

T-Cell Chronic Lymphocytic Leukemia: A Rare Case Report.

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Received: August 2017

Accepted: September 2017

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ABSTRACT

T-cell prolymphocytic leukemia is a rare and unusual malignancy characterized by the proliferation of small- to medium-sized prolymphocytes of postthymic origin with distinctive, morphologic, immunophenotypic, and cytogenetic features. Involvement of the peripheral blood, bone marrow, lymph nodes, liver, spleen, and skin can occur. The clinical course is typically very aggressive with poor response to conventional chemotherapy and short survival rates, and the only potential long-term curative treatment is hematopoietic stem cell transplantation. We report the case of a man with de novo T-cell prolymphocytic leukemia and discuss the distinctive clinical, morphologic, immunophenotypic, and cytogenetic features of this entity. Prolymphocytic leukemia (PLL) is a rare lymphocytic disorder characterized by marked lymphocytosis and splenomegaly and represents only 2% of all mature lymphocytic leukemias in adults over the age of 30. PLL is clearly defined into subtypes as B-cell prolymphocytic leukemia (B-PLL) and T-cell prolymphocytic leukemia (T-PLL), with T-PLL representing approximately 20% of the cases (1). While these subtypes have their similarities, T-cell and B-cell PLL are two distinct diseases with different clinical and laboratory features. T-PLL is more rare and more rapidly progressive and aggressive than B-PLL.

Keywords: Chronic Lymphocytic Leukemia, Prolymphocytic Leukemia.

INTRODUCTION

T-CLL accounts for less than 1% of all CLPDs. T-CLL is characterized by a marked lymphocytosis of primarily small, mature T-lymphocytes having some degree of nuclear irregularity, and inconspicuous nucleoli that do not meet the diagnostic criteria for prolymphocytes. Lymphadenopathy and splenomegaly are uncommonly found and, when present, are always mild-to-moderate without striking organomegaly. The immunophenotype is that of a mature T-cell that is usually CD4+, but may occasionally be CD8+. There is a rich history behind the extinct entity 'T-cell chronic lymphocytic leukemia (T-CLL)' and the now-established replacement, small-cell variant of T-cell prolymphocytic leukemia (T-PLL-sv). The history of the events, observations, and discussions that led to this replacement. There is also provided a systematic analysis of all previously reported cases of T-PLL-sv as well as four new additional case.^[1] A clonal evolution model has been proposed in which mature T-cell leukemias classified in the past as T-CLL are perhaps T-PLL diagnosed early in the course of the disease.^[2] Involvement of the peripheral blood, bone marrow, lymph nodes, liver, spleen, and skin can occur. The clinical course is typically very

aggressive with poor response to conventional chemotherapy and short survival rates, and the only

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potential long-term curative treatment is hematopoietic stem cell transplantation. We report the case of a man with de novo T-cell prolymphocytic leukemia and discuss the distinctive clinical, morphologic, immunophenotypic, and cytogenetic features of this entity. Prolymphocytic leukemia (PLL) is a rare lymphocytic disorder characterized by marked lymphocytosis and splenomegaly and represents only 2% of all mature lymphocytic leukemias in adults over the age of 30. PLL is clearly defined into subtypes as B-cell prolymphocytic leukemia (B-PLL) and T-cell prolymphocytic leukemia (T-PLL), with T-PLL representing approximately 20% of the cases.^[3] While these subtypes have their similarities, T-cell and B-cell PLL are two distinct diseases with different clinical and laboratory features. T-PLL is more rare and more rapidly progressive and aggressive than B-PLL.^[4]

CASE REPORT

A 55-year-old man presented to medicine opd at Rajindra Hospital Patiala. A 55 year male patient came to medicine opd at Rajindra Hospital Patiala with chief complaints of loss of weight, recurrent lymph node enlargement. On clinical examination, hepatosplenomegaly was present. Investigations were done. On CBC, Hb was 14.9g/dl, TLC was 100000/ cumm, DLC was lympho 80%, poly 20%, smudge cells were seen. Platelet count was 226000/cumm. Bilirubin was 0.8mg, SGOT 22 IU/L, SGPT 61IU/L, Blood urea 75mg/dl, serum creatinine 2mg/dl. USG was done it showed hepatosplenomegaly, CECT was done and it showed abdominal lymphadenopathy. FNAC was also done from right cervical lymph node and diagnosis was Non Hodgkins lymphoma (centrocytic centroblastic type).

Bone marrow aspiration was done on patient and it was diagnosed lymphoproliferative disorder-CLL (stable phase). Bone marrow biopsy was also taken and was diagnosed as CLL. Flow cytometry was done and it showed CD3, CD5, CD7, CD8 positivity. Thus was confirmed as T cell CLL.

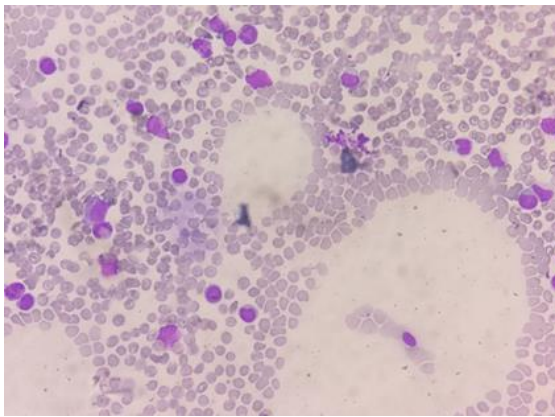


Figure-1: Photomicrograph of bone marrow aspiration of this patient

DISCUSSION & CONCLUSION

T-PLL is a well-published entity that shares many clinical and hematologic features with T-CLL; namely, both may present with a marked lymphocytosis and both usually, but not always, display a CD4+, mature T-cell immunophenotype.^[11-15] As opposed to T-CLL, patients with T-PLL often have striking splenomegaly with or without concurrent lymphadenopathy or hepatomegaly. In T-PLL cases, the lymphoid cells have characteristics of prolymphocytes, being intermediate in size, having a nuclear/cytoplasmic ratio that is lower than T-CLL with moderately condensed chromatin, and, as a hallmark, a single, prominent central nucleolus. Although in eight of our cases a small subpopulation

(< 10% of cells) of medium-sized cells could be identified, true pro-lymphocytes were infrequent. Morphologically, T-PLL was not a consideration when these cases were initially detected because of the homogeneous small lymphocyte appearance and lack of observable nucleoli. Significantly, in the largest published series of T-PLL? 21-20% of T-PLL cases were termed the "small cell variant," of T-PLL in which the nucleolus was not obvious by light microscopy and visible only by electron microscopy. It would appear that the cases we have termed T-CLL comprising our series probably correspond to this so-called small cell variant of T-PLL. Matutes et al have advocated using the term T-PLL to encompass both of these entities,^[14] with commentaries from other authors strongly discouraging the use of the term T-CLL.^[9]

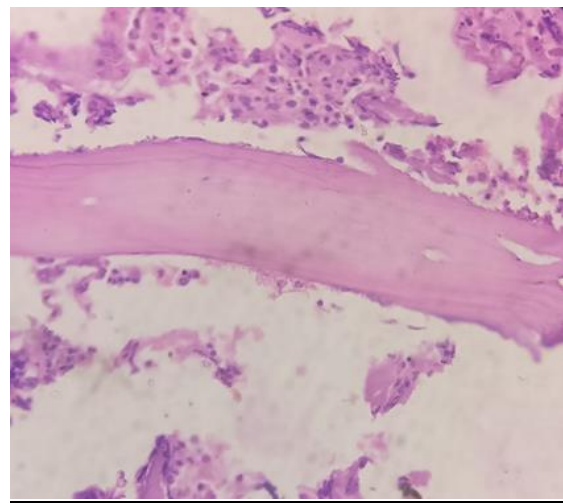


Figure 2: Photomicrograph of bone marrow biopsy of this patient.

The rationale presented has been that subdividing these T-cell disorders will discourage a further understanding of this group of mature T-cell processes and hinder development of effective treatments. Furthermore, it has been feared that using the term "CLL" to describe the small cell variant of T-PLL may cause clinicians to underestimate the aggressive nature of these cases. However, it is our contention that the mature T-cell classification system should have a category for T-CLL that is based on the morphologic finding of a small lymphocyte proliferation. Equally important is the distinction of T-CLL from the leukemic phase of PTCL.^[16,17] Both entities may present with varying degrees of lymphadenopathy and blood and marrow lymphocytosis.^[18] Similar to T-CLL, the majority of PTCL cases express a CD4+ immunophenotype. The morphology of circulating PTCL cells is usually more variable than in T-CLL. These lymphoma cells can be large to intermediate in size, with irregular nuclei, reticular nuclear chromatin, and may have prominent nucleoli. In our two cases in which lymph node biopsies were obtained, the morphology was

that of a small lymphocytic lymphoma, he designation T-CLL be used (as in our cases) in primarily marrow-based processes with significant involvement of the peripheral blood and BM by a small mature lymphocyte population and with only minimal secondary involvement of other organs such as lymph nodes or spleen. Conversely, the finding of prominent lymphadenopathy without marrow replacement would be more consistent with the diagnosis of a PTCL.^[2]

T-PLL, a rare hematological malignancy, was first described in 1973. It represents <2% of mature lymphocytic leukemias.^[3] T-PLL primarily affects older adults with an average age at presentation of 65 years with a slight male predominance. Most patients present with hepatosplenomegaly (splenomegaly in 82% to 92%) and generalized lymphadenopathy.^[3,19] A distinctive hematologic aspect is a rapidly rising white blood cell count with a doubling time of weeks to months.^[20] The key morphologic feature in the diagnosis of T-PLL is a population of prolymphocytes in the peripheral blood. The typical morphology consists of prolymphocytes of medium size with condensed nuclear chromatin, a single prominent nucleolus, and intensely basophilic nongranular cytoplasm with cytoplasmic protrusions or “blebs.” The nuclei can be round, oval, or irregular.^[21,22] In 5% the nuclear outline is markedly irregular and can even be cerebriform, mimicking Sézary cells.^[23] Both of these variants are otherwise similar to typical T-PLL, including immunophenotype and cytogenetics, and thus it is justified that all three are grouped together in a single category.^[22]

The bone marrow is diffusely infiltrated by prolymphocytes in most cases with variable residual hematopoiesis. Reticulin fibrosis is almost always present.^[21,22] On peripheral blood examination T-cell PLL cells have a prominent nucleolus and nucleus may be either round to oval in half the cases or irregular, often with convolutions.^[8] When the spleen is involved, histology finds a dense red pulp infiltrate with invasion into the splenic capsule, blood vessels, and extension into the atrophied white pulp. In lymph nodes, the involvement is diffuse with paracortical expansion by T prolymphocytes, sometimes with sparing of follicles.^[24] Immunophenotypically, T prolymphocytes are mature postthymic peripheral T cells that do not express TdT and the cortical thymic marker CD1a. The cells are positive for CD2, CD3, and CD5 and have strong CD7 staining. This strong CD7 intensity is in contrast to other mature T-cell malignancies, where this marker may be weak or negative. The membrane expression of CD3 may be weak or even negative in occasional cases, but T-cell receptor-beta/gamma chain genes are always rearranged. CD52 is usually expressed at high density in T prolymphocytes and can be used as a target of therapy by the monoclonal antibody

alemtuzumab.^[19,25] In 65% of patients, the cells are CD4+, CD8-, and in 13% they are CD4-, CD8+. In 21% the T prolymphocytes coexpress CD4 and CD8, which is a feature almost unique to T-PLL. The most specific markers for T-PLL by immunophenotyping are CD26 and TCL-1 protein expression, which are not detected in the other mature T-cell leukemia/lymphomas.^[22] The overexpression of the oncogene TCL1 is useful for detecting residual T-PLL in bone marrow sections after therapy.^[20]

T-PLL is characterized by complex chromosomal abnormalities, which suggests that chromosomal aberrations might occur progressively during the course of the disease, thus explaining the aggressive nature of this condition. Recurrent changes mainly affect chromosomes 14, 8, 11, and X.^[26] The most common characteristic chromosome abnormality, seen in 80% of cases, is inversion of chromosome 14 with breakpoints in the long arm at q11 and q32 (inv q11;q32).^[24] Reciprocal tandem translocations between the two chromosomes 14 occur in 10% (t(14;14)(q11;q32).^[26] These two rearrangements involve the 14q11 and 14q32.1 loci, where the genes coding for TCR α and the protooncogene TCL-1 are localized, respectively. The rearrangements result in juxtaposition of these two genes and lead to expression and activation of TCL-1.^[27] About 20% of patients have the translocation t(X;14) (q28;q11), which results in rearrangement of the MTCP1 gene.^[28] Both TCL-1 and MTCP-1 have oncogenic properties, as both can induce a T-cell leukemia (CD4-/CD8+) in transgenic mice.^[27,29,30] Abnormalities involving both arms of chromosome 8 are frequent, t(8;8) (p11-12;q12) as well as trisomy 8q, with both being seen in 70% to 80% of cases. Other alterations seen in T-PLL include deletions of 12p13 and 11q,^[22] with the latter being the locus for the ataxia telangiectasia mutated gene. Abnormalities of chromosome 6 and 17 and deletion of the TP53 gene are also not uncommonly encountered.^[21]

T-PLL is aggressive and often resistant to therapy. The overall prognosis is poor, with a median survival of approximately 7 months in patients treated with conventional regimens. Recently the average survival has been extended to >2 years following the introduction of newer therapies (22). The initial treatment of choice for most patients is the monoclonal antibody alemtuzumab (anti-CD52); the best responses have been seen with this agent, but responses are still transient and further disease progression is inevitable.^[5,31]

REFERENCES

1. Rashidi A, Fisher SI. T-cell chronic lymphocytic leukemia or small-cell variant of T-cell prolymphocytic leukemia: a historical perspective and search for consensus. *Eur J Haematol.* 2015 Sep;95(3):199-210.

2. J.D. Hoyer, C.W. ROSS, C.-Y. Li, T.E. Witzig, R.D. Gascoyne, G.W. Dewald, and C.A. Hanson. True T-cell Chronic Lymphocytic Leukemia: A Morphologic and Immunophenotypic Study of 25 Cases By 1995 86: 1163–1169.
3. Robak T, Robak P. Current treatment options in prolymphocytic leukemia. *Med Sci Monit.* 2007;13(4):RA69–RA80.
4. Madaris L. T-cell prolymphocytic leukemia: a rare disease in an elderly female. *J Am Acad Nurse Pract.* 2010;22(12):648–653.
5. Dearden CE, Matutes E, Cazin B, Tjønnfjord GE, Parreira A, Nomdedeu B, Leoni P, Clark FJ, Radia D, Rassam SM, Roques T, Ketterer N, Brito-Babapulle V, Dyer MJ, Catovsky D. High remission rate in T-cell prolymphocytic leukemia with CAMPATH-1H. *Blood.* 2001;98(6):1721–1726.
6. Del Giudice I, Davis Z, Matutes E, Osuji N, Parry-Jones N, Morilla A, Brito-Babapulle V, Oscier D, Catovsky D. IgVH genes mutation and usage, ZAP-70 and CD38 expression provide new insights on B-cell prolymphocytic leukemia (B-PLL) Leukemia. 2006;20(7):1231–1237.
7. Ruchlemer R, Parry-Jones N, Brito-Babapulle V, Attolico I, Wotherspoon AC, Matutes E, Catovsky D. B-prolymphocytic leukaemia with t(11;14) revisited: a splenomegalic form of mantle cell lymphoma evolving with leukaemia. *Br J Haematol.* 2004;125(3):330–336.
8. Wintrob's Clinical Hematology. Chronic lymphocytic leukemia. Edition(13):1904-1906.
9. Foon KA, Gale RP: Is there a T-cell form of chronic lymphocytic leukemia? *Leukemia* 6:867, 1992 9.
10. Matutes E, Catovsky D: CLL should be used only for the disease with B-cell phenotype. *Leukemia* 7:917, 1993 10.
11. Chan WC, Check IJ, Heffner LT, Gordon D, Whitsett C, Brynes RK: Prolymphocytic leukemia of helper cell phenotype. Re- port of a case and review of the scientific literature. *Am J Clin Pathol* 77:543, 1982:18.
12. Woessner S, La Fuente R, Sans-Sahrafen J, Vives J, Rozman C: Prolymphocytic leukemia of T-cell type: Immunologic, enzymatic, and ultrastructural morphometric characteristics. *Br J Haematol* 39:9, 1978
13. Volk JR, Kjeldsberg CR. Eyre HJ, Marty J: T-cell prolymphocytic leukemia: Clinical and immunologic characterization. *Cancer* 52:2047, 1983.
14. Lohmeyer J, Hadam M, Ho A, Hesse A, Pralle H: T-cell prolymphocytic leukemia (T-PLL) with unique surface phenotype. *Blut* 54:223, 1987.
15. Matutes E, Brito-Bahapulle V, Swansbury J, Ellis J, Morilla R, Dearden C, Sempere A, Catovsky D: Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. *Blood* 78:3269, 1991
16. Pinkus GS, O'Hara CJ, Said JW: PeripheraVpost-thymic T-cell lymphomas: A spectrum of disease. Clinical, pathologic and immunologic features of 78 cases. *Cancer* 65:971, 1990.
17. Armitage JO, Greer JP, Levine AM, Weisenburger DD, Formenti SC, Bast M, Conley S, Pierson J,Linder L, Cousar JB, Nathwani B: Peripheral T-cell lymphoma. *Cancer* 63:158, 1989.
18. Hanson CA, Brunning RD, Gajl-Peczalska KJ, Frizzera G, McKenna RW: Bone marrow manifestation of peripheral T-cell lymphoma. A study of 30 cases. *Am J Clin Pathol* 80:449, 1986.
19. Dearden CE. T-cell prolymphocytic leukemia. *Med Oncol.* 2006;23(1):17–22.
20. Herling M, Khoury JD, Washington LT, Duvic M, Keating MJ, Jones D. A systematic approach to diagnosis of mature T-cell leukemias reveals heterogeneity among WHO categories. *Blood.* 2004;104(2):328–335.
21. Catovsky D, Ralfkiaer E, Muller-Hermelink HK. T-cell prolymphocytic leukemia. Pathology and genetics of tumours of haemopoietic and lymphoid tissues. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. World Health Organisation Classification of Tumours. Lyon, France: IARC Press; 2008. pp. 270–271.
22. Dearden CE. T-cell prolymphocytic leukemia. *Clin Lymphoma Myeloma.* 2009;9(Suppl 3):S239–S243.
23. Pawson R, Matutes E, Brito-Babapulle V, Maljaie H, Hedges M, Mercieca J, Dyer M, Catovsky D. Sezary cell leukaemia: a distinct T cell disorder or a variant form of T prolymphocytic leukaemia? *Leukemia.* 1997;11(7):1009–1013.
24. Osuji N, Matutes E, Catovsky D, Lampert I, Wotherspoon A. Histopathology of the spleen in T-cell large granular lymphocyte leukemia and T-cell prolymphocytic leukemia: a comparative review. *Am J Surg Pathol.* 2005;29(7):935–941.
25. Matutes E. T-cell prolymphocytic leukemia. *Cancer Control.* 1998;5(1):19–24.
26. Maljaei SH, Brito-Babapulle V, Hiorns LR, Catovsky D. Abnormalities of chromosomes 8, 11, 14, and X in T-prolymphocytic leukemia studied by fluorescence in situ hybridization. *Cancer Genet Cytogenet.* 1998;103(2):110–116.
27. Pekarsky Y, Hallas C, Isobe M, Russo G, Croce CM. Abnormalities at 14q32.1 in T cell malignancies involve two oncogenes. *Proc Natl Acad Sci U S A.* 1999;96(6):2949–2951.
28. Stern MH, Soulier J, Rosenzweig M, Nakahara K, Canki-Klain N, Aurias A, Sigaux F, Kirsch IR. MTCP-1: a novel gene on the human chromosome Xq28 translocated to the T cell receptor alpha/delta locus in mature T cell proliferations. *Oncogene.* 1993;8(9):2475–2783.
29. Gritti C, Dastot H, Soulier J, Janin A, Daniel MT, Madani A, Grimber G, Briand P, Sigaux F, Stern MH. Transgenic mice for MTCP1 develop T-cell prolymphocytic leukemia. *Blood.* 1998;92(2):368–373.
30. Virgilio L, Lazzeri C, Bichi R, Nibu K, Narducci MG, Russo G, Rothstein JL, Croce CM. Deregulated expression of TCL1 causes T cell leukemia in mice. *Proc Natl Acad Sci U S A.* 1998;95(7):3885–3889.
31. Keating MJ, Cazin B, Coutré S, Birhiray R, Kovacovics T, Langer W, Leber B, Maughan T, Rai K, Tjønnfjord G, Bekradda M, Itzhaki M, Hérait P. Campath-1H treatment of T-cell prolymphocytic leukemia in patients for whom at least one prior chemotherapy regimen has failed. *J Clin Oncol.* 2002;20(1):205–213.

How to cite this article: Kaur M, Bodal VK, Kaur G, Kaur A. T-Cell Chronic Lymphocytic Leukemia: A Rare Case Report. *Ann. Int. Med. Den. Res.* 2017; 3(6):PT01-PT04.

Source of Support: Nil, **Conflict of Interest:** None declared