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Chylothorax as a Rare Complication of Chronic Lymphocytic Leukemia Relapse: A Case Report and Literature Review

Hale Afshar
Rasool Akram Hospital
Fatemeh Tajikrostami
Rasool Akram Hospital
Seyed-Soheil Hoseini
soheilhoseini153@gmail.com

Iran University of Medical Sciences

Case Report

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Abstract

Background: Chylothorax is an uncommon clinical manifestation of hematologic malignancies and is rarely associated with chronic lymphocytic leukemia (CLL). Case Presentation: We report a 55-year-old woman with a 7-year history of CLL who presented with progressive dyspnea. Imaging revealed extensive, diffuse bulky lymphadenopathy and a large left-sided pleural effusion. Ultrasonography-guided thoracentesis yielded yellowish, turbid fluid consistent with chylothorax. Bone marrow aspiration confirmed leukemic infiltration, and lymph node biopsy demonstrated a low-grade lymphoma pattern, indicative of CLL relapse. The patient received six cycles of Rituximab plus Bendamustine, resulting in complete resolution of both lymphadenopathy and pleural effusion. Conclusion: This case illustrates chylothorax as a rare but clinically significant complication of CLL relapse, likely secondary to thoracic duct obstruction from bulky lymphadenopathy. Early recognition of this unusual presentation is essential for timely diagnosis and management.

Introduction

Chronic lymphocytic leukemia (CLL) is a low-grade B-cell malignancy characterized by the clonal proliferation of mature but functionally incompetent lymphocytes. Common complications include cytopenia, recurrent infections, and autoimmune phenomena. Pleural effusion is an uncommon manifestation in CLL and is usually secondary to infection, heart failure, or leukemic infiltration.(1–4)

Chylothorax, defined as the accumulation of lymphatic fluid within the pleural space, is a particularly rare complication of CLL, with only a limited number of cases reported in the literature. The proposed mechanisms include thoracic duct obstruction or rupture resulting from lymphadenopathy or direct leukemic infiltration.(5–8)

Herein, we describe a case of CLL relapse presenting with left-sided chylothorax and provide a brief review of previously reported cases. We also aim to highlight the potential underlying mechanisms and therapeutic outcomes associated with this rare entity.

Case Presentation

A 55-year-old woman with a 7-year history of CLL presented with progressively worsening shortness of breath. On physical examination, multiple bulky cervical and axillary lymphadenopathies were noted, along with markedly diminished breath sounds over the left hemithorax. Chest computed tomography (CT) revealed extensive bulky lymphadenopathy involving the cervical, mediastinal, axillary, and para-aortic regions, along with a left-sided pleural effusion (Fig. 1). Ultrasound-guided thoracentesis yielded yellowish, turbid fluid (Fig. 1). The timeline of clinical course is presented in Table 1.

Table 1
The patient's timeline; from presentation to follow-up

Time	Clinical Event
7 years before presentation	Diagnosis of chronic lymphocytic leukemia (CLL)
At presentation	Progressive dyspnea and bulky cervical and axillary lymphadenopathy
Initial evaluation	Chest CT showed extensive lymphadenopathy and left-sided pleural effusion
Diagnostic work-up	Thoracentesis confirmed chylothorax; bone marrow and lymph node biopsies confirmed relapsed CLL
Treatment	Six cycles of rituximab plus Bendamustine were administered
During treatment	Pleural drainage was performed twice for symptomatic relief
Follow-up	Complete resolution of lymphadenopathy and pleural effusion on follow-up chest CT

Pleural fluid analysis demonstrated a white blood cell count of 7,000/μL (93% lymphocytes), lactate dehydrogenase (LDH) of 352 U/L, total protein of 4.9 g/dL, triglyceride concentration of 272 mg/dL, and cholesterol of 61 mg/dL—findings consistent with chylothorax.

Bone marrow aspiration and biopsy showed infiltration by CLL cells expressing CD20, CD5, and CD23, with a Ki-67 proliferation index of approximately 6% in atypical lymphocytes. Excisional biopsy of an enlarged cervical lymph node confirmed low-grade lymphoma consistent with relapsed CLL. Cytologic examination of the pleural fluid revealed no malignant cells.

The patient was treated with six cycles of **rituximab plus bendamustine**. During therapy, pleural drainage was required twice to alleviate dyspnea. Follow-up chest CT performed after completion of treatment demonstrated complete resolution of both lymphadenopathy and pleural effusion (Fig. 2).

Discussion

Chylothorax associated with chronic lymphocytic leukemia (CLL) is exceedingly rare, with fewer than 20 cases reported in the English-language literature.(6) In the general population, chylothorax carries substantial morbidity and mortality due to ongoing loss of lymphatic fluid rich in triglycerides, immunoglobulins and lymphocytes, which can result in malnutrition, immunosuppression, and respiratory compromise.(9)

Several mechanisms have been proposed to explain the development of chylothorax in CLL patients(8). Including:

1. **Mechanical obstruction** or compression of the thoracic duct by enlarged mediastinal or para-aortic lymph nodes.(5, 10)
2. **Direct leukemic infiltration** of the thoracic duct wall, leading to rupture.(11)

3. **Post-chemotherapy necrosis or fibrosis** causing delayed lymphatic leakage.(5, 12)
4. **Venous obstruction** (e.g., of the subclavian or superior vena cava) impairing lymphatic drainage.(5, 10)

In our patient, the presence of extensive mediastinal and para-aortic lymphadenopathy, a left-sided effusion (suggesting obstruction above the fifth thoracic vertebra), the absence of malignant cells in pleural fluid cytology, and the excellent response to chemo-immunotherapy together support a mechanical obstructive mechanism rather than direct leukemic or pleural infiltration. This may explain the complete resolution achieved following systemic therapy.

A review of previously published cases (Table 2 reveals several noteworthy trends:

- Lymphadenopathy and obstruction: Mediastinal lymphadenopathy was reported in several cases, suggesting lymphatic obstruction as a plausible mechanism in a subset of patients, consistent with our findings.
- Laterality: Although right-sided effusions are more common in nonmalignant chylothorax, CLL-associated cases frequently present with bilateral effusion, aligning with the anatomical principle that lesions above the T5 vertebral level typically result in left-sided chylothorax.(6)
- Pleural fluid characteristics: Reported triglyceride levels ranged from approximately 272–972 mg/dL; our patient's value (272 mg/dL) was at the lower end but clearly within the diagnostic threshold for chylothorax (>110 mg/dL).(13)
- Treatment outcomes: Therapeutic responses vary across reported cases. Some patients achieved remission with CLL-directed therapy alone, whereas others required additional interventions such as thoracic duct ligation, pleurodesis or prolonged drainage. Scholz et al. described a patient with persistent chylothorax despite hematologic response, necessitating surgical duct ligation.(14)

Our case contributes to the existing literature by demonstrating that prompt initiation of chemo-immunotherapy with Rituximab and Bendamustine can result in complete resolution of CLL-associated chylothorax without the need for invasive lymphatic interventions—particularly when the underlying mechanism is mechanical obstruction.

Nevertheless, several limitations must be acknowledged. The rarity of this complication limits the ability to derive prognostic conclusions. Published reports are heterogeneous in terms of treatment regimens and pleural management strategies, and long-term data regarding recurrence are scarce. Moreover, advanced imaging techniques such as lymphangiography or MR lymphangiography, which could localize the precise site of ductal injury, are infrequently performed in this setting.

Future research should focus on the systematic collection of data through registries of CLL patients with pleural complications, including chylous effusions. Standardized reporting of pleural fluid characteristics (volume, triglyceride concentration, cytology, and flowcytometry), detailed imaging of lymphatic anatomy, and correlation with the type and timing of CLL therapy—including targeted agents such as Bruton Tyrosine Kinase (BTK) inhibitors—will be crucial. Notably, recent case reports describing complete resolution of CLL-associated chylothorax with ibrutinib monotherapy suggest that targeted therapies may redefine management strategies in the near future. (15)

Table 2. Summary of reported cases of CLL-associated chylothorax

Case	Author (Year)	Age / Sex	Pleural Side	Pleural Fluid TG (mg/dL)	Pleural Fluid Characteristics	Imaging Findings	Histology / Flow Cytometry	Systemic Therapy Given	Outcome / Response
Case 1	Zimhony et al., 1994(16)	81/ F	Right	330	Milky	Mediastinal lymphadenopathy	CD5+, CD19+, CD23+	Mediastinal irradiation + chemotherapy (unsuccessful), followed by talc pleurodesis	Resolution o chylothorax after talc pleurodesis
Case 2	Philippakis et al., 2012(17)	83/ F	Right	900	Milky	No mediastinal adenopathy	-	Bleomycin pleurodesis	Complete resolution
Case 3	Scholz et al., 2011(18)	65/ M	Right	>700	Milky	Cervical, axillary & mediastinal lymphadenopathy	B-CLL phenotype	FCR (Fludarabine + Cyclophosphamide + Rituximab) + TPN → radiotherapy → thoracic duct ligation	Resolved by thoracic duct ligation
Case 4	Sharma et al., 2017(19)	71/ F	Bilateral	553	TG↑	No mediastinal obstruction; suspected lymphocyte sludging	Monotypic B cells (73%), CD38-	Thoracentesis + Pleurex catheter + chemotherapy	Improved after chemotherap
Case 5	Tanrıverdi et al., 2015(7)	71/ M	Right	575	Milky	No significant mediastinal or hilar lymphadenopathy reported	Positive flowcytometry of B-CLL	Fludarabine alone (patient had already been receiving fludarabine) + tube thoracostomy + low-fat diet	remission
Case 6	Sammartino et al., 2018(6)	78/ M	Bilateral	347	chylous	-	Positive (CD19+, dim CD20+, CD5+, CD23+)	Bendamustine + Rituximab (2 cycles)	Partial improvement with recurrence
Case 7	Sammartino et al., 2018(6)	81/ F	Bilateral	-	chylous	Extensive axillary, mediastinal and hilar lymphadenopathy	flow cytometry: monoclonal B-cell CLL	Bendamustine + Rituximab (3 cycles)	Partial response wit persistent chylothorax. Expired due t pulmonary complicatior
Case 8	Sammartino et al., 2018(6)	77/ F	Bilateral	311	chylous	Recurrent CLL-associated chylothorax; treated with mediastinal/thoracic duct radiotherapy	-	Obinutuzumab (1 cycle) → Idelalisib → radiotherapy	remission
Case 9	Cheng et al., 2021(15)	67/ M	Bilateral	972	Chylous	lymphadenopathy	Typical CLL immunophenotype	One cycle FCR, then ibrutinib	Complete resolution after 2 months of ibrutinib
Our Case	—	55/ F	Left	272	Milky	Bulky mediastinal adenopathy compressing thoracic duct	CD34+, CD20+, CD3+, Ki-67	Rituximab + Bendamustine	Complete response

Conclusion

Chylothorax should be recognized as a rare but potentially reversible manifestation of CLL relapse, typically presenting with progressive dyspnea. Prompt diagnostic evaluation, including pleural fluid analysis and early initiation of effective CLL-directed chemo-immunotherapy can lead to complete remission. Clinicians should maintain a high index of suspicion for chylothorax in patients with known CLL who present with pleural effusion, as timely intervention can prevent complications and obviate the need for invasive surgical management.

Declarations

Ethics and consent to participate

According to our institutional policy, ethics committee approval was not required for this single-patient case report. Written informed consent was obtained from the patient.

Patient Perspective

The patient reported satisfaction with the treatment process and clinical outcome.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Competing interests

The authors declare that they have no competing interests.

Authors' information

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Author Contribution

S.S.H. performed the literature review, wrote the manuscript, and revised the final version. H.A. was one of the primary physicians responsible for the patient's diagnosis and clinical management and contributed to writing and critically reviewing the manuscript. F.T. was one of the primary physicians responsible for the patient's diagnosis and clinical management and contributed to the clinical information used in this report. All authors read and approved the final manuscript.

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Availability of data and materials

The data supporting the findings of this case report are available from the corresponding author upon reasonable request.

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Figures

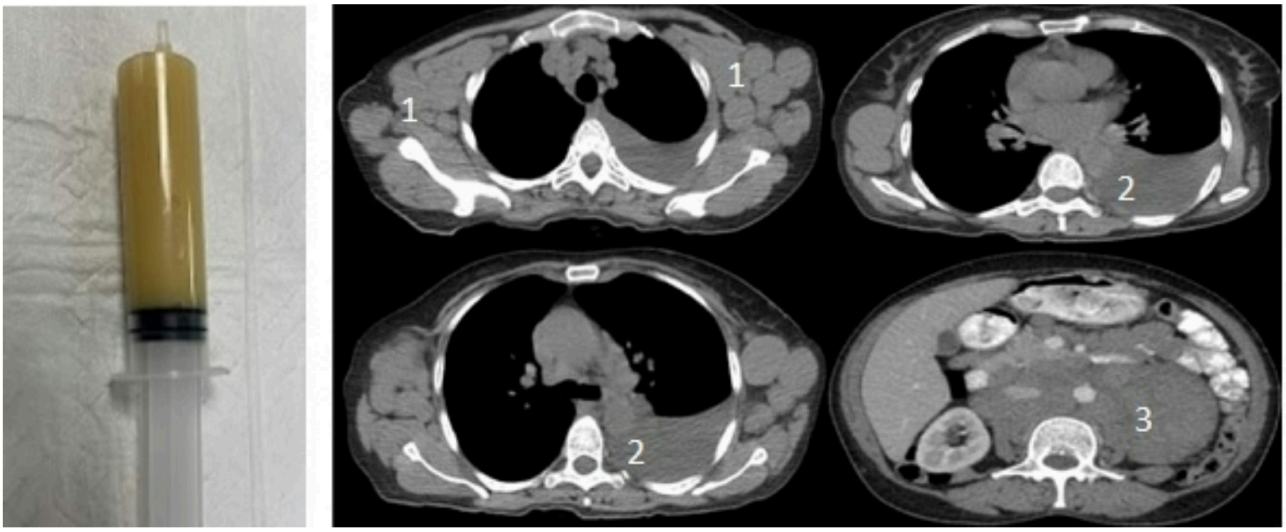


Figure 1

Yellowish pleural fluid and Axial mediastinal views of chest and abdominal CT-scan at initial work ups, revealed extensive massive axillary (number 1) and paraaortic (number 3) lymphadenopathies accompanied by a left-sided pleural effusion (number 2).

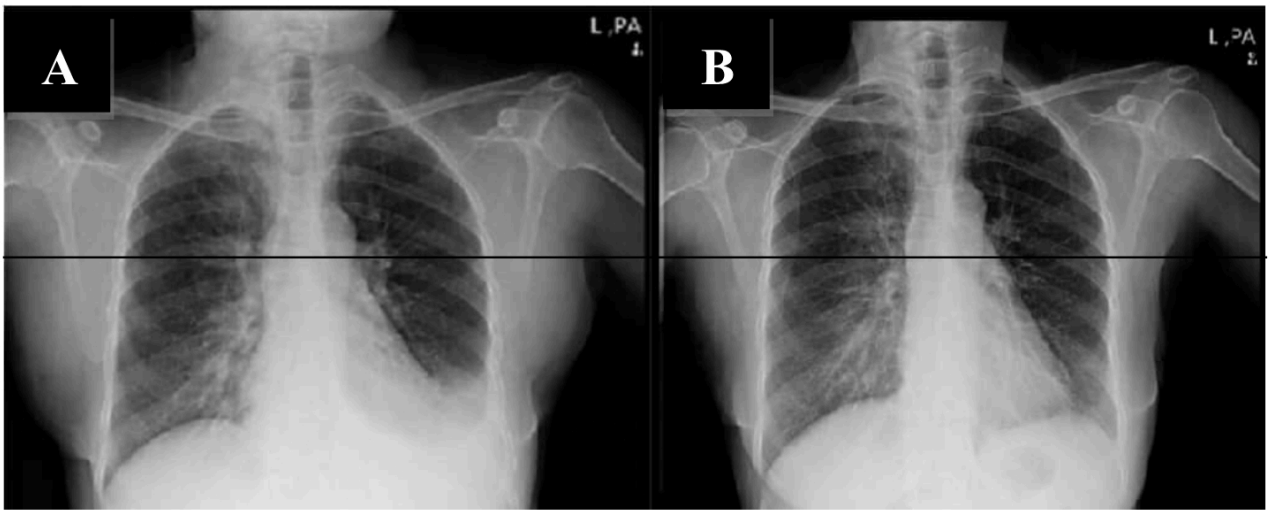


Figure 2

pre- treatment chest X-ray (A) and follow-up chest X-ray (B) after 6 courses of chemotherapy revealed nearly complete resolution of the effusion.