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# Diagnostic burdens in patient with CLL/SLL in the primary care clinic - A case report

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## ABSTRACT

**Introduction:** Chronic lymphocytic leukemia (CLL) together with small lymphocytic lymphoma (SLL) are considered different manifestations of the same disease from the group of low-grade B-cell lymphomas. The diagnosis of each is made based on either a blood count or a lymph node biopsy. However, the diagnostic tools for evaluating lymphadenopathy in primary care are limited, which contributes to the diagnostic challenges in determining its underlying causes. **Case Report:** A 67-year-old woman reported to the general practitioner (GP) clinic due to an increase in the abdominal circumference over the past 2 weeks. Additionally, she noted recent mild enlargement of the lymph nodes in the submandibular and left axillary area. Physical examination revealed one small lymph node on the left submandibular side, and in the central region of the left axilla, two lymph nodes of about 10-15 mm in size. The results of blood tests revealed no abnormalities. The chest X-ray examination revealed suspicion of fluid in both pleural cavities. Finally, the ultrasound examination of the abdomen and breasts showed numerous enlarged lymph nodes. After the referral to a surgical oncology clinic, SLL was initially diagnosed. **Conclusion:** Early recognition and understanding of the benign and malignant etiologies of lymphadenopathy play a critical role for prompt diagnosis and treatment initiation.

**Keywords:** CLL/SLL, diagnostic, primary care

## 1. INTRODUCTION

Chronic lymphocytic leukemia (CLL) together with small lymphocytic lymphoma (SLL), within the non-Hodgkin lymphoma group (NHL), distinguished by the accumulation of functionally incompetent lymphocytes in blood, bone marrow, and lymphoid tissues (Tees and Flinn, 2017). They differ mainly in the location of cancer cells and clinical symptoms, rather than in their biological nature. In the case of CLL, the cancer cells are located primarily in the blood and bone marrow, causing symptoms such as fatigue, infections, hepatomegaly and splenomegaly. In contrast, in SLL they are located in the lymph nodes and lymphatic tissues, which is why it often manifests as enlarged lymph nodes without general symptoms (Ben-Ezra et al., 1989). The diagnosis of CLL is based on a blood count showing significant lymphocytosis, which distinguishes it from SLL, as well as on the

immunophenotype of B cells. On the other hand, the diagnosis of SLL is based on a lymph node biopsy (Li, 2022). Globally, CLL accounts for approximately 28% of leukemia cases in men and 24% in women, with higher incidence rates observed in countries with very high Human Development Index (Daltveit et al., 2025).

Lymphadenopathy is defined as an increase in lymph node size >1cm or >2cm of inguinal lymph nodes. There are numerous possible causes of lymphadenopathy encountered in primary care, ranging from benign, self-limiting viral, bacterial, parasitic, or fungal infections to malignant diseases. Among primary care patients with lymphadenopathy, the most common causes are benign viral infections, such as CMV, HIV, and Epstein-Barr virus, or bacterial infections, including streptococcal pharyngitis (Ferrer, 1998). In contrast, a neoplastic cause, such as malignant hematologic or metastatic diseases, is found in approximately 1.1% of patients (Habermann and Steensma, 2000). Moreover, the causes of lymphadenopathy include sarcoidosis, tuberculosis and autoimmune diseases, including rheumatoid arthritis and systemic lupus erythematosus, or the use of certain drugs (Rodolfi et al., 2024).

Simultaneously, diagnostic tools for evaluating lymphadenopathy in primary care are limited, which contributes to the diagnostic challenges in determining its underlying causes (Habermann and Steensma, 2000). Therefore, we would like to present the case of a patient with CLL/SLL, whose nodal manifestation in the right breast area caused diagnostic difficulties in the primary care physician's office.

## 2. CASE REPORT

A 67-year-old female patient reported to the general practitioner (GP) clinic due to an abdominal hernia that had been present for approximately 3 years, which, according to the patient, had enlarged over the last two weeks, causing an increase in the abdominal circumference. In the past, the patient had already been qualified for hernia repair, but at that time, she did not decide to undergo the procedure. Additionally, she noticed a slight enlargement of the lymph nodes in the submandibular and left axillary area. So far, the patient has been treated only for spondylosis and bilateral coxarthrosis during the period of exacerbation of the symptoms. She did not suffer from other chronic diseases and did not take any medications chronically.

Physical examination revealed a soft, painless abdomen with normal peristalsis and no peritoneal signs. In the central part of the abdomen above the umbilicus, a ventral hernia was visible, which becomes visible during tension of the abdominal press muscles. Additionally, one small lymph node was palpable on the left submandibular side, and in the central area of the left axilla, two lymph nodes of about 10-15 mm in size were palpable. Both the right and left breasts were fibrous and difficult to assess on palpation. No inflammatory changes or redness in the skin of the breasts were visible. Nipples were normal, without pathological discharge. To deepen the diagnostics, the patient was referred to a surgical clinic to order imaging tests of the breasts and axillary area. Laboratory tests and a gynecological check-up were also recommended.

After about 2 weeks, the patient returned with the test results. Except for CRP 10.4 mg/l (norm up to 5 mg/l), the results were within the normal range. Detailed values of laboratory tests are presented in Table 1. In the meantime, she had a surgical visit - to deepen the diagnostics, a CT scan was ordered - the date was set in 1 month. The patient reported that she had scheduled a gynecological check-up in 2 months. At the same time, during the visit, she reported new complaints: a feeling of shortness of breath, which occurs especially before falling asleep. She provides the result of a chest X-ray from 2 years ago - linear fibrosis in both lung fields, otherwise no abnormalities were visible. Physical examination was consistent with the previous visit; additionally, slightly decreased breath sounds were heard at the base of the right lung. Otherwise, vesicular breath sounds were symmetrical and present bilaterally. A new chest X-ray was ordered, and the patient was advised to return for follow-up with the results.

**Table 1:** Values of laboratory tests performed.

Parameter	Result	Normal Value
White blood cells	6900/ $\mu$ l	4000-10000
Red blood cells	4.78 million / $\mu$ l	3.9-5.2
Hemoglobin	14.2 g/dl	11.2-15.7
Hematocrit	41 %	34-46
Mean Corpuscular Volume	85.7 fl	75-97
Mean Corpuscular Hemoglobin	29.6 pg	25.6-33
Mean Corpuscular Hemoglobin Concentration	34.5 g/dl	31-37
Red Cell Distribution Width - Coefficient of Variation	14 %	11.7-14.4

Red Cell Distribution Width - Standard Deviation	41.6 fl	36.4-46.3
Platelet Count	191.000 / $\mu$ l	125.000-396.000
Mean Platelet Volume	10 fl	9.4-12.6
Alanine transaminase	18.7 U/l	Max 35
Aspartate aminotransferase	24.3 U/l	Max 35
Creatinine	0.84 mg/dl	0.51-0.95
Estimated Glomerular Filtration Rate	67 ml/min/1.73 <sup>2</sup>	
C-reactive protein	10.4 mg/l	Max 5
Erythrocyte sedimentation rate	5 mm/h	3 - 20

After 7 days, the patient reported mild dyspnea and coughing, providing the current result of a chest X-ray. The chest X-ray examination revealed: small linear fibrosis in the lung fields, thickening of the small and large interlobular fissure, suspicion of fluid in both pleural cavities - ultrasound indicated, diaphragmatic-pleural adhesions, sclerotic plaque in the aortic arch, and degenerative changes in the thoracic spine. The physical examination revealed no changes compared to the previous visit.

The ultrasound examination of the abdomen and breasts was performed. The report described numerous enlarged lymph nodes: in the pancreatic region and around the aorta measuring 40×25 mm, 42×19 mm, 49×43 mm; in the left axillary region 20×26 mm, 12×19 mm, 18×21 mm; in the right axillary region 14×12 mm, 8×12 mm; in the left supraclavicular area 8×15 mm; and near the iliac vessels—on the left side 21 mm and 27 mm, on the right side 28×20 mm (Figure 1). Additionally, fluid was noted in both pleural cavities: approximately 704 ml on the right and 156 ml on the left. For this reason, the patient was referred to the oncological surgery outpatient clinic.



Figure 1. Lymph node on ultrasound examination.

As a result of further diagnostics based on lymph node excision, small lymphocytic lymphoma (SLL) was initially diagnosed, then due to the multiple lymphocytosis above 5000/ $\mu$ l, the diagnosis was changed to chronic lymphocytic leukemia (CLL). The treatment in accordance with the Obinutuzumab with Venetoclax regimen was administered to the patient. The patient has experienced clinical improvement with treatment, including a reduction in symptoms, and lymph node enlargement. Currently, the patient continues treatment in a hematology-oncology center with good clinical response.

### 3. DISCUSSION

Non-Hodgkin Lymphoma is a rare diagnosis with an incidence of 19.6 cases per 100,000 people per year for NHL (Non-Hodgkin Lymphoma - cancer stat facts, 2025). Polish National Histopathological Lymphoma Register reports that CLL/SLL accounts for approximately 21.4% of mature B-cell neoplasms (Szumera-Ciećkiewicz et al., 2014). CLL is diagnosed primarily in older adults. The median age at diagnosis is 69 years. There is a significant age-related increase in the incidence of the disease, reaching over 30 cases per 100,000 per year in people over 80 years old (Eichhorst et al., 2021). Thus, CLL and SLL are uncommon disorders in primary care, but their prevalence is anticipated to rise with an aging population, highlighting the need for increased vigilance among primary care providers. Data from the Polish National Cancer Registry show that the incidence of CLL in the general population rose from 1.4 per 100,000 in 1999 to 2.4 per 100,000 in 2013. Morbidity reaches its highest level in men aged 60–79 years (Monica et al., 2018). A study conducted by Parry et al. showed that 43% of patients with early-stage (A0) CLL were treated in primary care without compromising clinical outcomes. This suggests that primary care may play an important role in managing patients with early-stage CLL/SLL (Parry et al., 2015).

Both lymphoma and breast cancer metastases may cause enlarged axillary lymph nodes, and it may be challenging to distinguish these two diseases based on history and physical examination. The axillary lymph nodes in both lymphoma and breast cancer metastasis are usually painless. However, in metastasis it is single, hard, immovable, and asymmetric, whereas in lymphoma usually several lymph nodes are enlarged, soft or rubbery, and movable (Gaddey et al., 2016; Karpf et al., 1990). Ultrasound is the best method for characterizing lymph nodes allowing for the assessment of shape, cortical thickness and fatty hilum (Chung et al., 2021; Dialani et al., 2015; Pinheiro et al., 2014). On grayscale sonography, metastatic nodes are usually hypoechoic, round, and lack an echogenic hilum (Sambhaji et al., 2009). The ability to perform an ultrasound of the lymph nodes helps in making an initial diagnosis of lymphadenopathy. Unfortunately, access to breast ultrasound is not universally available to family doctors in all primary health care clinics.

Another diagnostic parameter may be lactate dehydrogenase (LDH), an enzyme that can increase in the blood as a result of cell damage. In the case of lymphoma, this reflects the rapid growth of cancer cells (Ruan et al., 2021). It is worth noting, however, that a normal LDH level does not rule out lymphoma, as in the case we described. Especially in the early stages of the disease LDH may remain within the normal range (Colomo et al., 2003). Moreover, the study by Hiramani et al., (2023) in patients after remission indicates that LDH is not necessarily effective in detecting relapse – only about 33% of patients with relapse, had LDH above the normal range.

There is no specific blood marker for lymphomas available in primary care. Therefore, diagnostic vigilance by primary care physicians is necessary. Ultimately, lymph node surgical excision is the standard of care for lymphoma diagnosis (Syrykh et al., 2022). Blood cancers are challenging to diagnose due to non-specific heterogeneous symptoms, and the correct diagnosis is often made with delay - nearly one-third of patients with blood cancer are diagnosed only after an emergency presentation to the hospital (Black et al., 2023).

### 4. CONCLUSION

Although CLL/SLL are infrequent, they are serious hematologic malignancies that may first appear with non-specific symptoms like lymphadenopathy, making early detection in primary care essential. Strengthening diagnostic pathways and access to imaging in a primary care setting contributes to better patient outcomes and helps reduce diagnostic delays.

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**Author's Contribution**

Karol Miklusiak was author of the concept, involved in gathering the necessary clinical data. Karol Miklusiak and Klaudia Miklusiak performed the initial analysis, drafted the introduction, case report, discussion and conclusion sections.

**Informed consent**

Written & Oral informed consent was obtained from individual participants included in the study.

**Ethical approval**

Not applicable.

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**Conflict of interest**

The authors declare that there is no conflict of interest.

**Data and materials availability**

All data associated with this work are present in the paper.

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