

## CORRESPONDENCE

## Large Cell Non-Hodgkin's Lymphoma and Hodgkin's Disease Arising Synchronously in a Patient With Chronic Lymphocytic Leukemia: Importance of Immunocytochemistry

To the Editor:

Transformation of chronic lymphocytic leukemia (CLL) into a more aggressive hematologic malignancy is a well-described phenomenon known as Richter's syndrome (RS) and has been reported to result in non-Hodgkin's lymphoma (NHL), Hodgkin's disease (HD), or multiple myeloma in 3%, 0.5%, and 0.1% of patients, respectively.<sup>1</sup> Although there have been cases of patients with both de novo HD and high-grade B-cell lymphoma, as well as sequential HD, follicular NHL, and high-grade B-cell NHL, we have not been able to identify any patients with HD and NHL concurrently arising in the setting of CLL.<sup>2-4</sup> Here we report the synchronous occurrence of both diffuse large B-cell NHL and nodular sclerosing HD in a patient with CLL.

A 51-year-old man with anemia and lymphocytosis was diagnosed with CLL. His disease did not respond to chlorambucil, but responded well to fludarabine. A subsequent hemolytic anemia resolved with splenectomy. Three years after diagnosis, the patient developed night sweats, distal femur swelling, and ipsilateral inguinal lymphadenopathy. Biopsies of both posterior iliac crests and of the distal femoral mass were performed. The bone marrow was 90% cellular largely due to an infiltrate consisting of large lymphoid cells in a background of small round lymphocytes. The mass in the distal femur consisted of a subset of cells containing multiple nuclei and prominent nucleoli with Reed-Sternberg-like morphology within a background of small round lymphocytes. The immunocytochemical and morphological findings were interpreted as showing CD20<sup>+</sup>, CD15<sup>-</sup>, CD30<sup>-</sup>, CD5<sup>-</sup>, CD3<sup>-</sup> large cell NHL in the bone marrow; CD15<sup>+</sup>, CD30<sup>+</sup>, Fascin<sup>+</sup>, CD20<sup>-</sup> nodular sclerosing HD in the femoral mass; and a background of CD5<sup>+</sup>, CD19<sup>+</sup>, dim CD20<sup>+</sup>, CD10<sup>-</sup> CLL in both biopsy specimens.

The patient was treated with 5 cycles of cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP), with a dramatic response in his night sweats and inguinal adenopathy along with normalization of his bone marrow. However, the mass in his distal femur increased in size after only a brief response. Repeat biopsy of this area revealed extensive necrosis with evidence of CLL and a persistent subset of large malignant-appearing lymphoid cells. Because of this extensive necrosis, repeat immunocytochemical studies could not differentiate residual HD from large cell NHL. Radiotherapy to his femur resulted in local improvement, although subsequent treatment with dexamethasone, cytosine arabinoside, and cisplatin (DHAP) and then mesna, ifosfamide, mitoxantrone, and etoposide (MINE) yielded only transient minor responses. The patient died with progressive lymphoma 11 months after the recognition of apparent RS, and postmortem examination was not performed.

Based on the observed incidence of NHL and HD in RS patients with CLL, the likelihood of developing both HD and NHL in the same patient should be exceedingly rare (0.015%, ie, 3% × 0.5%). With 7,400 new cases of CLL in the United States each year,<sup>5</sup> the estimated frequency of RS resulting in both HD and NHL in the same patient would be expected to be, at most, 1 patient per year. The events we report may be even less likely because the two diseases presented simultaneously. Unfortunately, the quantity of these samples did not allow us to definitively confirm clonality between the three histologies. Because multiple biopsies and pathological evaluations including

detailed immunocytochemistry of each area were required to establish the diagnosis in our patient, the synchronous occurrence of NHL and HD might have occurred in previous patients but not been recognized.

Therapy in the rare situations of so called "composite lymphomas" has traditionally been directed against the more aggressive subtype.<sup>6</sup> We treated both of his newly diagnosed lymphomas with CHOP. Initially, he responded well, but ultimately progressed and died with systemic disease, although faring better than the median survival of 5 months of RS with NHL.<sup>1</sup> Perhaps similar or even more complex transformations as manifestations of RS will be identified as clinicians more aggressively evaluate and biopsy patients with an unexplained change in their disease course and more broadly apply immunocytochemical techniques. This approach may ultimately lead to both a clearer understanding of the pathophysiology as well as improved therapies for this phenomenon.

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Ajay K. Gopal  
Scott M. Schuetze  
David G. Maloney  
*Department of Medicine*  
*Division of Medical Oncology*  
*University of Washington Medical Center*  
*Seattle, WA*  
Paul L. Weiden  
*Section of Hematology*  
*The Virginia Mason Medical Center*  
*Seattle, WA*

### REFERENCES

- Giles FJ, O'Brien SM, Keating MJ: Chronic lymphocytic leukemia in (Richter's) transformation. *Semin Oncol* 25:117, 1998
- Amini RM, Enblad G, Sundstrom C, Glimelius B: Patients suffering from both Hodgkin's disease and non-Hodgkin's lymphoma: A clinico-pathological and immuno-histochemical population-based study of 32 patients. *Int J Cancer* 71:510, 1997
- Brauninger A, Hansmann ML, Strickler JG, Dummer R, Burg G, Rajewsky K, Kuppers R: Identification of common germinal-center B-cell precursors in two patients with both Hodgkin's disease and non-Hodgkin's lymphoma. *N Engl J Med* 340:1239, 1999
- Hell K, Hansmann ML, Pringle JH, Lauder I, Fischer R: Combination of Hodgkin's disease and diffuse large cell lymphoma: An in situ hybridization study for immunoglobulin light chain messenger RNA. *Histopathology* 27:491, 1995
- Parker SL, Tong T, Bolden S, Wingo PA: Cancer statistics, 1997 [published erratum appears in *CA Cancer J Clin* 47:68, 1997]. *CA Cancer J Clin* 47:5, 1997
- Jaffe ES, Zarate-Osorno A, Medeiros LJ: The interrelationship of Hodgkin's disease and non-Hodgkin's lymphomas—Lessons learned from composite and sequential malignancies. *Semin Diagn Pathol* 9:297, 1992