To the Editor:

In their recent report in *Blood*, Wormsley et al concluded that CD11c+, CD5+ B-cell chronic leukemias are subgroups of chronic lymphocytic leukemia (CLL) and prolymphocytic leukemia (PLL) rather than of hairy cell leukemia (HCL). We do not disagree that chronic B-cell lymphoproliferative disorders other than HCL may demonstrate CD11c+, and have previously reported on such cases; but we do have reservations regarding the implication that HCL should be excluded as a diagnostic possibility when the leukemic cells possess the CD5 antigen in addition to CD11c and B-cell markers. We have recently encountered a case of HCL with CD5+, CD11c+, CD20+ leukemic cells, which points out the need for cautious interpretation of immune surface markers in the context of clinical, morphologic, and cytochemical findings.

The patient is an 85-year-old retired physician who had been in excellent health until 1985, when moderate splenomegaly was discovered on a routine physical examination at another institution. A CBC performed at that time showed a white blood cell count (WBC) of 6,700/µL with 9% neutrophils and 37% "atypical lymphocytes," a hemoglobin (Hgb) level of 12.3 g/dL, and a platelet count of 177,000/µL. A bone marrow biopsy was performed and a tentative diagnosis of HCL was made. The patient was followed with no medical intervention, but has had routine physical examinations every 6 months.

The patient was referred to the University of Chicago for additional evaluation in July 1990. Moderate splenomegaly was present, but he had no lymphadenopathy or hepatomegaly. The WBC was 9,100/µL with 52% "hairy cells," 33% small lymphocytes, 12% neutrophils, and 3% monocytes. The Hgb was 11.8 g/dL and the platelet count was 110,000/µL. The "hairy cells" were large (12 to 15 µm), and had round to oval, eccentrically placed nuclei with delicate chromatin and inconspicuous nucleoli, as well as abundant cytoplasm with villous margins (Fig 1). More than one half of the hairy cells had tartrate-resistant acid phosphatase reactivity. A bone marrow biopsy specimen was only 10% cellular, but nearly one half of the marrow cells had histologic features consistent with those of HCL. Immunophenotypic studies of peripheral-blood mononuclear cells were performed by flow cytometry as well as by the alkaline-phosphatase-anti-alkaline phosphatase (APAAP) technique on peripheral blood smears. The immunophenotype of the neoplastic cells was CD5+, CD11c+, CD19+, CD20+, and CD25+. This immunophenotype was confirmed by examination of the hairy cells on APAAP-stained peripheral blood smears. Dual staining by flow cytometry showed that CD5 and CD20 as well as CD19 and...
CD11c were coexpressed on the neoplastic cells. Therefore, the leukemic cells from our patient were CD5+, CD11c+, CD20+, but the clinical, morphologic, and cytochemical findings were those of HCL.

Although we agree with Wormsley et al that additional prospective studies of CD11c+, CD5+ B-cell leukemias are required to show whether they are a clinically significant subgroup of lymphocytic neoplasms, we consider our case as demonstrating that this phenotype is not necessarily confined to B-CLL or B-PLL, but may, in fact, be found in HCL as well. Until additional information regarding such unusual cases is acquired, we believe that it is prudent to interpret monoclonal antibody studies cautiously, and to rely on current clinical and morphologic findings for diagnostic purposes.

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RESPONSE

We agree that the results of immunophenotypic analyses should be interpreted in the context of conventional morphologic, cytochemical, and clinical diagnostic criteria. However, it is well recognized that the diagnosis of a small proportion of chronic B-cell leukemias will be problematic owing to the considerable heterogeneity of these diseases and their overlap of morphologic, immunophenotypic, and clinical features. These difficulties are reflected by the case of CD5+, CD11c+ hairy cell leukemia (HCL) described by Heimann et al, our series of CD5+, CD11c+ chronic lymphocytic leukemias (CLL), and the recent report by Hanson et al describing CD11c+ B-cell leukemias with CLL morphology and clinical characteristics associated with HCL.

It should be noted that the case described by Heimann et al is uncommon, as CD5 is rarely expressed by leukemias with HCL morphology. In our series of 119 patients with CD5+ B-cell immunophenotypes, 26 (22%) were CD11c+ and all CD11c+ cases with peripheral blood smears available for review (n = 14) had CLL morphology. Many of our cases with CD5+, CD11c+ B-cell immunophenotypes were characterized by the presence of large lymphocytes with abundant cytoplasm. Similar large lymphocyte morphologic features were reported by Hanson et al in their study of CD11c+ B-cell leukemias with CLL morphology. While our CD11c+ cases shared morphologic characteristics with those reported by Hanson et al, the presenting clinical features of our cases were different in some respects. In our patients, lymphadenopathy was common (9 of 14 cases) and splenomegaly was present in 6 of 14 patients. In the patients studied by Hanson, et al., generalized lymphadenopathy was uncommon (1 of 14 cases) and splenomegaly was frequently observed (11 of 14 cases). All of the patients in our study had CD5 immunophenotypes, whereas only 7 of 14 patients evaluated by Hanson et al were CD5+. As the number of patients evaluated in these studies was small, definition of the morphologic, immunophenotypic, and clinical characteristics of CD11c+ B-cell leukemias with CLL morphology will require assessment of a larger number of patients. Nevertheless, our results and those of others indicate that CD11c is not restricted to cases with HCL morphology and that CD11c may be expressed by B-cell leukemias with CLL morphology. Prospective studies of larger numbers of patients will be necessary to determine whether CD11c+ B-cell leukemias with CLL morphology represent a distinct pathologic entity of clinical significance.

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CD5+, CD11c+, CD20+ hairy cell leukemia [letter; comment]

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