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Silent but significant: Asymptomatic chronic lymphocytic leukemia in a young adult presenting with leukocytosis and radiologic lymphadenopathy

Abstract

Background: Chronic Lymphocytic Leukemia (CLL) represents the most prevalent adult leukemia in Western populations, with a median age at diagnosis of approximately 70 years. The disease is exceptionally rare in patients under 40 years of age, and such presentations are frequently under-recognized in clinical practice. This case report presents a comprehensive analysis of CLL diagnosed in a 34-year-old male patient with significant lymphocytosis and extensive radiologically confirmed nodal involvement.

Case presentation: A 34-year-old asymptomatic male was referred for hematologic evaluation following the incidental discovery of persistent leukocytosis during a routine health screening examination. Laboratory investigations revealed a white blood cell count of 31,500/µL with lymphocytes comprising 83.3% of the differential. Peripheral blood smear examination demonstrated lymphocytosis with atypical lymphocytes exhibiting mature nuclear chromatin and characteristic smudge cells. Comprehensive flow cytometric immunophenotyping confirmed a clonal B-cell population expressing CD19, CD20, CD5, CD23, and CD200 with lambda light chain restriction, findings pathognomonic for CLL. Contrast-enhanced computed tomography imaging demonstrated extensive mesenteric, retroperitoneal, and inguinal lymphadenopathy, along with borderline splenomegaly.

Molecular risk stratification through next-generation sequencing did not reveal pathogenic mutations, and conventional karyotyping showed a normal 46, XY chromosomal complement. Given the absence of treatment indications per international guidelines, the patient was managed conservatively with active surveillance.

Conclusion: This case illustrates an uncommon presentation of CLL in a young adult with extensive nodal involvement but no constitutional symptoms. It highlights the critical diagnostic value of flow cytometry in evaluating unexplained lymphocytosis and reinforces the principle that even extensive radiological findings do not necessarily mandate immediate therapeutic intervention in early-stage, asymptomatic CLL when appropriate risk stratification is performed.

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Introduction

Chronic Lymphocytic Leukemia (CLL) is a clonal lymphoproliferative disorder characterized by the accumulation of mature-appearing CD5-positive B lymphocytes in the peripheral blood, bone marrow, and secondary lymphoid tissues [1,2]. The disease represents the most common adult leukemia in Western countries, accounting for approximately 25-30% of all leukemia cases in this demographic [3]. The pathogenesis of CLL involves a complex interplay of genetic alterations, dysregulated apoptosis, and aberrant microenvironmental signaling that promotes malignant B-cell survival and proliferation [4].

The epidemiology of CLL demonstrates a striking age predilection, with the median age at diagnosis ranging from 70 to 72 years in population-based studies [5]. The incidence rises dramatically with advancing age, with approximately 70% of patients diagnosed after age 65 years. CLL is distinctly uncommon in individuals under 40 years of age, representing less than 5% of all cases, and extremely rare in patients younger than 35 years, accounting for fewer than 1% of diagnoses [6].

This age-related distribution has significant implications for both diagnostic awareness and long-term management considerations in younger patients.

The clinical presentation of CLL is remarkably heterogeneous, ranging from asymptomatic disease discovered incidentally on routine blood counts to advanced-stage disease with significant cytopenias, massive lymphadenopathy, and constitutional symptoms [7,8].

The Rai and Binet staging systems, developed in the 1970s and 1980s respectively, remain the cornerstone of clinical staging and provide important prognostic information. The Rai system classifies patients into five stages (0-IV) based on the presence of lymphocytosis, lymphadenopathy, hepatosplenomegaly, and cytopenias, while the Binet system categorizes patients into three stages (A-C) based on the number of involved lymphoid regions and the presence of anemia or thrombocytopenia [7,8].

Contemporary CLL management has been transformed by the integration of molecular prognostication into clinical decision-making.

The Immunoglobulin Heavy Chain Variable region (IGHV) mutation status represents one of the most powerful predictors of clinical outcome, with mutated IGHV associated with indolent disease course and prolonged survival compared to unmutated IGHV [9,10].

Cytogenetic abnormalities detected by Fluorescence in Situ Hybridization (FISH), particularly del(17p) and TP53 mutations, identify high-risk populations with inferior responses to chemoimmunotherapy and shorter progression-free survival [11]. The International Prognostic Score for Early-stage CLL (IPS-E) provides refined risk stratification for patients with early-stage disease, incorporating IGHV mutation status, absolute lymphocyte count, and palpable lymphadenopathy to predict treatment probability at one and five years [6].

Treatment decisions in CLL are guided by the presence of active disease as defined by the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria, which include progressive marrow failure, massive or progressive lymphadenopathy, symptomatic splenomegaly, constitutional symptoms, autoimmune complications, and recurrent infections [1].

The emergence of targeted therapies, including Bruton Tyrosine Kinase (BTK) inhibitors and BCL-2 antagonists, has fundamentally altered the therapeutic landscape, offering highly effective treatment options with improved safety profiles compared to traditional chemoimmunotherapy [12,13].

We present a case of CLL diagnosed in a 34-year-old asymptomatic male with extensive radiologic lymphadenopathy, emphasizing the diagnostic approach, risk stratification, and management considerations specific to young-onset CLL. This case underscores the importance of maintaining diagnostic vigilance for hematologic malignancies even in young, asymptomatic patients with incidentally discovered lymphocytosis.

Case presentation

Initial presentation and clinical evaluation

A 34-year-old male was referred to the hematology clinic following the incidental discovery of leukocytosis during a routine annual health examination. The patient was entirely asymptomatic, with no reported history of fever, night sweats, unintentional weight loss, fatigue, or recurrent infections.

He denied any personal history of malignancy, autoimmune disease, or significant medical comorbidities. There was no family history of hematologic malignancies. The patient was a non-smoker with occasional alcohol consumption and worked in an administrative capacity.

Physical examination revealed a well-appearing young adult in no apparent distress. Vital signs were stable and within normal limits. Comprehensive lymph node examination demonstrated no clinically palpable cervical, supraclavicular, axillary, or inguinal lymphadenopathy. Abdominal examination revealed no hepatosplenomegaly on palpation. The remainder of the physical examination was entirely unremarkable.

Laboratory investigations

Initial complete blood count demonstrated a markedly elevated white blood cell count of 31,500/μL (reference range: 4,000-11,000/μL) with an absolute lymphocyte count of 26,240/μL.

The differential count revealed lymphocytes comprising 83.3% of the total leukocyte population. Hemoglobin was 15.1 g/dL (reference range: 13.5-17.5 g/dL) and platelet count was 190×10^9/L (reference range: 150-400$\times10^9$/L), both within normal limits. Lactate dehydrogenase was 153 U/L (reference range: 125-220 U/L), and β_2-microglobulin was elevated at 1,930 ng/mL (reference range: 1,010-1,730 ng/mL). Infectious workup including Epstein-Barr virus and cytomegalovirus quantitative polymerase chain reaction testing was negative.

Peripheral blood smear examination demonstrated absolute lymphocytosis with predominantly small, mature-appearing lymphocytes exhibiting dense chromatin and scant cytoplasm. Characteristic smudge cells (Gumprecht shadows) were identified, representing mechanically fragile lymphocytes disrupted during slide preparation. Atypical lymphocytes with irregular nuclear contours were also observed. No blast forms were identified.

Table 1: Summary of laboratory findings at diagnosis.

Parameter	Value
White blood cell count	31,500 /µL
Lymphocyte percentage	83.3%
Absolute lymphocyte count	26,240 /µL
Hemoglobin	15.1 g/dL
Platelet count	190 × 10^9/L
Lactate dehydrogenase	153 U/L
β_2-Microglobulin	1,930 ng/mL

Summary of key laboratory findings at diagnosis demonstrating marked lymphocytosis with preserved hemoglobin and platelet counts.

Flow cytometric immunophenotyping

Comprehensive flow cytometric immunophenotyping of peripheral blood was performed using a standardized chronic lymphoproliferative disorder panel. Analysis revealed that 55.1% of total leukocytes represented a clonal B-cell population with the following immunophenotypic profile: positive for CD19, CD20 (dim), CD5, CD23, and CD200; negative for CD10, FMC-7, CD25, and CD38. Light chain analysis demonstrated lambda light chain restriction with a kappa-to-lambda ratio of 0.3.

The immunophenotypic pattern (CD5+, CD23+, CD200+, CD10-, FMC-7-, dim CD20) is diagnostic of CLL with a Matutes score of 5, effectively excluding other B-cell lymphoproliferative disorders including mantle cell lymphoma, follicular lymphoma, and marginal zone lymphoma [14].

Cytogenetic and molecular analysis

Conventional G-banded karyotype analysis of bone marrow aspirate demonstrated a normal male chromosomal complement of 46, XY in all metaphases examined. Fluorescence in situ hybridization analysis for common CLL-associated abnormalities including del(13q), del(11q), del(17p), and trisomy 12 was negative.

Next-generation sequencing analysis of a comprehensive CLL-focused gene panel did not detect pathogenic mutations in TP53, SF3B1, NOTCH1, ATM, or other recurrently mutated genes. IGHV mutation status analysis revealed an unmutated IGHV sequence with 100% germline homology, placing the patient in the prognostically unfavorable unmutated IGHV category.

Radiologic evaluation

Contrast-enhanced computed tomography of the chest, abdomen, and pelvis was performed for comprehensive staging evaluation. The imaging revealed multiple enlarged, homogeneously enhancing lymph nodes distributed throughout multiple anatomic regions.

In the abdomen and pelvis, enlarged lymph nodes were identified in the mesenteric, retroperitoneal, periportal, peripancreatic, perigastric, aortocaval, paracaval, retrocaval, and bilateral inguinal regions. The largest lymph node in the right colic region measured 16.6×19.8 mm, while the largest para-aortic node measured 13.3×19.6 mm. The spleen demonstrated borderline enlargement with a craniocaudal dimension of 11.8 cm (upper limit of normal approximately 11 cm). No hepatomegaly or ascites was present.

Chest computed tomography demonstrated multiple enlarged lymph nodes in the bilateral axillary and mediastinal regions. The largest left axillary lymph node measured 18×12 mm, while the largest right axillary node measured 12×14 mm. A right lower paratracheal lymph node measured 5.4×6.4 mm. The lungs were clear without evidence of consolidation, nodules, or ground-glass opacities.

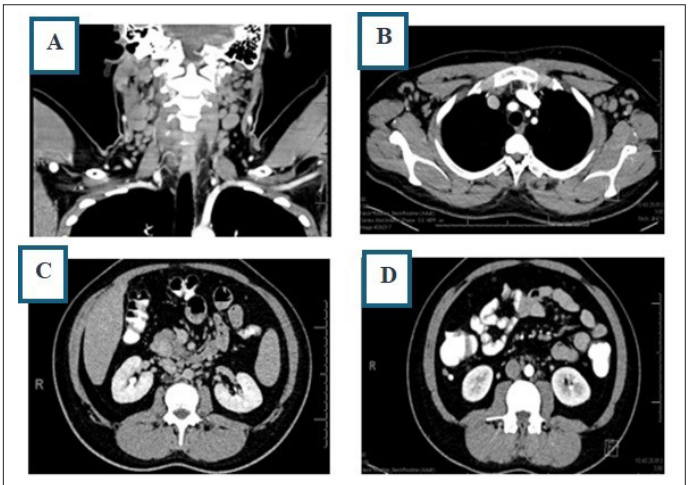

Figure 1: Contrast-enhanced CT imaging demonstrating extensive lymphadenopathy. **(A)** Coronal view of the neck and upper chest showing cervical lymphadenopathy. **(B)** Axial chest CT demonstrating bilateral axillary and mediastinal lymph nodes. **(C)** Axial abdominal CT showing mesenteric lymphadenopathy. **(D)** Axial abdominal CT demonstrating retroperitoneal lymphadenopathy.

Diagnosis and risk stratification

Based on the integration of clinical, laboratory, immunophenotypic, and radiologic findings, a diagnosis of Chronic Lymphocytic Leukemia was established. The patient was classified as Rai Stage II (lymphocytosis with lymphadenopathy) and Binet Stage B (three or more lymph node regions involved without anemia or thrombocytopenia).

Risk stratification using the IPS-E scoring system identified two adverse risk factors: unmutated IGHV status and absolute lymphocyte count greater than 15,000/µL, placing the patient in the high-risk category with an estimated 14% probability of requiring treatment at one year and 61% at five years [6].

Management and follow-up

Despite radiologic evidence of extensive lymphadenopathy involving multiple anatomic regions, the patient remained entirely asymptomatic with preserved hematologic function and normal hemoglobin and platelet counts. Repeat complete blood count performed four weeks after initial evaluation demonstrated stable white blood cell count without evidence of progressive lymphocytosis. In accordance with current international guidelines, the patient did not meet criteria for treatment initiation per iwCLL or National Comprehensive Cancer Network (NCCN) criteria [1,15].

The patient was counseled regarding the diagnosis, natural history of CLL, and the rationale for active surveillance. A comprehensive management plan was established including observation with regular follow-up every two to three months with complete blood count monitoring, physical examination for assessment of lymphadenopathy and splenomegaly, and periodic imaging if clinically indicated. The patient was educated

regarding symptoms requiring prompt medical attention, including fever, night sweats, weight loss, rapid increase in lymph node size, or signs of infection.

Given the young age at diagnosis and unmutated IGHV status, close monitoring was emphasized with consideration of early intervention should disease progression occur.

Discussion

Epidemiology and clinical features of young-onset CLL

The presentation of CLL in a 34-year-old individual represents a distinctly uncommon clinical scenario that warrants particular attention to both diagnostic and management considerations. Population-based registries consistently demonstrate that CLL is predominantly a disease of older adults, with incidence rates rising exponentially after age 60 and peaking in the eighth decade of life [5]. Young-onset CLL, variably defined as diagnosis before age 40 or 50 years, accounts for only 2-5% of all cases, with patients under 35 years representing an even smaller fraction of the total CLL population [6,16].

Despite its rarity, young-onset CLL exhibits several distinctive characteristics that differentiate it from typical presentations in older adults.

Younger patients are more likely to present with asymptomatic disease discovered incidentally during routine health evaluations, as exemplified by the current case [16].

The frequency of incidental diagnosis in young patients may reflect higher rates of health screening engagement and the lower threshold for diagnostic suspicion for malignancy in this demographic. Additionally, young patients tend to present with earlier Rai and Binet stages, potentially reflecting earlier detection rather than inherently different disease biology.

The clinical, morphologic, and immunophenotypic features of CLL in young adults are generally similar to those observed in older patients. The characteristic immunophenotypic profile of CD5+, CD23+, CD200+, dim CD20+ with light chain restriction is consistently observed across age groups, underscoring the diagnostic utility of flow cytometry regardless of patient age [14]. However, the differential diagnosis of lymphocytosis in young adults is broader than in older individuals and includes reactive processes related to viral infections, particularly Epstein-Barr virus and cytomegalovirus, which must be excluded through appropriate serologic and molecular testing.

Prognostic implications of IGHV mutation status

The IGHV mutation status represents one of the most powerful and clinically validated prognostic markers in CLL, with implications that extend across the disease spectrum from initial risk stratification to treatment selection [9,10]. The presence of somatic hypermutation in the immunoglobulin variable region genes, defined as greater than 2% deviation from germline sequence, identifies patients with mutated IGHV who typically experience an indolent disease course with prolonged survival even without treatment. Conversely, patients with unmutated IGHV, as demonstrated in the current case, have a more aggressive clinical course with shorter time to first treatment and inferior overall survival.

The biological basis for the prognostic significance of IGHV mutation status relates to the ontogeny of the leukemic clone. Mutated IGHV suggests origin from post-germinal center B cells that have undergone antigen-driven selection and somatic hypermutation, whereas unmutated IGHV indicates derivation from naive B cells with limited antigen exposure [4].

This distinction has profound implications for disease behavior, with unmutated CLL demonstrating greater proliferative capacity, enhanced B-cell receptor signaling, and increased resistance to apoptosis.

In the context of young-onset CLL, IGHV mutation status assumes particular importance given the extended anticipated survival and the potential for multiple lines of therapy over the disease course.

Young patients with unmutated IGHV, as in the current case, require particularly close monitoring and may benefit from earlier intervention if disease progression is documented. The integration of IGHV status into the IPS-E scoring system provides a framework for risk stratification that can inform surveillance intensity and patient counseling [6].

Molecular and cytogenetic risk stratification

Contemporary CLL management relies heavily on molecular and cytogenetic characterization to inform prognosis and guide treatment selection.

Fluorescence in situ hybridization analysis for recurrent chromosomal abnormalities has established a hierarchical risk stratification model, with del(17p) and TP53 mutations conferring the highest risk, followed by del(11q), normal karyotype/trisomy 12, and del(13q) as the most favorable abnormality [11]. The absence of detectable cytogenetic abnormalities in the current case, while generally associated with intermediate prognosis, does not negate the adverse prognostic impact of unmutated IGHV status.

Next-generation sequencing has expanded our understanding of the mutational landscape of CLL, identifying recurrent mutations in genes involved in DNA damage response (TP53, ATM), RNA splicing (SF3B1), and cell signaling (NOTCH1, BIRC3) [17]. These mutations can refine prognostication beyond FISH-based risk stratification and may have implications for treatment selection, particularly in the context of novel targeted therapies. The absence of pathogenic mutations in the current case is somewhat reassuring, though the unmutated IGHV status remains the dominant adverse prognostic factor.

The IPS-E score and early-stage risk stratification

The International Prognostic Score for Early-stage CLL (IPS-E) was developed to address the need for refined risk stratification in patients with early-stage disease who do not require immediate treatment [6]. The score incorporates three readily available clinical parameters: unmutated IGHV status, absolute lymphocyte count greater than 15,000/μL, and presence of palpable lymphadenopathy. Patients are categorized into low-risk (no factors), intermediate-risk (one factor), and high-risk (two or three factors) groups with markedly different probabilities of requiring treatment at one and five years.

The current patient was classified as high-risk by IPS-E criteria based on the presence of two adverse factors: unmutated IGHV status and elevated lymphocyte count. This classification carries important implications for clinical management, as high-risk patients have a 14% probability of requiring treatment at one year and 61% at five years [6]. This information facilitates informed patient counseling regarding prognosis and guides

the intensity of surveillance, with high-risk patients warranting more frequent monitoring and lower threshold for intervention if progression is documented.

Treatment indications and the watch-and-wait approach

The management of early-stage, asymptomatic CLL has been revolutionized by the recognition that immediate treatment in the absence of active disease does not improve survival and may expose patients to unnecessary toxicity [18,19]. Current international guidelines, including those from the iwCLL and NCCN, recommend active surveillance for patients who do not meet criteria for treatment initiation [1,15]. These criteria include progressive marrow failure, massive or progressive lymphadenopathy, symptomatic splenomegaly, constitutional symptoms, autoimmune complications, and recurrent infections.

The watch-and-wait approach requires careful patient selection, comprehensive baseline evaluation, and structured follow-up to ensure timely intervention when treatment criteria are met. For young patients with early-stage disease, the psychological impact of a leukemia diagnosis without immediate treatment can be substantial, necessitating thorough patient education and ongoing supportive care [20]. The current patient was counseled extensively regarding the rationale for observation, the natural history of CLL, and symptoms requiring prompt medical attention.

Therapeutic considerations for young-onset CLL

When treatment becomes necessary, young patients with CLL are candidates for the full spectrum of therapeutic options, including chemoimmunotherapy, targeted agents, and cellular therapies. The emergence of Bruton tyrosine kinase inhibitors (ibrutinib, acalabrutinib, zanubrutinib) and the BCL-2 antagonist venetoclax has fundamentally transformed the treatment landscape, offering highly effective regimens with improved safety profiles compared to traditional fludarabine-based chemoimmunotherapy [12,13].

For young patients with unmutated IGHV and high-risk features, the choice between continuous therapy with BTK inhibitors and time-limited therapy with venetoclax-based combinations requires careful consideration of efficacy, toxicity, and patient preferences [21]. Clinical trials have demonstrated that both approaches achieve high rates of deep remission, though long-term follow-up is needed to determine optimal sequencing strategies. The potential for treatment-free remission after fixed-duration venetoclax-based therapy is particularly appealing for young patients who may require multiple lines of treatment over their lifetime.

Long-term considerations and survivorship

Young patients diagnosed with CLL face unique challenges related to the extended anticipated disease course and the potential for multiple treatment exposures over decades. Long-term considerations include fertility preservation, career planning, psychosocial support, and management of treatment-related toxicities [20]. The psychosocial impact of a leukemia diagnosis at a young age should not be underestimated, with many patients experiencing significant anxiety, depression, and uncertainty about the future.

The risk of second malignancies is elevated in CLL patients, reflecting both disease-related immune dysfunction and treatment-related effects [22]. Young patients have a longer cumulative exposure to these risks and require appropriate screening and preventive interventions. Additionally, the potential for disease transformation to aggressive lymphoma (Richter transformation) remains a concern, though the incidence appears lower in young patients compared to older individuals [23].

Familial predisposition and genetic counseling

Familial clustering of CLL has been well-documented, with first-degree relatives of CLL patients having a two- to seven-fold increased risk of developing the disease [24]. While the majority of CLL cases are sporadic, approximately 5-10% occur in familial clusters, and young-onset disease may be more frequently associated with inherited predisposition [25]. Despite extensive research, no single high-penetrance germline mutation has been identified, suggesting that familial CLL risk reflects the combined effects of multiple common genetic variants.

For young patients with CLL, particularly those with a family history of hematologic malignancies, genetic counseling may be appropriate to discuss the implications for family members and the potential for screening. While no established screening protocols exist for at-risk relatives, awareness of the increased familial risk may prompt earlier evaluation of suggestive symptoms or abnormalities in first-degree relatives.

Conclusion

This case report presents a comprehensive analysis of chronic lymphocytic leukemia diagnosed in a 34-year-old asymptomatic male, highlighting several important clinical considerations. The presentation of CLL in young adults, while uncommon, requires heightened diagnostic awareness given the typically indolent and asymptomatic nature of early-stage disease. The incidental discovery of lymphocytosis during routine health screening underscores the importance of appropriate evaluation of persistent hematologic abnormalities, regardless of patient age or symptom status.

The diagnostic approach in this case exemplifies current best practices, incorporating peripheral blood smear examination, comprehensive flow cytometric immunophenotyping, cytogenetic analysis, and molecular profiling to establish diagnosis and risk stratification. The characteristic immunophenotypic profile of CLL, with expression of CD5, CD23, and CD200 and absence of CD10 and FMC-7, provides a reliable means of distinguishing CLL from other lymphoproliferative disorders. The integration of IGHV mutation status into the IPS-E scoring system facilitates refined risk stratification and informs surveillance intensity.

The management approach of active surveillance, despite extensive radiologic lymphadenopathy, aligns with current international guidelines that emphasize the absence of survival benefit from early treatment in asymptomatic patients. The high-risk IPS-E classification, based on unmutated IGHV status and elevated lymphocyte count, mandates close monitoring with regular clinical and laboratory evaluation to ensure timely intervention when treatment criteria are met.

This case reinforces several key principles in the management of young-onset CLL: the importance of maintaining diagnostic vigilance for hematologic malignancies in young patients with unexplained lymphocytosis; the critical role of flow cytometry in establishing the diagnosis and excluding reactive processes; the value of comprehensive molecular and cytogenetic profiling for

risk stratification; and the appropriateness of active surveillance for early-stage, asymptomatic disease even in the presence of extensive nodal involvement.

As the therapeutic armamentarium for CLL continues to expand, the principles of individualized care based on disease biology and patient characteristics remain paramount.

References

1. Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Dohner H, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018; 131: 2745–60.
2. Eichhorst B, Robak T, Montserrat E, Ghia P, Niemann CU, Kater AP, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2021; 32: 23–33.
3. Kipps TJ, Stevenson FK, Wu CJ, Croce CM, Packham G, Wierda WG, et al. Chronic lymphocytic leukaemia. Nature Reviews Disease Primers. 2017; 3: 17008.
4. Chiorazzi N, Rai KR, Ferrarini M. Chronic lymphocytic leukemia. New England Journal of Medicine. 2005; 352: 804–15.
5. Santos T, Gomes P, Ribeiro AC, Coutinho MM, Lopes C, Ribeiro AM. Chronic lymphocytic leukemia: A clinical and molecular approach of a heterogeneous disease. Journal of Clinical Oncology. 2021; 39: 19507.
6. Parikh SA, Rabe KG, Kay NE, Call TG, Ding W, Leis JF, et al. The International Prognostic Score for Early-stage Chronic Lymphocytic Leukemia Identifies Patients with High Risk of Disease Progression in the Era of Novel Targeted Therapies. Blood Cancer Journal. 2021; 11: 1–9.
7. Rai KR, Sawitsky A, Cronkite EP, Chanana AD, Levy RN, Pasternack BS. Clinical staging of chronic lymphocytic leukemia. Blood. 1975; 46: 219–34.
8. Binet JL, Auquier A, Dighiero G, Chastang C, Piguet H, Goasguen J, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer. 1981; 48: 198–206.
9. Hamblin TJ, Davis Z, Gardiner A, Oscier DG, Stevenson FK. Unmutated Ig V(H) genes are associated with a more aggressive form of chronic lymphocytic leukemia. Blood. 1999; 94: 1848–54.
10. Damle RN, Wasil T, Fais F, Ghiotto F, Valetto A, Allen SL, et al. Ig V gene mutation status and CD38 expression as novel prognostic indicators in chronic lymphocytic leukemia. Blood. 1999; 94: 1840–7.
11. Dohner H, Stilgenbauer S, Benner A, Leupolt E, Krober A, Bullinger L, et al. Genomic aberrations and survival in chronic lymphocytic leukemia. New England Journal of Medicine. 2000; 343: 1910–6.
12. Sharman JP, Egyed M, Jurczak W, Skarbnik A, Pagel JM, Flinn IW, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukaemia (ELEVATE-TN): A randomised, controlled, phase 3 trial. The Lancet Oncology. 2022; 23: 1105–18.
13. Fischer K, Al-Sawaf O, Bahlo J, Fink AM, Tandon M, Dixon R, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. New England Journal of Medicine. 2023; 380: 2225–36.
14. Matutes E, Owusu-Ankomah K, Morilla R, Garcia Marco J, Houlihan A, Que TH, et al. The immunological profile of B-cell disorders and proposal of a scoring system for the diagnosis of CLL. Leukemia. 1994; 8: 1640–5.
15. Network NCC. NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. 2024.
16. Mauer C, Hsu M, Geyer SM, Chen T, Liu X, Coignet L, et al. Comprehensive mutational profiling in chronic lymphocytic leukemia: Clinical implications for young patients. Leukemia & Lymphoma. 2014; 55: 1265–72.
17. Landau DA, Tausch E, Taylor-Weiner AN, Stewart C, Reiter JG, Bahlo J, et al. Mutations driving CLL and their evolution in progression and relapse. Nature. 2015; 526: 525–30.
18. Dighiero G, Maloum K, Desablens B, Cazin B, Navarro M, Leblond V, et al. Chlorambucil in indolent chronic lymphocytic leukemia. New England Journal of Medicine. 1988; 338: 1506–14.
19. Oscier DG, Gardiner AC, Mould SJ, Glide S, Davis ZA, Ibbotson RE, et al. Multivariate analysis of prognostic factors in CLL: Clinical stage, IGVH gene mutational status, and loss or mutation of the p53 gene are independent prognostic factors. Blood. 2012; 100: 1177–84.
20. Shanafelt TD, Bowen D, Venkat C, Slager SL, Zent CS, Kay NE, et al. Quality of life in chronic lymphocytic leukemia: An international survey of 1482 patients. British Journal of Haematology. 2007; 139: 255–64.
21. Al-Sawaf O, Zhang C, Tandon M, Robrecht S, Chua C, Bahlo J, et al. Venetoclax plus obinutuzumab versus chlorambucil plus obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL14): Follow-up results from a multicentre, open-label, randomised, phase 3 trial. The Lancet Oncology. 2020; 21: 1188–200.
22. Morton LM, Landgren O, Engels EA. The evolving landscape of HIV-related malignancies: Implications for cancer prevention and treatment. AIDS. 2014; 28: 663–70.
23. Tsimberidou AM, Keating MJ, Bueso-Ramos CE, Kurzrock R, Wierda WG. Clinical outcomes and prognostic factors in patients with Richter's syndrome treated with chemotherapy or chemoimmunotherapy with or without stem-cell transplantation. Journal of Clinical Oncology. 2013; 31: 2349–57.
24. Goldin LR, Bjorkholm M, Kristjansson SY, Turesson I, Landgren O. Highly increased familial risks for specific lymphoma subtypes. British Journal of Haematology. 2010; 146: 86–90.
25. Slager SL, Benavente Y, Blair A, Vermeulen R, Cerhan JR, Costantini AS, et al. Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project. Journal of the National Cancer Institute. 2018; 105: 1041–9.