph node fibrosis (Kinmonth syndrome).¹⁻³ There are based on two basic mechanisms of secondary LE; lymphatic obstruction and lymphatic interruption.³ The most common cause of LE in the developing world is secondary to an infection by the nematode *Wuchereria bancrofti*, also known as filariasis.^{1,2} The most common cause of LE in the industrialized world is malignancy and malignancy-associated. Secondary LE can also be caused by surgery, radiation, trauma, infection, tumor blockage, chronic venous insufficiency, immobility, or tourniquet effects.^{3,4} Once damage has occurred to the lymphatic system, transport capacity is permanently diminished in the affected region, thereby predisposing that region to LE. Cancer, its treatment and other types of trauma are causes of secondary LE.³⁻⁶ Recurrent and metastatic malignancy; Hodgkin and non-Hodgkin lymphomas; any treatments, whether surgical or irradiation; lymphadenectomy or surgical excision of the inguinal, iliac, or auxiliary lymph nodes; and the most common non-infectious cause worldwide, especially following breast cancer treatment; nonsurgical trauma, e.g. radiation therapy to lymph node groups, surgery of the prostate, uterus, or cervix.³⁻⁵

The accumulation of lymph fluid in the interstitial may not be clinically evident in the early stages of the disease, but will occur if the lymphatic load increases above the reduced transport capacity of the lymphatic system. Therefore, a subclinical LE exists after surgery or radiation therapy, referred to as the latency stage or Stage 0. In this stage, there are no clinical signs of LE because the reduced transport capacity exceeds the lymphatic load of the tissues. Stage I lymphedema is referred to as reversible lymphedema. In this stage, the patient presents with very soft, pitting edema with no fibrosis. Prolonged elevation of the limb leads to complete resolution. Stage II lymphedema, also called spontaneously irreversible lymphedema, presents with intradermal fibrosis that decreases

tissue suppleness and reduces the ability of the skin to indent with pressure. In this stage, resolution of clinically evident lymphedema is not possible with elevation. Stage III lymphedema is also called lymphostatic elephantiasis. It is associated with a significant increase in the severity of the fibrotic response, tissue volume, and other skin changes such as papillomas, cysts, fistulas, and hyperkeratosis. Skin folds on the wrists and ankles more deep. Recurrent bacterial and fungal infections of the skin and nails are more common in this stage. In Stage II and III the formation of adipose tissue is mainly responsible for the excess volume in swollen limbs that do not present with pitting. The comparative volumetric differences between the affected compared to the unaffected limb can be used as a supplement to further characterize the severity of each stage. Minimal severity represents a situation in which the affected limb has a measured volume that is less than 20% greater than the unaffected limb. A 20% to 40% difference represents moderate severity, and a difference of more than 40% is considered severe.^{1,4}

In the case of LE and lymphoma, a case study expressed that LE could maintain the persistence of an occult localization of lymphoma, despite routine investigations found an apparent complete remission of disease. The impaired lymphatic drainage area is like a safe place for the lymphoma cells to skip the anti proliferative effect of chemotherapy. In addition, the local immunodeficiency in the immune deficient district of LE might have promoted the chemotherapy resistance of malignant cells.⁶⁻⁸

The patient in the case illustration had stage II lymphedema, with lymphedema that was not reversible with elevation, decreased tissue suppleness and reduced ability of the skin to indent with pressure (non pitting).^{9,10} The skin also had hyperkeratosis and hyperpigmentation. Although the right leg seemed to be less in dimension to the left leg (72 vs. 77 centimeters), but it was not that the right leg was not affected. The lymphedema affected both legs, but with a greater extent to the left than the right leg.

The lymphedema in this patient seemed to be secondary in nature, as the patient was 57 year-old, with no history of similar complaints in her life. The filariasis as a common etiology for lymphedema in this part of the world was negative, but the biopsy of the lymph node revealed lymphoma. Other etiologies of secondary lymphedema such as deep vein thrombosis or obstruction by a pelvic mass were negative.

In conclusion, the stage II lymphedema of both legs of this patient was caused by bilateral inguinal lymphadenopathy, causing lymphatic obstruction. The large B cell lymphoma lymphadenopathy also caused lymphatic interruption.

REFERENCE

1. Simonian SJ, Morgan CL, Tretbar LL, Blondeau. Lymphedema: Diagnosis and Treatment. In Differential diagnosis of lymphedema. Ed. Tretbar LL, Morgan CL, Lee BB, Simonian SJ, Blondeau B. London: Springer; 2007:12-20.
2. Morgan CL. Lymphedema: Diagnosis and Treatment. In Medical management of lymphedema. Ed. Tretbar LL, Morgan CL, Lee BB, Simonian SJ, Blondeau B. London: Springer; 2007:43-54.
3. Paskett ED, Dean JA, Oliveri JM, Harrop JP. Cancer-related lymphedema risk factors, diagnosis, treatment, and impact: a review. *J Clin Oncol*. 2012;30:3726-33.
4. Földi M, Földi E, Kubik S. Textbook of lymphology. Munich, Germany: Urban & Fischer; 2003:22-5.
5. Ely JW, Osheroff JA, Chambliss ML, Ebell MH. Approach to leg edema of unclear etiology. *J Am Board Fam Med* 2006;19:148-60.
6. Lacovara JE, Yoder LH. Secondary lymphedema in the cancer patient. *Medsurg Nurs*. 2006;15:302-6.
7. Kerchner K, Fleischer A, Yosipovitch G: Lower extremity lymphedema update: pathophysiology, diagnosis, and treatment guidelines. *J Am Acad Dermatol* 2008, 59:324-31.
8. Massini G, Hohaus S, D'Álo F, Bozzoli V Vannata B, et.al. Mantle Cell Lymphoma Relapsing at the Lymphomatous Arm. *Mediterr J Hematol Infect Dis* 2013,5(1):16.
9. Dawes DJ, Meterissian S, Goldberg M, Mayo NE. Impact of lymphoedema on arm function and health-related quality of life in women following breast cancer surgery. *J Rehabil Med*. 2008;40:651-8.
10. Soligo CG, Godoy JM, Godoy MF, Taglietto VR. New technique of lymphatic drainage improving the lymphoscintigraphic pattern in traumatic lymphedema: case report. *Arq Ciêc Saúde*. 2008;15: 43-5.