## *HemeImage*

# T Prolymphocytic Leukemia Lacking Surface CD3 Expression

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A 65-year-old male presented initially with asymptomatic peripheral lymphocytosis in December 2022 (White blood count: 17.9 x $10^9$ cells/L, absolute lymphocyte count: 10.0 x $10^9$ cells/L). Peripheral blood smear revealed a subset of lymphocytes appearing small to medium sized with variably round-indented contours, coarsely clumped chromatin, and small nucleoli. The cytoplasm was somewhat basophilic with peripheral blebs (Figure 1A).

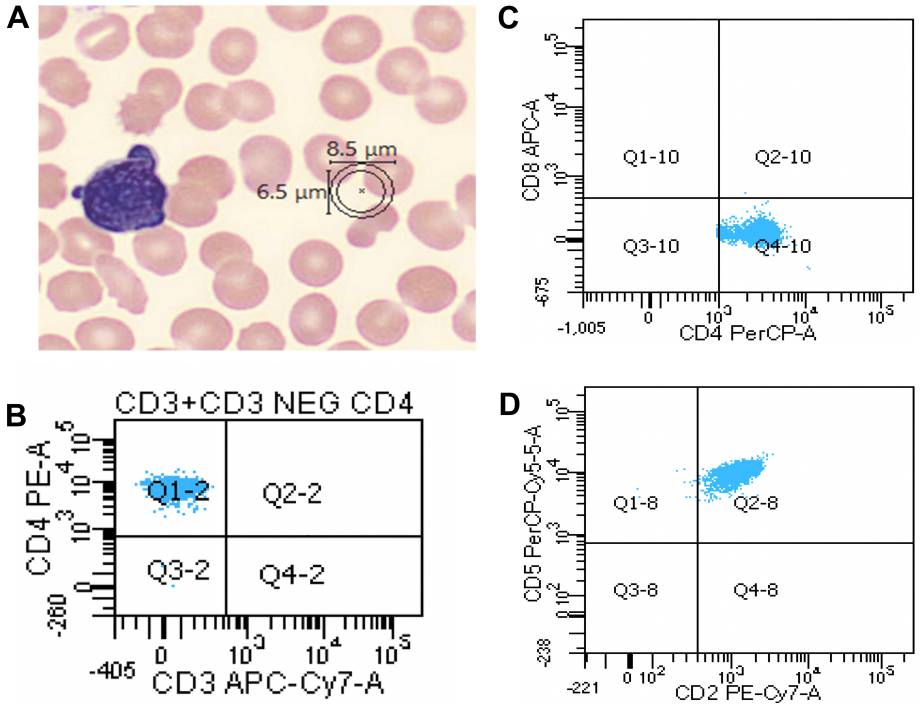


**Figure 1: Peripheral smear**. (A) A small to medium sized lymphocyte with course chromatin, irregular nuclear membranes, and peripheral blebs, consistent with the morphology of T prolymphocytic leukemia (May-Grünwald-Giemsa stain x1000 magnification). Flow cytometry of the peripheral blood revealed these cells to be sCD3-/CD4+ T cells (B). They were negative for CD8 (C), positive for CD5 and CD2 (D).

Flow cytometry on the peripheral blood showed a T-cell population (comprising of approximately 30% of events) that was positive for CD2, CD4, CD5, CD7, CD25, CD26, CD45 and negative for surface CD3 (sCD3), CD1a, CD8, CD10, CD16, CD34, CD56, CD57, TCR$\alpha/\beta$ and TCR$\gamma/\delta$ (Figure 1B-D). T-cell

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clonality study was positive. Right neck lymph node biopsy showed diffuse paracortical infiltration and attenuation of germinal centres by neoplastic lymphocytes (Figure 2A). These cells showed a small to medium sized morphology with irregular hyperchromatic nuclei and occasional nucleoli (Figure 2B). Immunohistochemical staining of these cells showed the following pattern: Positive for cCD3, CD2, CD4, CD5, TCR$\beta$ (BF1), CD43 and PD-1 (CD279), and negative for CD30, CD56, CD8, CD20. CD10, PAX5, TCR$\gamma$, TIA-1, CXCL13, ICOS, Granzyme B and TdT (Figure 2C-G). The flow cytometric analysis of the lymph node showed a similar immunophenotype to what was described before in the blood smear. FISH studies done on the lymph node showed 40% of nuclei with *TCL1A* rearrangement (14q11.2) in 50% of the nuclei and a *TRAD* rearrangement (14q32) in 31% of nuclei (Figure 2H). The combination of both indicate either an inv(14) or t(14:14). These rearrangements confirmed the diagnosis of T prolymphocytic leukemia. CD52 testing on flow cytometry was positive. He remained in the dormant phase of this disease until Feb 2023 (14 months) were he progressed and was started on Alemtuzumab and his disease has been controlled up until this report.

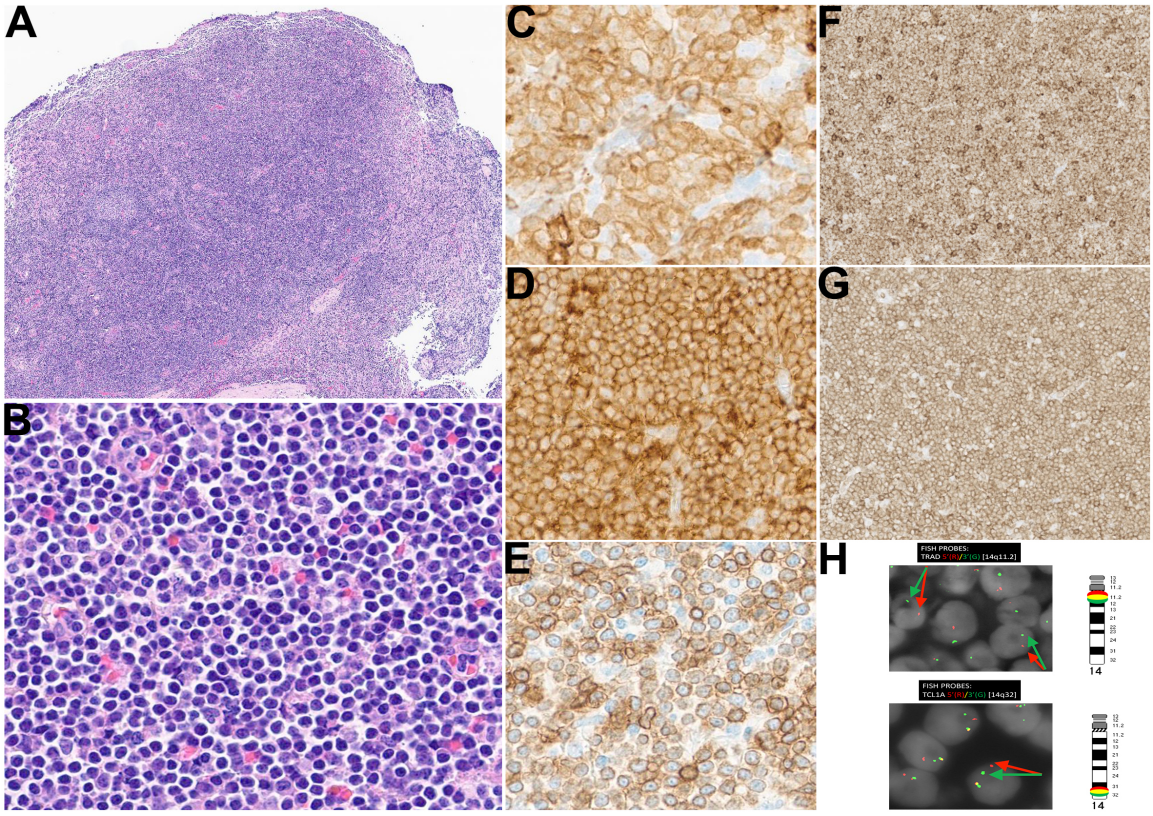


**Figure 2: Lymph node**. (A) Diffuse paracortical involvement of lymph node by neoplastic lymphocytes while showing the interface between preserved and attenuated germinal centres (H&E, 40x magnification). The lymphocytes were monomorphic exhibiting a small to medium size morphology with irregular nuclear membranes and occasional prominent nucleoli (B, H&E, 400x magnification). These lymphocytes were positive for cytoplasmic CD3 (C), CD4 (D), TCR$\beta$ (E) (400x magnification), CD2 (F) and CD5 (G) (100x magnification). FISH results showing *TRAD* and *TCL1A* separation are demonstrated in (H).

T prolymphocytic leukemia (T-PLL) is a rare, aggressive type of T-cell leukemia, with a median survival

of 1.4 years [1]. The disease is characterized by proliferation of post-thymic T-lymphocytes with a small to medium-sized morphology and a mature T-cell immunophenotype. As T cells mature from the pre-thymic phase to the post-thymic stage, CD3 expression changes from cytoplasmic to surface [2]. While T-PLL typically shows a mature T-cell immunophenotype, our case demonstrated a lack of sCD3 expression. This can potentially be confused with T acute lymphoblastic leukemia (T-ALL), which shows an immature T-cell immunophenotype with cytoplasmic CD3 expression and absent sCD3 [3]. Utilizing immaturity immunohistochemical markers like TdT and CD1a can help distinguish both diseases [4]. Moreover, sCD3-/CD4+ cells in the setting of mature T-cell lymphomas have been described in angioimmunoblastic T-cell lymphoma [5]. Testing for *RHOA* p.G17V mutations can be helpful in this case [4]. While sCD3 negative T-PLL is uncommon, our case emphasizes the importance of recognizing this unusual immunophenotype for this aggressive disease as it can potentially pose diagnostic hurdles, especially in patients presenting initially with clinically indolent disease [6]. In such cases, a high index of suspicion is warranted and emphasis on combining all diagnostic modalities is crucial to reach a diagnosis.

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