had a lower probability of DFS than patients with MRD < 1/10[3]. These data are comparable to those previously reported.[4-6,9,10] In summary, MRD after induction therapy is a relevant prognostic factor in children with B-precursor ALL. Our study indicates the need for MRD evaluation by PCR in all patients at the end of the induction period.

David Ruano, Miguel Angel Diaz,* Olga Tutor,° Felix Garcia-Sanchez,# Pedro Martinez,° Luis Madero**

**"Niño Jesús" Children's Hospital, Madrid; °Molecular Genetics Lab. Hospital Nacional de Paraplejicos, Toledo; #Centro de Transfusión, Comunidad de Madrid, Madrid, Spain*

Key words

Childhood ALL, minimal residual disease.

Correspondence

Luis Madero, M.D., Department of Pediatrics, Bone Marrow Transplant Unit, Hospital Niño Jesús, Menendez Pelayo 65, 28009 Madrid, Spain. Phone: international +34-1-5035900 – Fax: international +34-1-5744669.

References

1. Reiter A, Schrappe M, Luwdig WD, et al. Chemotherapy in 998 unselected childhood acute lymphoblastic leukemia patients. Results and conclusions of the multicenter trial ALL-BFM 86. Blood 1994; 84:3122-33.
2. Wan JH, Trainor KJ, Brisco MJ, Morley AA. Monoclonality in B-cell lymphoma detected in paraffin wax embedded using the polymerase chain reaction. J Clin Pathol 1990; 43:888-90.
3. Brisco M, Condon J, Hughes E, et al. Outcome prediction in childhood acute lymphoblastic leukemia by molecular quantification of residual disease at the end of induction. Lancet 1994; 343:196-200.
4. Yokota S, Hansen-Hagge TE, Luwdig WD, et al. Use of polymerase chain reaction to monitor minimal residual disease in acute lymphoblastic leukemia patients. Blood 1991; 77:331-9.
5. Wasserman R, Galili N, Ito Y, et al. Residual disease at the end of induction therapy as a predictor of relapse during therapy in childhood B-lineage acute lymphoblastic leukemia. J Clin Oncol 1992; 10:1879-88.
6. Jacquy C, Delepant B, Van Daele S, et al. A prospective study of minimal residual disease in childhood B-lineage acute lymphoblastic leukemia: MRD level at the end of induction is a strong predictive factor of relapse. Br J Haematol 1997; 98:140-6.
7. Nizet Y, Martiat P, Vaerman JL, et al. Follow-up of residual disease (MRD) in B-lineage acute leukemia using a simplified PCR strategy: evolution of MRD rather than its detection is correlated with clinical outcome. Br J Haematol 1991; 79:205-10.
8. Roberts WM, Estrov Z, Ouspenskaia M, Johnston DA, McClain KL, Zipf TF. Measurement of residual leukemia during remission in childhood acute lymphoblastic leukemia. N Engl J Med 1997; 336:317-23.
9. Steenbergen EJ, Verhagen OJ, van Leewen EI, et al. Prolonged persistence of PCR detectable minimal residual disease after diagnosis or first relapse predicts poor outcome in childhood B-precursor acute lymphoblastic leukemia. Leukemia 1995; 9:1726-34.
10. Cave H, van der Werff ten Bosch J, Suciu S, et al. Clinical significance of minimal residual disease in childhood acute lymphoblastic leukemia. European Organization for Research and Treatment of Cancer Childhood Leukemia Cooperative Group. N Engl J Med 1998; 339:591-8.

Chronic lymphocytic leukemia and Hodgkin's disease. Clinicopathologic study of three cases with good prognosis

Lymphadenopathy during the course of chronic lymphocytic leukemia is common. However, when patients develop associated symptoms, a lymph node biopsy is warranted. We report three patients with chronic lymphocytic leukemia who subsequently developed Hodgkin's disease and who achieved complete remission after chemotherapy and radiotherapy.

Sir,

B-cell chronic lymphocytic leukemia (CLL) is the most common form of leukemia, affecting older patients; 10% develop diffuse large cell lymphoma (Richter's syndrome)[1]. Hodgkin's disease (HD) sometimes occurs in patients with a longstanding history of CLL[2] and survival is usually short. We report 3 cases of HD in CLL patients. All patients achieved complete remission (CR) of HD.

Case #1. In 1990 a 62-year old man was diagnosed as having Binet stage A CLL. Chlorambucil was administered over 3 years. In 1997 axillary lymphadenopathies appeared with anemia and thrombocytopenia. Lymph node biopsy showed Reed Sternberg (RS) cells. According to the Ann Arbor classification he had stage III disease. Blood lymphocyte immunophenotyping and bone marrow biopsy are detailed in Table 1. Three courses of intensive chemotherapy (Stanford V regimen) produced CR. When last seen in 1999 he was still in CR from HD.

Case #2. In 1990 a 62-year old woman developed a Binet stage A CLL (Table 1). In 1996 lymphadenopathies and night sweats appeared. Lymph node biopsy revealed RS cells and $CD5^+$ lymphocytes. The patient was considered as having stage III disease according to the Ann Arbor classification. She received 3 courses of intensive chemotherapy (Stanford V regimen) followed by radiotherapy. She achieved a CR. In 1999 she was still in CR from HD.

Case #3. In 1991 a 60-year old man was diagnosed as having a Binet stage C CLL. He received 11 courses of mitoxantrone, etoposide, and steroids. Only a partial response was achieved (Table 1). In 1995, he developed a CLL related cytopenia. Six courses of fludarabine were delivered. In 1996 submandibular lymph nodes and splenomegaly appeared. Lymphadenopathy biopsy showed RS cells. Three courses of MOPP/ABVD were completed by radiotherapy. Thirty-six months later he was still in CR from HD.

The occurrence of HD in the course of CLL has been reported in the literature.[3-6] In Fayad's study,[4] 7 CLL patients out of 1,374 developed HD (0.6%) with a mean interval of 45 months. The median age upon diagnosis of HD was 71 years. They all received chemotherapy, but only one achieved CR.

In contrast, the prognosis of our patients remained as good as those of patients with HD without CLL. This could be because they were younger or because of the late occurrence of HD and intensive chemotherapy. Nevertheless, such an outcome is rare. Butts[5] reported two cases of HD in patients with CLL, with-

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]