

# Unusual Presentation of Non-Hodgkin's B-Cell Lymphoma with Unilateral Right Limb Lymphedema

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## Abstract

**Background:** In clinical practice and setting of general practice it is common to see patients with leg edema. To correctly identify the etiology of the edema and then properly manage the cause is not always easy. The unilateral lymphedema of the lower limb has rarely been reported as an initial presentation for lymphoma, especially in females, usually without classic signs or symptoms, but often with inguinal lymphadenopathy or abdominal masses. **Case Report:** In this article, we report a rare case of unilateral lower limb edema in a healthy obese woman who complained about the appearance of the disease for several months and for whom deep vein thrombosis and other diseases had been excluded. The histological examination of the biopsy of an enlarged lymph node in the right groin, which was compressing the iliac and femoral vein, revealed the presence of B cell non-Hodgkin lymphoma with high-grade malignancy. **Conclusions:** A common challenge for primary care physicians is to determine the cause and find an effective treatment for leg edema of unclear etiology. Non-Hodgkin's B-cell Lymphoma should be considered in the differential diagnosis in patients with unilateral leg edema when the swelling is chronic and deep venous thrombosis is promptly excluded.

## Keywords

Component, Unilateral Leg Edema, Non-Hodgkin's B-Cell Lymphoma, Inguinal Lymphadenopathy

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## 1. Introduction

A common challenge for primary care physicians is to determine the cause and find an effective treatment for

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leg edema of unclear etiology. The most likely cause of leg edema in patients over 50 years of age is venous insufficiency. There are two types of leg edema: venous edema and lymphedema. Venous edema consists of excess low-viscosity, protein-poor interstitial fluid resulting from increased capillary filtration that cannot be accommodated by a normal lymphatic system [1].

Lymphedema consists of excess protein-rich interstitial fluid within the skin and subcutaneous tissue resulting from lymphatic dysfunction [2].

Primary lymphedema is a rare disorder that is divided into 3 types according to age of presentation [3].

Unilateral leg edema is a frequent clinical problem, usually reflecting underlying vascular disease. Unilateral leg edema is generally due to a local cause such as deep vein thrombosis, venous insufficiency, or lymphedema. Bilateral edema can be due to a local cause or systemic disease, such as heart failure or kidney disease. Generalized edema is due to systemic disease [4].

Secondary lymphedema is much more common than primary, and the cause is generally apparent from the history [5]. The most common causes of leg lymphedema are tumors (e.g., lymphoma, prostate cancer, ovarian cancer), surgery involving lymphatics, radiation therapy, and infection (bacterial infection or filariasis) [6].

To our knowledge there has been only one previous report of a case of unilateral lymphoma-related leg edema [7] in the English-language literature. An original study [8] retrospectively found a 1.1 percent prevalence of malignancy in primary care patients presenting themselves to the office with unexplained lymphadenopathy.

This report describes an uncommon cause of obstructive lymphedema due to enlarged lumbar aortic, iliac and inguinal lymphadenopathy of malignant lymphoma, in a 70-year-old obese female in the setting of general practice. For this patient, the diagnosis of lymphoma was overlooked during the initial consultation due to lack of symptoms and signs of systemic disease.

## 2. Case Report

A 70-year-old female suffering from obesity and high blood pressure presented herself to our office complaining of pain with swelling of the right leg which had started some months before. She denied any weakness, fever, night sweats, weight loss, dyspnea, exercise intolerance, cough and headache. She reported no prolonged immobilization or bed rest. Cardiac examination was normal and the chest was clinically clear.

No hepatosplenomegaly was found but enlarged right inguinal lymph nodes were observed. No other lymphadenopathies were palpable in the neck and axilla.

Physical examination of the lower extremities revealed severe right leg swelling with pitting edema, erythematous skin, increased warmth and pain on pressure of the calf. The right leg appeared grossly swollen as compared to the left lower limb. Femoral and popliteal arterial pulses were not palpable because of edema (See **Figure 1**).

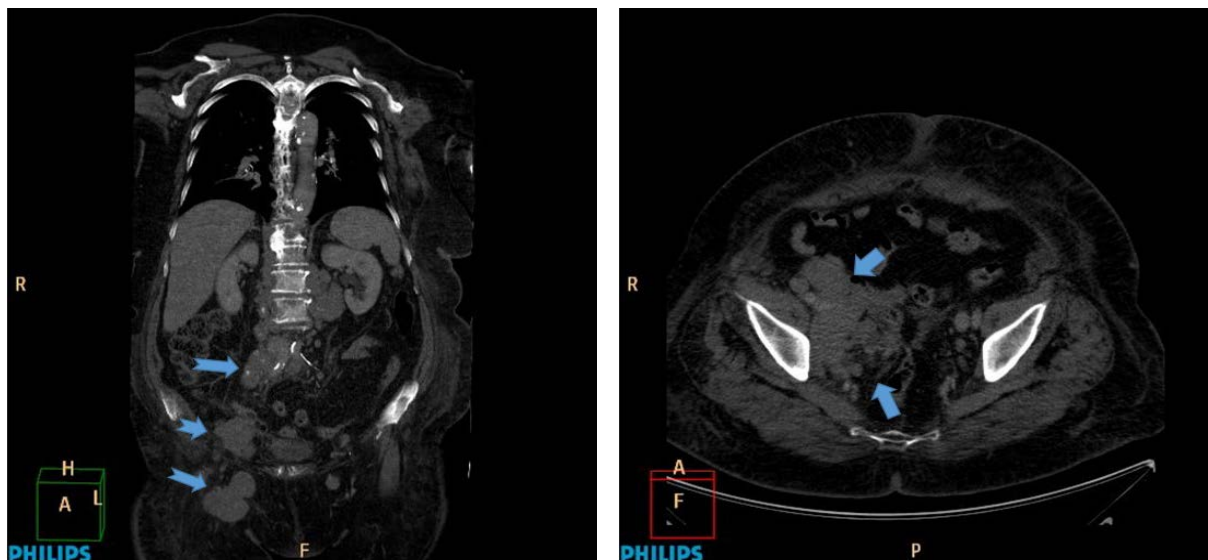
The chest X-ray and the two-dimensional transthoracic echocardiography exam were normal.



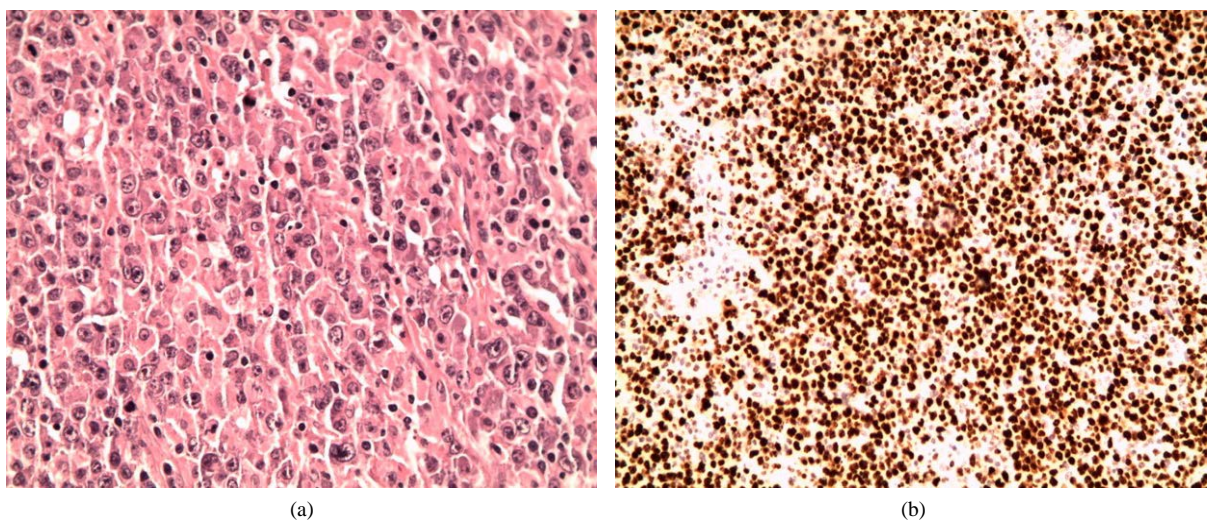
**Figure 1.** Unilateral limb edema.

Laboratory evaluation was unremarkable except for the presence of mildly elevated inflammatory markers with a slight increase in d-dimer (>700 mg/dl). Subsequently a Doppler ultrasonography of the lower extremities was performed but no sign of deep vein thrombosis was detected. Therefore the patient underwent to an abdomen ultrasound scan that showed the presence of a complex right inguinal lymphadenopathy compressing the ipsilateral femoral and iliac vein. Also the abdomen CT scan showed enlarged right lumbar para-aortic lymph nodes extended to iliac-obturator stations as well as the ipsilateral inguinal-femoral lymph nodes, as seen by ultrasonography (See **Figure 2**).

It was concluded that the mechanical obstruction of the blood vessels in the groin determined the lower limb lymphedema. Consequently, the patient was admitted to hospital to carry out a biopsy of an enlarged inguinal lymph node for histological definition of suspected lymphoproliferative disease. In fact biopsy showed complete effacement of nodal architecture by malignant tumor, comprising diffused cells having large pleomorphic vesicular nuclei with prominent nucleoli, suggesting the existence of diffused B-cell lymphoblastic non-Hodgkin's lymphoma. Consequently the patient was referred to the oncology department and underwent chemotherapy with improvement of the right limb lymphedema (See **Figure 3**).



**Figure 2.** Abdomen CT scan showing enlarged right lumbar para-aortic, iliac and inguinal lymph nodes (see arrows).



**Figure 3.** Histopathology findings—Panel A shows intense positivity of lymphoid elements with CD-20, a marker of B lymphocytes; Panel B shows intense diffuse positivity for Ki-67 as expression of high proliferative index.

### 3. Discussion

Lymph node enlargement may occur because of proliferation of cells of the lymphocyte and monocyte-macrophage systems, usually in response to antigenic stimulus, or may be due to infiltration by inflammatory cells in infections involving lymph nodes (lymphadenitis).

*In situ* proliferation of malignant lymphocytes or macrophages, infiltration of nodes by metastatic malignant cells or infiltration of lymph nodes by metabolite laden macrophages are the storage of diseases [9].

When the cause for the lymphadenopathy remains unexplained, the physician must decide whether to pursue a specific diagnosis. The decision will depend primarily on the clinical setting as determined by the patient's age, the duration of the lymphadenopathy and the characteristics and location of the nodes.

Using the factors above as guidance, a thorough history and physical examination should allow physicians to categorize individual cases of lymphadenopathy according to the algorithm as posted by Ferrer [10].

In developed countries, the most common cause of secondary lymphoedema is malignancy.

On the other hand, filariasis is considered the most common cause of secondary lymphoedema in developing countries [11].

The appearance of pronounced lymphedema of a lower extremity due to an obstruction of iliac and femoral vein in the groin, as the first clinical manifestation and presenting sign of Hodgkin's disease is extremely rare [12] [13].

The development of lymphedema is a slow, insidious process starting in the most distal portion of the extremity.

Ninety-five percent of unilateral lymphedema involves obstruction of lymphatics due to infection, postoperative lymphatic disruption and malignancy. Carcinoma of prostate in males and lymphomas and pelvic tumours in females are commonly responsible. Presentation of lymphoma, as leg edema, is uncommon, especially in the absence of generalized lymphadenopathy.

Diffuse large cell lymphomas are the most common types of NHL and account for 60% - 70% of aggressive lymphoid neoplasm and 85% of these originate in B-cells. The mean age of presentation is 65 - 70 years of age and patients present rapid symptomatic lymphadenopathy. B-symptoms (fever, night sweats, weight loss > 10% of normal body weight), skin rash and symptoms pertinent to extra-nodal involvement were absent [14].

Notoriously non-Hodgkin's lymphoma typically presents with painless progressive lymphadenopathy and commonly with bilateral leg edema [15].

Unilateral lower extremity lymphedema is considered a possible but rare initial presentation for non-Hodgkin's lymphoma [16].

This case report confirms that this is more common in women [17] and there are usually no associated B-symptoms (e.g., weight loss, anorexia and night sweats), making for low clinical suspicion in our female patient. A close examination for inguinal lymphadenopathy or abdominal masses may provide a key clue for the diagnosis of lymphoma.

It follows that to make an early diagnosis of non-Hodgkin's lymphoma subtype an excisional biopsy with histological examination of the lymph nodes is mandatory [18].

Although the advent of new immunohistochemical analytic techniques has increased the sensitivity and specificity of fine-needle aspiration [19] excisional biopsy remains the gold standard diagnostic procedure.

### 4. Conclusions

In conclusion, the aim of this case is to draw physicians attention as they should not underestimate the unusual presentation of lymphedema in patients over 50 years old, given the need to perform an early diagnosis and specific therapy for lymphoma.

This entity should be considered in the differential diagnosis in patients with unilateral leg edema when the swelling is chronic and deep venous thrombosis is promptly excluded.

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### Manuscript Type

Case report.



Both authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.

Both authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

## Competing Interests

None declared.

## Conflict of Interests

None declared.

## Consent

Written informed consent was obtained from the patient for publication of this case study and the accompanying images are for scientific purposes.

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