Case report

Unveiling T- Cell Prolymphocytic Leukaemia: A Case study highlighting diagnostic markers and challenges.

Abstract

T-PLL is a rare T cell Chronic Lymphoproliferative disorder (T-CLPD), representing about 2% of mature lymphocytic leukaemia in adults over 30, with a median diagnosis age of 65. It commonly presents with symptoms like hepatosplenomegaly, generalized lymphadenopathy, and occasionally skin infiltration or serous effusion.

The subject, a 40- year-old male, presented with symptoms such as high white blood cell counts, anemia, lymphadenopathy, and hepatosplenomegaly. Flow cytometric immunophenotyping of peripheral blood revealed specific markers consistent with T-PLL, including expression patterns for CD markers (CD2, CD3, CD4, CD5, CD7, CD8) and strong positivity for CD38, indicative of T-cell activation. The diagnosis utilized flow cytometry to identify T-PLL's characteristic CD marker profile, notably CD4+/CD8- in most cases, with rare co-expression of CD4 and CD8.

The findings aligned with the known features of T-PLL, including mature T- cell immunophenotype, typically CD2+, CD5+, CD7+, and CD16-, and emphasized flow cytometry' role in improving diagnosis accuracy. It concludes that the observed dim to negative surface CD3 expression is compatible with T-PLL.

Key words: Flow cytometry immunophenotyping, T-cell prolymphocytic leukaemia, T-PLL, T-CLPD

Introduction

T-cell prolymphocytic leukemia (T-PLL) is an extremely rare T- Cell Chronic Lymphoproliferative disorder,accounting for approximately 2% of cases of mature lymphocytic leukaemias in adults aged > 30 years(1). And the median patient age is 65 years. It is very uncommon among young individuals aged less than 30 years. It is characterized by the proliferation of small to medium- sized prolymphocytes with a mature post-thymic T- cell phenotype, involving the peripheral blood, bone marrow(2,3).

Most patients present with hepatosplenomegaly and generalized lymphadenopathy.Skin infiltration is seen in 20% of cases, and serous effusions in a minority(4). Absolute lymphocytosis is common in peripheral blood and bone marrow (often more than 100 $\times 10^3/\mu L$)(5). Most patients present with thrombocytopenia and anemia. A predominance of small to medium- sized lymphoid cells with non- granular basophilic cytoplasm; round, oval, or markedly irregular nuclei, and visible nucleoli are seen in the peripheral blood films.

The diagnosis of T-PLL is difficult to make on the basis of peripheral blood and bone marrow histology alone.Flowcytometry immunophenotyping (FCI) plays an important role in the detection of T-PLL. Characteristic expression of Cluster of Differentiation (CD) markers is a key factor that involving accurate diagnosis of T-PLL.

Peripheral T Lymphocytes in T-PLL are Terminal deoxynucleotidyl transferase (TDT) negative(6). And they are usually positive for CD2, CD5, CD3, and CD7; the surface membrane expression of CD3 may be weak(2).

In 60% of cases of T- PLL, the T cells are CD4 positive and CD8 negative in expression. In 25% cases, they coexpress CD4 and CD8.The other 15% of cases are CD4negative and CD8 positive(2).This is typically aggressive malignancy, with a median survival of 1- 2 years.

The aim of this case study was to describe an extremely rare case of T- PLL with the flowcytometry immunophenotyping pattern.

Case report

This report was of a 40-year-old male patient. He was admitted to the Sri Jayewardenepura GeneralHospital, Colombo, Sri Lanka with the history of rapidly increasing leucocytosis, anemia, generalized lymphadenopathyand hepatosplenomegaly. Full Blood Count (FBC) andimmunophenotyping by flowcytometry were requested.

Investigations of peripheral blood revealed White Blood Cells (WBC) of $154\times10^3/\mu L$, platelet count of $19\times10^3/\mu L$, absolute count of lymphocytesis $138.6\times10^3/\mu L$ (90%).

Many atypical lymphoid cells characterized bysmall to medium cells with relativelyclumped chromatin and small nucleoli were noted in the stained blood film. Smudge cells were also

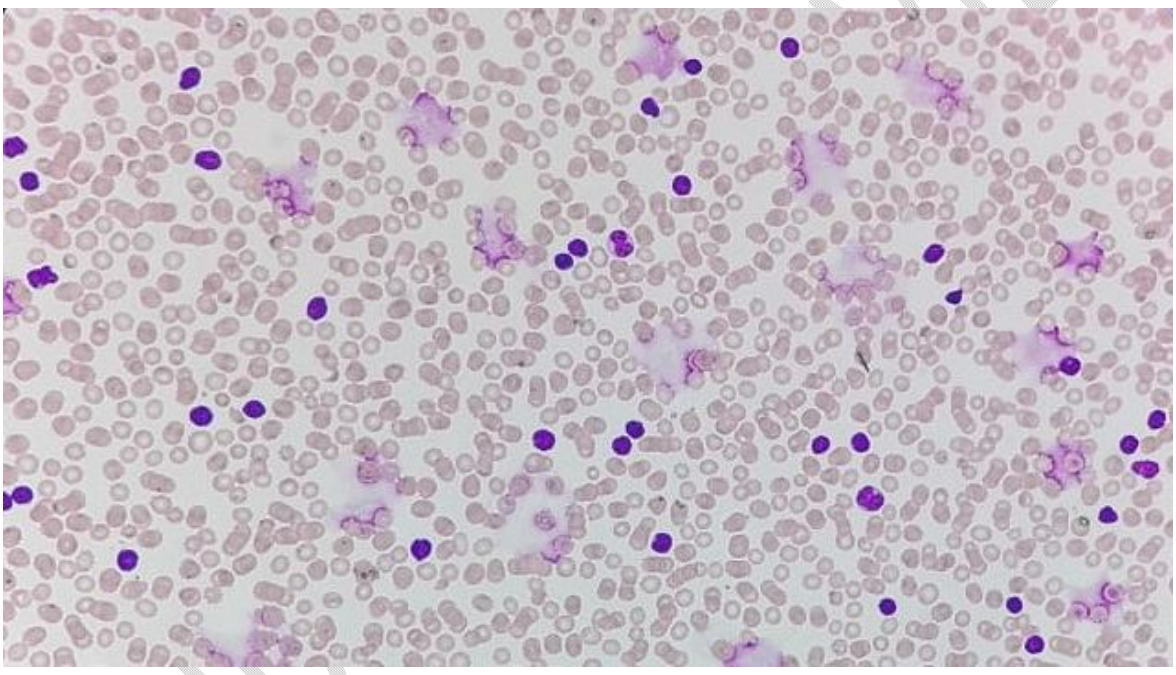

Figure 1: Morphology of peripheral blood (High power)

observed(7).

Live cells were gated by CD45 andtwo distinct populations as lymphocytes andgranulocytes were identified. Lymphocytes weregated by smCD3 and CD19.

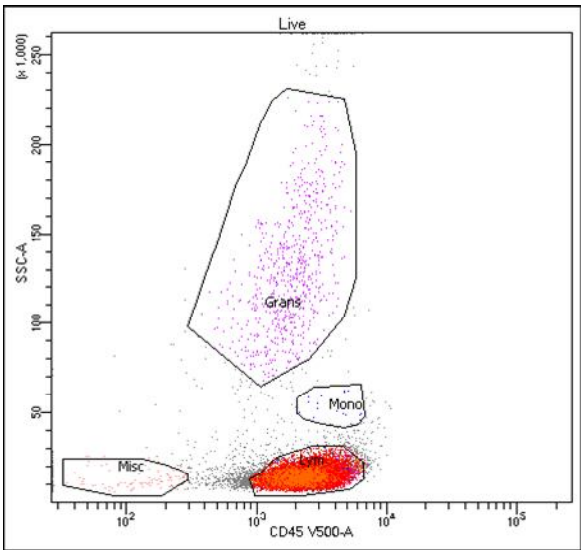

Figure 2: CD45 gated cells

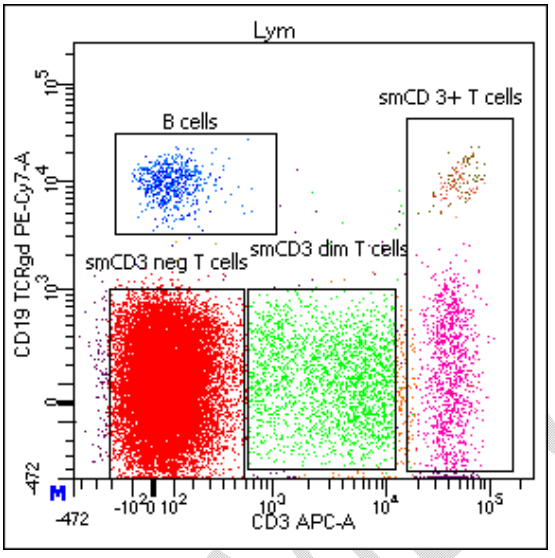

Figure 3: CD3, CD19, TCRgd gated lymphocytes

CD45 gated lymphoid cells (92.2%) revealed a non-clonal B cell population of 2.6% with anormal NK cell population of 2%.

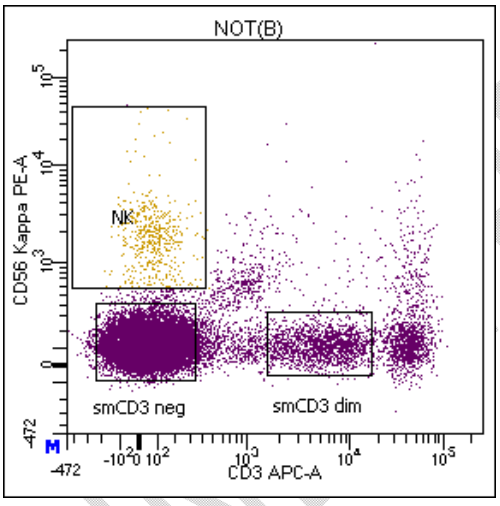

Figure 4: CD3, CD56 gated T cells and NK cells

T cell population revealed,a small population of smCD3 positive cells (4%) with TCR αβ expression,positive panT cell antigens & positive CD4, CD8 expression.

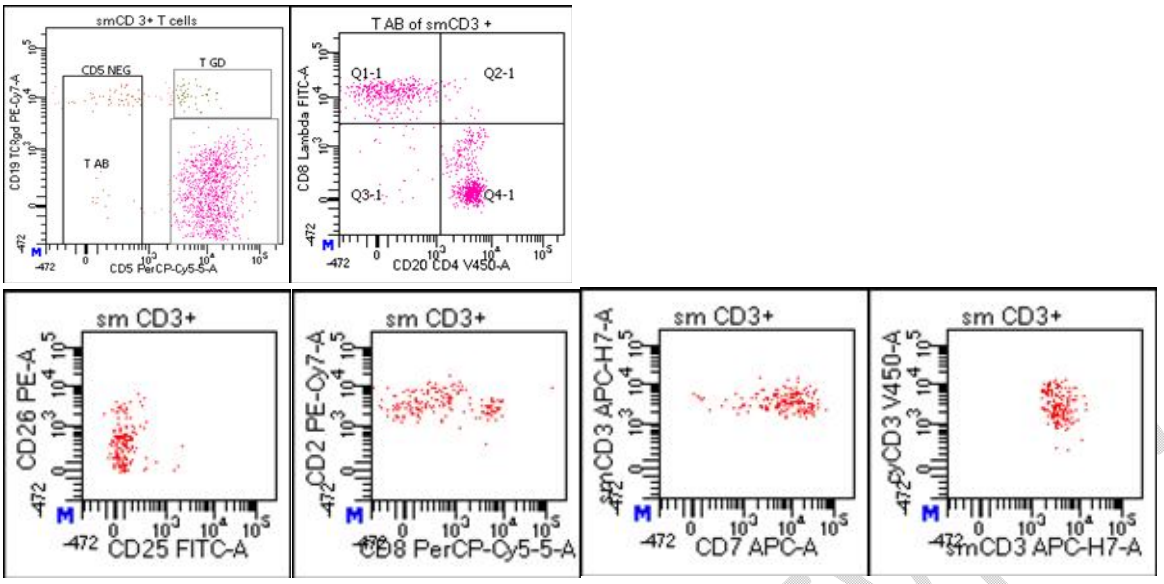

Figure 5: CD markers expression of smCD3 positive T cells

A population of T cells(6%) showed, dim positivity for smCD3 with TCR αβ expression, positive expression for CD2, CD5, CD7, CD4 & dim expression of CD8.

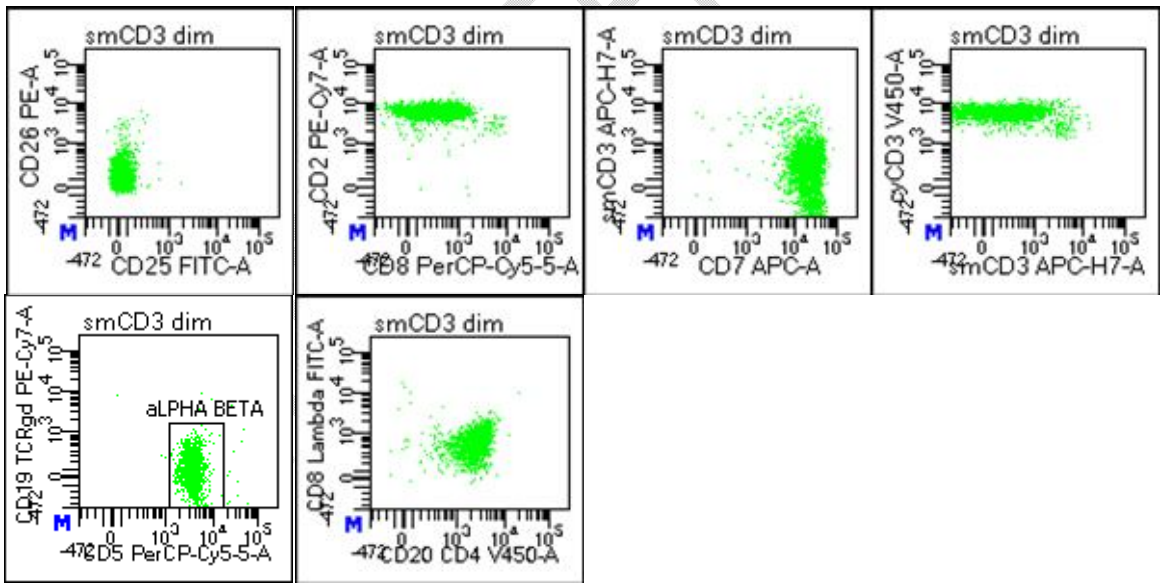

Figure 6: CD markers expression of smCD3 dim positive T cells

Strong positivity forCD38 noted indicating T cell activation.The larger T cell population of (76%) showed negativity for smCD3 with TCR αβ expression, positive expression for CD2,CD5,CD7,CD4 & dim expression for CD8.

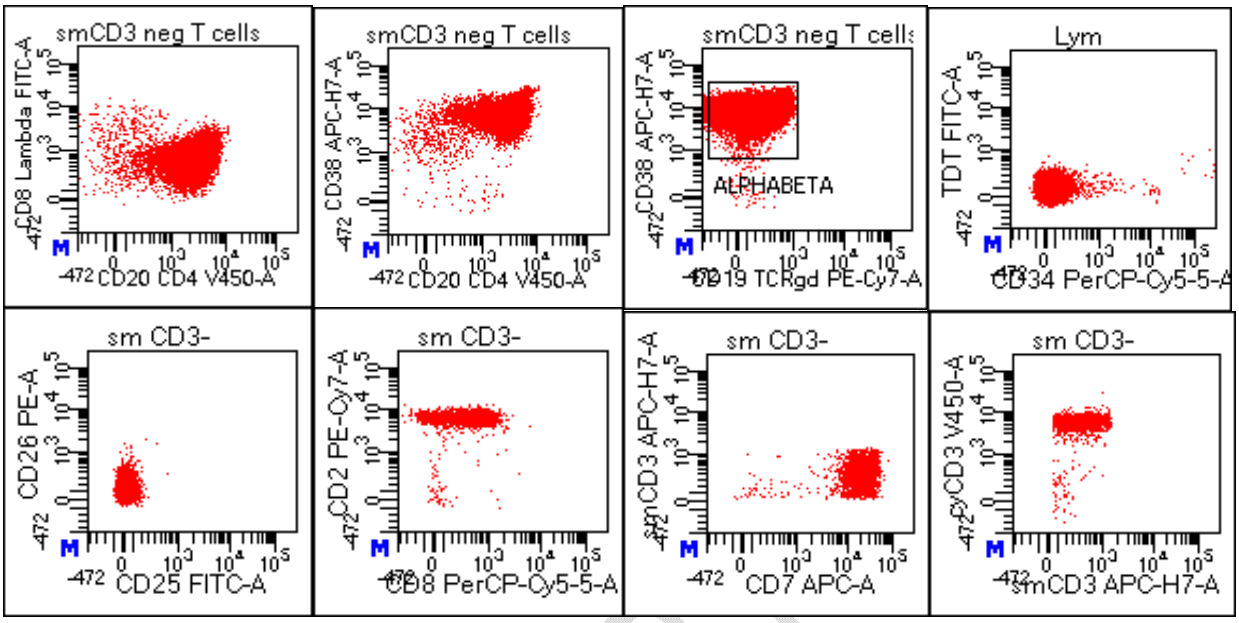

Figure 7: CD markers expression of smCD3 negative T cells

Strong positivity for CD38 noted indicating T cell activation.The total T cell population was positive for cy CD3, negative for CD34 & TDT.

Discussion

In Our study, the T-PLL exhibits a TDT negative, mature T-cell immunophenotype (CD2+, CD5+, CD7+, CD16–, and CD56-) and co-expresses CD4 and CD8.The leukemic lymphocytes are generally CD4+/CD8- in majority of cases and a CD4-/CD8- phenotype has also been reported in very rare cases (8). CD7 is also generally highly expressed. The cells of T-PLL patients are of mostly the TCR αβ phenotype. Only rare cases of TCR γδ expression have been reported (3).

Surface membrane CD3 may be lacking T-PLL cells, but they are always found in the cytoplasm. It causes to the positive of expression cytoCD3.Such cytoCD3 expression can be expected in immature T cells that do not yet express the CD3 antigen on the cell surface membrane (5,9–11).

In T-PLL, markers related to T-cell activation, such as CD25, CD38 may or may not be expressed (12). In our study showed, negative expression of CD25 with bright positivity of CD38. The weak expression ofsurface membrane CD3 and CD45, expression of both CD4 and CD8, and bright expression CD7 suggest that T-cell prolymphocytes might be at an intermediate stage of differentiation between thymic and post-thymic T cells (5).But in our case revealed high CD45 expression and some rare cases have reported with the lower expression of CD45 (12).

T-PLL is a rare disease with a poor prognosis. Flowcytometry has led to better characterization of the cells involved in this disease and cytogenetics and molecular biology have revealed much about its pathophysiology (5).

Conclusion

In keeping with the morphological features and negativity for immature markers, the findingsfavour a diagnosis of T -chronic lymphoproliferative disorder.With dim to negative smCD3 activity more in favours the diagnosis of **T - Prolymphocytic leukaemia**.

References

1. Delgado J, Buston JG, Jimenez MC, Quevedo E, Hernandez-Navarro F. Are activation markers (CD25, CD38 and CD103) predictive of sensitivity to purine analogues in patients with T-cell prolymphocytic leukemia and other lymphoproliferative disorders? Leuk Lymphoma. 2002;43(12):2331–4.

2. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. WHO classification of tumours of haematopoietic and lymphoid tissues, 4th edition (IARC WHO Classification of Tumours, Volume 2). Histopathology. 2017. 417 p.

3. Matutes E, Brito-Babapulle V, Swansbury J, Ellis J, Morilla R, Dearden C, et al. Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. Blood. 1991;78(12):3269–74.

4. Garand R, Goasguen J, Brizard A, Buisine J, Charpentier A, Claisse JF, et al. Indolent course as a relatively frequent presentation in T- prolymphocytic leukaemia. Br J

Haematol. 1998;103(2):488–94.

5. Laribi K, Lemaire P, Sandrini J, de Materre AB. Advances in the understanding and management of T-cell prolymphocytic leukemia. Oncotarget. 2017;8(61):104664–86.

6. Uchida T, Kawachi Y. B-cell prolymphocytic leukemia. Ryoikibetsu Shokogun Shirizu. 1998;75246(22 Pt 3):99–101.

7. Vivekanandarajah A, Atallah JP, Gupta S. T-cell prolymphocytic leukaemia (T-PLL): A rare disease with a grave prognosis. BMJ Case Rep. 2013;1–3.

8. Sun S, Fang W. Current understandings on T-cell prolymphocytic leukemia and its association with TCL1 proto-oncogene. Biomed Pharmacother [Internet]. 2020;126(February):110107. Available from: https://doi.org/10.1016/j.biopha.2020.110107

9. Matutes E. T-cell prolymphocytic leukemia. Cancer Control. 1998;5(1):19–24.

10. Gorczyca W, Weisberger J, Liu Z, Tsang P, Hossein M, Wu CD, et al. An Approach to Diagnosis of T-cell Lymphoproliferative Disorders by Flow Cytometry. Clin Cytom. 2002;50(3):177–90.

11. van Dongen J, Krissansen G, Wolvers-Tettero I, Comans-Bitter W, Adriaansen H, Hooijkaas H, et al. Cytoplasmic expression of the CD3 antigen as a diagnostic marker for immature T-cell malignancies. Blood. 1988;71(3):603–12.

12. Chen X, Cherian S. Immunophenotypic characterization of T-cell prolymphocytic leukemia. Am J Clin Pathol. 2013;140(5):727–35.