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Case Report

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Pulmonary nodular infiltration in a young patient with chronic lymphocytic leukaemia and isolated Del (13q): Atypical clinical aggressiveness with typical immunophenotype

Abstract

Chronic lymphocytic leukaemia (CLL) is a mature B-cell neoplasm predominantly affecting older adults and is often diagnosed incidentally. We report a case of a 45-year-old male presenting with severe anaemia, thrombocytopenia, massive lymphadenopathy, and bilateral pulmonary nodular lesions. Peripheral smear, flow cytometry, lymph node biopsy, and lung biopsy confirmed CLL/small lymphocytic lymphoma (SLL) with pulmonary infiltration. Fluorescence in situ hybridisation (FISH) revealed an isolated deletion of chromosome 13q14 in 75% of cells. Due to financial constraints, the patient received rituximab and chlorambucil instead of a Bruton tyrosine kinase inhibitor. Clinical improvement, with reduced lymphadenopathy and symptomatic relief, was observed at subsequent follow-up. This case highlights that typical morphology and immunophenotype may coexist with aggressive clinical features in younger patients and underscores the importance of extended molecular evaluation.

Keywords: chronic lymphocytic leukaemia, Del (13q), pulmonary infiltration, young-onset cll, extranodal involvement

Volume 14 Issue 1 - 2026

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Received: April 24, 2026 | **Published:** May 20, 2026

Introduction

Chronic lymphocytic leukaemia is characterised by monoclonal proliferation of small mature B lymphocytes involving peripheral blood, bone marrow, lymph nodes and spleen. It primarily affects elderly individuals, with a median age at diagnosis in the seventh decade. Younger patients are uncommon and may exhibit distinct biological behaviour. Extranodal pulmonary involvement is rare but clinically significant. We describe a young patient presenting with advanced-stage CLL and pulmonary nodular infiltration despite a typical immunophenotype and isolated Del (13q).

Case presentation

A 45-year-old male presented with a 20-day history of cough and intermittent fever. Examination revealed marked pallor and bilateral cervical lymphadenopathy. Laboratory investigations showed haemoglobin 4.1 g/dL, platelet count 60,000/µL, and absolute lymphocyte count 271 × 10^3/µL. Peripheral smear demonstrated 99% small mature lymphocytes with smudge cells

PET–CT revealed widespread metabolically active lymphadenopathy along with bilateral pulmonary nodules. Flow cytometric immunophenotyping demonstrated dim-to-moderate CD20 expression with positivity for CD19, CD5, CD23, CD43, and CD200, along with light-chain restriction, consistent with a classical CLL immunophenotype (Figure 1). CD10 and CD79b were negative. Lymph node biopsy showed diffuse effacement of nodal architecture by small mature lymphoid cells exhibiting clumped chromatin (Figure 2). Histopathological examination of the lung biopsy revealed diffuse interstitial/parenchymal infiltration by small monomorphic lymphoid cells expanding the alveolar septae. The infiltrating cells exhibited round to mildly irregular nuclei, densely clumped chromatin, inconspicuous nucleoli, and scant cytoplasm, morphologically consistent with small mature lymphocytes. No granulomas, fungal elements, necrosis, or significant acute inflammatory infiltrate were identified. Immunohistochemistry demonstrated diffuse membranous positivity for CD20, co-expression of CD5 and CD23, and nuclear positivity for PAX5 in the infiltrating lymphoid cells. The cells were negative for CD10, Cyclin D1, and BCL6. The Ki-67 proliferation index was low. The overall morphological and immunophenotypic features were consistent with pulmonary infiltration by CLL/SLL (Figure a–c). FISH revealed isolated Del (13q14) in 75% of cells. The patient was classified as Rai stage IV due to severe anaemia and thrombocytopenia. Although infectious etiologies were considered in the differential diagnosis, definitive evidence of infection was not identified clinically, radiologically, or histopathologically. Lung biopsy with immunohistochemistry supported leukemic infiltration by CLL/SLL.

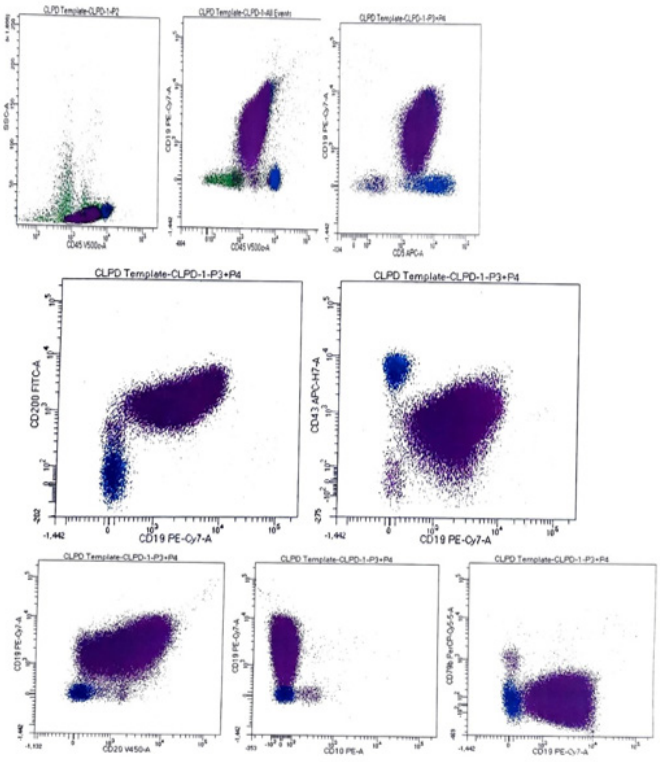

Figure 1 Immunophenotype of CLL showing moderate CD45 & low SSC and dim to moderate CD19 positivity, dim to moderate CD20 positivity & negative for CD10 & CD79b and dim CD 43 & CD200 positivity.

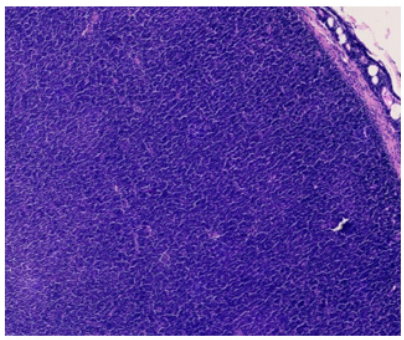

Figure 2 Lung biopsy showing diffuse interstitial infiltration by small mature lymphoid cells.

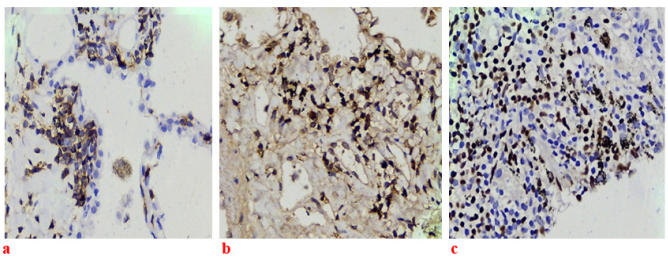

Figure a–c Immunohistochemical staining demonstrates positivity for CD5 (Fig. a), CD20 (Fig. b), and PAX5 (Fig. c) in infiltrating lymphoid cell.

Management and outcome

Considering the advanced-stage disease with pulmonary involvement, targeted therapy with a Bruton tyrosine kinase (BTK) inhibitor was initially considered. However, due to financial constraints, the patient was treated with rituximab and chlorambucil-based chemoimmunotherapy. Rituximab was administered at a dose of 375 mg/m² along with chlorambucil-based therapy for 6 cycles. Response assessment was performed clinically, hematologically, and radiologically. At 3 months of follow-up, the patient demonstrated significant symptomatic improvement, with resolution/reduction of fever and cough, reduction in cervical lymphadenopathy, and improvement in haematological parameters, including an increase in haemoglobin from 4.1 g/dL to 8 g/dL and a improvement in platelet count from 60,000/µL to 1,10,000/µL. Follow-up imaging showed significant reduction in pulmonary nodular lesions and lymphadenopathy, consistent with a favourable treatment response.

Discussion

Chronic lymphocytic leukaemia (CLL) exhibits significant biological and clinical heterogeneity, and the present case highlights a clear clinicopathological discordance wherein classical morphology and immunophenotype coexist with aggressive clinical features, including severe cytopenias and extranodal pulmonary involvement. Although CLL predominantly affects elderly individuals, younger patients represent a distinct subgroup with variable disease behaviour. Studies have shown that patients ≤55 years may present with more advanced-stage disease and require earlier therapeutic intervention despite otherwise favourable baseline characteristics, indicating that younger age does not necessarily predict indolent biology.[1] The current case, presenting at Rai stage IV with marked cytopenias, aligns with this observation.

Pulmonary involvement in CLL is most commonly infectious due to underlying immune dysfunction; however, direct leukemic infiltration, as confirmed in this case by histopathology and immunohistochemistry (CD5, CD20, CD23, PAX5 positivity), is rare and often under-recognised. Radiologically, such lesions may mimic infection or metastasis, making tissue diagnosis essential for accurate characterization.[2] The presence of extranodal disease suggests altered tumor-microenvironment interactions, including dysregulation of chemokine-mediated homing pathways such as CXCR4, which may contribute to a more disseminated and aggressive phenotype.[6]

Cytogenetically, an isolated deletion of chromosome 13q14 is traditionally considered a favourable prognostic marker, particularly when present as a sole abnormality. However, emerging evidence indicates that the prognostic impact of Del (13q) is influenced by the proportion of cells affected. A higher clonal burden has been associated with increased tumour load, advanced clinical stage, and shorter time to first treatment.[3,7] In the present case, the deletion was identified in 75% of cells, which may explain the aggressive clinical presentation despite otherwise favourable cytogenetics, underscoring the limitation of interpreting cytogenetic abnormalities in isolation.

Further complexity arises from the absence of extended molecular profiling. Mutations in genes such as TP53, NOTCH1, SF3B1, ATM, and BIRC3, along with IGHV mutation status, are now recognised as critical determinants of prognosis and therapeutic response.[4,8] In particular, TP53 abnormalities are strongly associated with resistance to conventional chemoimmunotherapy and poor clinical outcomes. The aggressive phenotype observed in this patient raises the

possibility of coexisting high-risk molecular alterations, highlighting the importance of comprehensive genomic evaluation, especially in younger patients with atypical presentations.

The therapeutic landscape of CLL has evolved with the introduction of targeted agents such as Bruton tyrosine kinase inhibitors, which have demonstrated superior efficacy across risk groups.[5,9,10] Current international guidelines recommend assessment of TP53 aberrations, IGHV mutation status, and molecular risk stratification prior to initiation of therapy, as these biomarkers significantly influence prognosis and therapeutic selection.[11,12] However, in resource-limited settings, access to these therapies remains constrained. The use of rituximab combined with chlorambucil in this case reflects a pragmatic approach, and the observed clinical improvement supports its continued relevance as an alternative in such contexts, although long-term outcomes may be inferior compared to targeted therapies. Contemporary treatment guidelines increasingly favour targeted agents such as BTK inhibitors and BCL2 inhibitors over conventional chemoimmunotherapy, particularly in patients with high-risk molecular features.[11,13]

Overall, this case underscores the need for an integrated diagnostic and prognostic approach in CLL that incorporates clinical staging, quantitative cytogenetics, and molecular profiling. It also emphasises that younger age and favourable cytogenetic findings do not preclude aggressive disease, and that extranodal involvement, such as pulmonary infiltration, although rare, should be considered in the differential diagnosis of atypical radiological findings. Given the inherent limitations of a single case report, the present findings should be interpreted cautiously. Nevertheless, the case highlights a potential association between high-burden isolated Del (13q), younger age, and aggressive extranodal disease, which may warrant further investigation in larger cohorts.

Learning points

- CLL can present aggressively in younger patients despite a typical immunophenotype.
- Pulmonary nodular lesions may represent leukemic infiltration rather than infection.
- High-percentage isolated Del (13q) may not always indicate indolent behaviour.
- Extended molecular profiling is recommended in clinically discordant cases.

Conclusion

Young age and aggressive clinical presentation may rarely coexist with classical immunophenotypic and cytogenetic features of CLL. This case highlights the importance of comprehensive molecular evaluation in clinically discordant presentations and serves as a hypothesis-generating observation requiring validation in larger cohorts.

Author contributions

Dr Seema Acharya: Concept, supervision, analysis, critical revision.

Dr Saqib Ahmed: Concept, supervision, drafting, analysis, critical revision

Dr Sanjhali Singh: Concept, manuscript drafting

Dr Rachit Ahuja: Clinical correlation, data acquisition.

Acknowledgements

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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