Table 1. Characteristics of the 3 patients.

	Blood lymphocyte immunophenotyping at the diagnosis of CLL	*Blood lymphocyte immunophenotyping at the diagnosis of HD*	*Bone marrow lymphocytic infiltration at the diagnosis of HD*	*Outcome*
Patient #1	Lymphocytes: 46.44×10^9/L	Lymphocytes: 0.3×10^9/L	Slight lymphocytic infiltration and no RS cells	HD complete remission
	96% monoclonal κ light chain $CD5^+$, $CD19^+$, $CD23^+$	75% monoclonal kappa light chain $CD5^+$, $CD19^+$, $CD23^+$		
Patient #2	Lymphocytes: 15.4×10^9/L 70% monoclonal κ light chain $CD5^+$	Lymphocytes: 2.57×10^9/L 40% monoclonal κ light chain $CD5^+$, $CD19^+$, $CD23^+$	Nodular infiltration by mature and small lymphocytes without RS cells	HD complete remission Persisting CLL (Lymphocytes: 6×10^9/L with 86% B monoclonal lymphocytes)
Patient #3	Lymphocytes: 7.8×10^9/L 91% monoclonal κ light chain $CD5^+$, $CD19^+$, $CD23^+$	Not done	Mild bone marrow infiltration by lymphocytes without RS cells	HD complete remission Persisting CLL (Lymphocytes: 2×10^9/L 60% B monoclonal lymphocytes)

out relapse.

In CLL patients, the risk of a secondary neoplasm is related to an immunologic deficiency and/or treatment such as chlorambucil.[7] Recent data show that RS cells and CLL cells belong to the same clonal population.[8,9] RS cells, occurring in CLL or in classical HD, have the same genetic, morphologic and immunophenotypic features.

The good prognosis of HD after CLL distinguishes it from Richter's syndrome. Indeed it might be considered as a complication of CLL and not only as a coincidental finding. It should be searched for when patients develop signs suggestive of progression or transformation of CLL. Intensive treatment seems to be useful for obtaining CR.

Christine Serratrice-de Roux, Diane Coso,° Reda Bouabdallah,° Jacques Serratrice,* Patrick Disdier,* Pierre Jean Weiller**

**Service de Médecine Interne, CHU Timone, Marseille; °Service d'Hématologie Générale, Institut Paoli Calmettes, Marseille, France*

Key words

Chronic lymphocytic leukemia. Hodgkin's disease.

Correspondence

Patrick Disdier, M.D., Service de médecine interne du Pr PJ Weiller, CHU Timone, 264 rue Saint Pierre, 13385 Marseille Cedex 5, France. Phone: international +33-4-91386039 – Fax: international +33-4-91347401 – E mail: pdisdier@ap-hm.fr

References

1. Harousseau JL, Flandrin G, Tricot G, Brouet JC, Seligmann M, Bernard J. Malignant lymphoma supervening in chronic lymphocytic leukemia and related disorders. Richter's syndrome: a study of 25 cases. Cancer 1981; 48:1302-8.
2. Choi H, Keller RH. Coexistence of chronic lymphocytic leukemia and Hodgkin's disease. Cancer 1981; 48:48-57.
3. Weisenberg E, Anastasi J, Adeyanju M, Variakojis D, Vardiman JW. Hodgkin's disease associated with chronic lymphocytic leukemia. Eight additional cases, including two of the nodular predominant type. Am J Clin Pathol 1995; 103:479-84.
4. Fayad L, Robertson LE, O'Brian S, et al. Hodgkin's disease variant of Richter's syndrome: experience at a single institution. Leuk Lymphoma 1996; 23:333-7.
5. Butts C, Drouin J, Taylor R, McLeish W. Hodgkin's disease in CLL. Am J Hematol 1995; 48:134-5.
6. Schmidt HH, Sill H, Eibl M, et al. Hodgkin's disease developing after spontaneous remission of chronic lymphocytic leukemia. Ann Hematol 1995; 71:247-52.
7. Manusow D, Weinrman BH. Subsequent neoplasia in chronic lymphocytic leukemia. JAMA 1975; 232:267-9.
8. Ohno T, Smir B, Weisenburger D, Gascoyne R, Hinrichs S, Chan W. Origin of the Hodgkin/Reed-Stenberg cells in chronic lymphocytic leukemia with Hodgkin's transformation. Blood 1998; 91:1757-61.
9. Kanzler H, Kuppers R, Hansmann ML, Rajewsky K. Hodgkin and Reed-Stenberg cells in Hodgkin's disease represent the outgrowth of a dominant tumor clone derived from (crippled) germinal center B cells. J Exp Med 1996; 184:1495-505.

$CD3^-$ large granular lymphocyte leukemia with clonal rearrangement of the γ and β genes of the T-cell receptor

We report the case of a patient with large granular lymphocyte leukemia with a CD3-phenotype and evidence of a monoclonal rearrangement of the TCRγ and β genes.This case seems to show that the proliferation originated from an immature T-thymic progenitor.

Sir,

Large granular lymphocyte (LGL) proliferation of $CD3^+$ cells with clonal T-cell receptor (TCR) gene rearrangements are referred to as T-LGL leukemia; LGL proliferations of $CD3^-$ cells without TCR gene rearrangements are classified as natural killer (NK)-LGL leukemia.[1-5]

©Ferrata Storti Foundation

We report a well documented case of LGL leukemia with unusual biological features. A 46-year old woman was sent to our Hematology Department for study of a stable, isolated chronic severe neutropenia (neutrophils 0.145x10^9/L, lymphocytes 2.904x10^9/L) of 5 years of duration. Morphologic evaluation of the peripheral blood and bone marrow aspiration smears showed the presence of 40% and 13% LGLs, respectively. The LGs in peripheral blood showed expression of CD2, CD7, CD94, CD11c and CD16 and negativity for surface and cytoplasmic CD3, CD56, CD57, TCRαβ, TCRγδ, CD5, CD34 and TdT. Conventional cytogenetics performed on peripheral blood stimulated with PHA showed a normal karyotype. The molecular analysis by polymerase chain reaction and Southern blot revealed rearrangement of the TCRγ and β genes. To our knowledge, this is the second case reported of TCR gene rearrangement in a patient with CD3$^-$ LGL leukemia. Among seven patients with CD3$^-$ LGL leukemia analyzed for rearrangement of the TCR genes, Hara *et al.*[6] found one patient with TCR-δ gene rearrangement. Their findings indicate that CD3- LGLs include not only cells belonging to the NK-cell lineage but also precursor cells committed to the T-cell lineage. In the human thymus there are progenitors cells with the capacity to develop into T, NK, and dendritic cells.[7] It has been recently shown that the TCR genes of early thymocyte subpopulations rearrange in an ordered way during human T-cell differentiation; TCRδ rearrange first followed by TCRγ and TCRβ.[8] The rearrangement of the TCR-β gene initiates in T-thymic progenitors.

Taken together, an attractive hypothesis to explain the CD3$^-$ phenotype and the TCRγ and β genes rearrangement in our case would be that the LGL clone may have arisen in a T-thymic progenitor. Since rearrangement of the TCRβ gene strongly suggests T-cell commitment,[8] the cells of this patient may have been arrested at a differentiation stage earlier than the stage of TCRα gene rearrangement and would have differentiated to CD3$^+$ T-cells bearing the gδ or αβ heterodimer. This concept may be supported by the absence on the cell surface in this patient of CD5, TCRγδ, TCRαβ and CD56, which are antigens with lineage-specific and maturation dependent expression, and the positivity for HLA-DR and CD7, antigens that may be associated with immaturity. Overall, our case would support the theory that some cases of CD3$^-$ LGL leukemia may represent immature proliferations originating in T-thymic progenitors rather than true peripheral NK neoplasias. Molecular characterization of TCR gene rearrangement status in a greater number of cases of CD3$^-$ LGL leukemia would be of great interest to increase our knowledge of this rare pathology.

Rosa Manteiga, Lourdes Florensa, Francesc Solé, Margarita Prat, Carles Besses,° Soledad Woessner#*

*Laboratori de Citologia Hematològica; Unitat d'Hematologia 1973; Laboratori de Referència de Catalunya; Institut Municipal d'Assistència Sanitària (IMAS), Institut Municipal d'Investigació Mèdica (IMIM); °Servei d'Hematologia Clínica; Hospital del Mar; #Escola de Citologia Hematològica "S. Woessner-IMAS"; Barcelona; *Servei d'Hematologia; Hospital Sant Pau i Santa Tecla; Tarragona, Spain*

Key words

Large granular lymphocyte leukemia, CD3, T-cell receptor gene rearrangement.

Acknowledgments

The authors are grateful to Dra. Colomer from the "Hospital Clínic", Spain, who performed the molecular analysis. Supported in part by grant FIS 99/0574 from the "Ministerio de Sanidad y Consumo", Spain.

Correspondence

Lourdes Florensa, Laboratori de Citologia Hematològica, Unitat d'Hematologia 1973, Laboratori de Referència de Catalunya, Hospital del Mar, Passeig Marítim 25-29, 08003 Barcelona, Spain. Phone: international +34-93-2211010-1073 – Fax: international +34-93-2212920 – E-mail: e0037@imas.imim.es

References

1. Loughran T Jr. Clonal diseases of large granular lymphocytes. Blood 1993; 82:1-14.
2. Lanier LL, Phillips JH, Hackett J Jr, Tutt M, Kumar V. Natural killer cells: definition of a cell type rather than a function. J Immunol 1986; 137:2735-9.
3. Pelicci PG, Allavena P, Subar M, et al. T cell receptor (α, β, γ) gene rearrangements and expression in normal and leukemic large granular lymphocytes/natural killer cells. Blood 1987; 70:1500-8.
4. Loughran T Jr, Starkebaum G, Aprile JA. Rearrangement and expression of T-cell receptor genes in large granular lymphocyte leukemia. Blood 1988; 71:822-4.
5. Chan WC, Dahl C, Waldmann T, et al. Large granular lymphocyte proliferation: an analysis of T cell receptor gene arrangement and expression and the effect of in vitro culture with inducing agents. Blood 1988; 71:52-8.
6. Hara J, Yumura-Yagi K, Tagawa S, et al. Molecular analysis of T cell receptor and CD3 genes in CD3- large granular lymphocytes (LGLs): evidence for the existence of CD3- LGLs committed to the T cell lineage. Leukemia 1990; 4:580-3.
7. Res P, Martínez-Cáceres E, Jaleco AC, et al. CD34+ CD38^{dim} cells in the human thymus can differentiate into T, natural killer, and dendritic cells but are distinct from pluripotent stem cells. Blood 1996; 87:5196-206.
8. Blom B, Verschuren MCM, Heemskerk MHM, et al. TCR gene rearrangements and expression of the pre-T cell receptor complex during human T-cell differentiation. Blood 1999; 93:3033-43.

Successful treatment of angioimmunoblastic lymphadenopathy with dysproteinemia-type T-cell lymphoma by combined methotrexate and prednisone

Angioimmunoblastic lymphadenopathy with dysproteinemia (AILD)-type T-cell lymphoma has a very poor prognosis in most patients. Here we report a complete clinical response in a patient treated with low-dose oral methotrexate (10 mg/m^2 weekly) in combination with prednisone (15 mg/day) in whom conventional chemotherapy was not effective. This regimen was not associated with