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T-cell Prolymphocytic Leukemia Initially Mimicking Chronic Lymphocytic Leukemia: A Diagnostic Pitfall

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Abstract

T-cell prolymphocytic leukemia (T-PLL) is a rare and highly aggressive post-thymic T-cell neoplasm that accounts for approximately 2% of adult leukemias1. Its clinical presentation often overlaps with more common lymphoid malignancies such as chronic lymphocytic leukemia (CLL), making early diagnosis challenging. T-PLL often presents with three primary symptoms, which include swollen lymph nodes, enlarged liver and spleen, and elevated white blood cell counts [1]. In several instances, T-PLLs develop promyelocytic characteristics which make these infrequent morphologic variants challenging to diagnose because they share similarities with DLBCL, CLL and AML. We present a case of a 60-year-old man with T-PLL that initially presented as acute left upper quadrant pain for two days and was suspected to have CLL. This case highlights the diagnostic overlap of T-PLL and CLL and emphasizes the need for early recognition and treatment. Its importance stems from disease's aggressiveness and rarity, its morphological and clinical overlap with CLL, and the challenges of treating an older patient.

Keywords: T- cell Prolymphocytic Leukemia, Chronic Lymphocytic Leukemia, Diagnostic Pitfall, Anchoring Bias, Extreme Lymphocytosis, Flow Cytometry, Constitutional Symptoms, Delayed Diagnosis, Aggressive Leukemia.

Introduction

Mature lymphoid leukemias present on a spectrum from indolent to very aggressive, which poses great challenges in diagnosis and treatment selection. Chronic lymphocytic leukemia (CLL) is the most common adult leukemia with an incidence of 23,690 new cases annually per 100,000 persons, and prevalence of 200,000 cases (in the US) [2, 3]. Adults present with asymptomatic lymphocytosis, non-specific general fatigue, and mild lymphadenopathy. Flow cytometry demonstrates expression of CD19, CD20, and CD23 and atypical co-expression of CD5. The pathogenesis of CLL stems from clonal expansion of mature B cells due to cytogenetic abnormalities, chronic B-cell receptor signaling, and defects in apoptosis [4]. Treatment of CLL is reserved for symptomatic patients and it includes BTK or BCL2 inhibitors3. The 5-year survival rate is high at 89.3% [5].

In contrast, T-cell prolymphocytic leukemia (T-PLL) is a rare, aggressive, and rapidly progressive disease that presents with substantial lymphocytosis, anemia, thrombocytopenia, and extensive hepatosplenomegaly [6].

T-PLL involves mature, post-thymic cells, with the "prolymphocytic" part of the name being a misnomer. The pathogenesis of T-PLL is strongly connected to TCL1 overexpression and ATM loss6. Additional genomic aberrations have been identified in the JAK/STAT pathways [6]. Flow cytometry shows a mature post-thymic T-cell phenotype with strong CD2, CD3, CD5, and CD7 expression, frequently accompanied by CD52 expression. At the moment, alemtuzumab remains the main modality of treatment, followed by hematopoietic stem cell transplant in eligible and stable candidates. The median survival is 1-2 years [7].

Due to overlapping symptomology of CLL and T-PLL, as well as CD5 expression, early distinction is crucial for patient out-

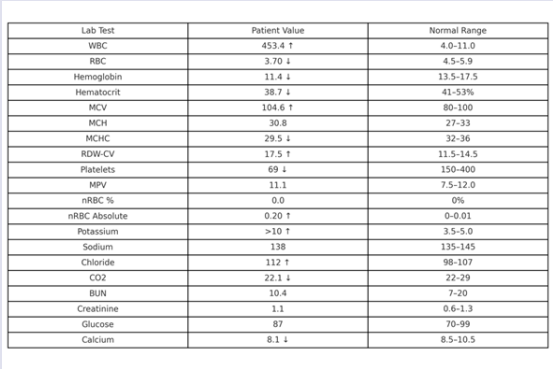
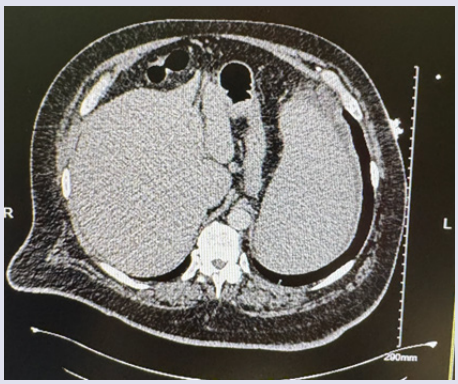
comes. Below, we present a 60-year-old Caucasian male who initially presented with symptomatology aligned with CLL, only to later be diagnosed with T-PLL. This case stresses the importance of early diagnostic intervention and the consequences of delayed management

Case Report

Initial Presentation

A 60-year-old Caucasian male with no significant past medical history presented to the emergency room with two days of left upper quadrant pain and left-sided chest pain, worsened by inspiration. He also reported bilateral peripheral lower leg edema and night sweats that began three months prior. Social history was negative. The patient denied smoking, illicit drug use and reported occasional alcohol consumption. The patient had no personal history of malignancy, but had a brother with bladder cancer.

Table 1: Initial Presentation (only noting remarkable findings)

Vital Signs	Oxygen: 92%
Physical Exam	Abdominal: Hepatosplenomegaly Musculoskeletal: Bilateral lower extremity pitting edema Skin: Pallor Neurologic: AxO X 3
Labs	
Imaging	 CT of the abdomen and pelvis • marked hepatosplenomegaly

With these findings, the patient was admitted to the hospital for oncology consultation. Given the patient's age, clinical presentation, and marked lymphocytosis (453.4x10⁹/L), the initial diagnostic workup was suggestive of symptomatic CLL. The patient was started on cytoreductive therapy which consisted of hydroxyurea two grams twice daily, while awaiting further diagnostic studies.

Table 2: Flow cytometry was collected and demonstrated mature T-cell population comprising 97% of lymphoid cells, expressing the following markers

Positive markers	Negative markers
CD45	CD4
CD3 (surface and cytoplasmic)	TdT
CD2	CD34
CD5	CD1a
CD7	MPO
CD8	TCRγ/δ.
TCRα/β	
Partial CD117	

No blast population was present. These findings shifted the diagnosis to T-PLL. Genetic testing by FISH was conducted and ruled out any BCR/ABL mutations.

Treatment

Due to administrative regulations surrounding MabCampath (alemtuzumab) administration inpatient, the patient received one dose of bendamustin 70.0 mg/m2 to further advance cytoreduction. After stabilization, the patient was discharged and outpatient treatment was revised to MabCampath (two doses, 30.0 mg/m2) to facilitate cytoreductive stabilization followed by stem cell transplant (if deemed appropriate). Despite treatment and a small reduction in lymphocytosis, the patient developed ascites, shortness of breath, and profound pancytopenia. The patient was readmitted and received three units of platelets, and two units packed RBCs, along with a paracentesis. Given the complexity of his condition, we arranged a referral to a leukemia/lymphoma specialist at the regional cancer center to support the best possible outcome.

Discussion

This case highlights three main types of diagnostic issues:

Diagnostic Delay

First, this case illustrates the diagnostic challenges and clinical consequences of delayed presentation and treatment of an aggressive hematologic malignancy. This patient experienced three months of night sweats, worsening lower extremity edema, and fatigue prior to seeking medical assistance. This delay facilitated marked disease progression, a progression of extensive leukemic burden, as witnessed by a white blood cell count exceeding 450 × 10^9/L, and a significant hepatosplenomegaly at the time of admission.

Diagnostic Pitfall Potential

Secondly, based on the patient's presentation and age, the diagnosis initially aligned closely better with symptomatic CLL. Therefore, hydroxyurea was started for rapid cytoreduction while further work- up was pending. Flow cytometry, however, revealed a population of mature post thymic T-cells, ruling out CLL and confirming T-PLL: a diagnosis with a markedly different prognosis and management course.

The case highlights that T-PLL can closely mimic other lymphoid malignancies in the early diagnostic stages, which in turn can lead to a diagnostic pitfall and back to point one a diagnostic delay.

Clinical Systems

From a clinical systems perspective, this case highlights three important considerations:

1. The importance of immediate flow cytometry in cases of extreme leukocytosis, regardless of suspected diagnosis. Early flow cytometry in the emergency department may expedite diagnosis and provide the oncologist with actionable data upon first evaluation.
2. The value of provider patient education in recognizing constitutional symptoms, leading to early detection that can improve patient outcome. In the same vein, his case underscores the importance to not discredit patients' symptoms as simply functions of “old age” or chronic venous insufficiency.
3. Broader hospital access to medication to prevent treatment delay. As illustrated in this case, the patient was administered bendamustine until the patient was stable enough to be discharged and initiated alemtuzumab.

Conclusion

Consequently, this case demonstrates how an aggressive cancer can masquerade as a common one, and how both public health education combined with provider vigilance should go hand in hand to improve outcomes for patients in diseases such as T-PLL, where every month of delay carries a significant consequence in prognosis and treatment options.

Prior Presentation

There was no prior presentation of this case.

Conflicts of Interest

The authors have no conflict of interest to declare.

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References

1. Cancer.org. (2025). Key Statistics for CLL. American Cancer Society. https://www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/about/key-statistics.html
2. Gutierrez, M., Bladek, P., Goksu, B., Murga-Zamalloa, C., Bixby, D., & Wilcox, R. (2023). T-Cell Prolymphocytic Leukemia: Diagnosis, Pathogenesis, and Treatment. International Journal of Molecular Sciences, 24(15), 12106. https://doi.org/10.3390/ijms241512106
3. Kaseb, H., Madan, A., & Hozayen, S. (2021). T Cell Prolymphocytic Leukemia. In StatPearls. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK541000/
4. Matutes, E., Brito-Babapulle, V., Swansbury, J., Talavera, J. G., de Jesus, M. L., de Saldanha, P. H., & Catovsky, D. (1991). Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. Blood, 78(12), 3269–3274. https://pubmed.ncbi.nlm.nih.gov/1742486/
5. SEER. (2018). Chronic Lymphocytic Leukemia - Cancer Stat Facts. National Cancer Institute Surveillance, Epidemiology, and End Results Program. https://seer.cancer.gov/statfacts/html/clyl.html
6. Shadman, M. (2023). Diagnosis and Treatment of Chronic Lymphocytic Leukemia. JAMA, 329(11), 918. https://doi.org/10.1001/jama.2023.1946
7. Sobczyńska-Konefał, A., Jasek, M., Karabon, L., & Jaskuła, E. (2024). Insights into genetic aberrations and signalling pathway interactions in chronic lymphocytic leukemia: from pathogenesis to treatment strategies. Biomarker Research, 12(1). https://doi.org/10.1186/s40364-024-00710-w