To the Editor:

We read with interest the two recent reports in Blood1,2 outlining a unique subset of the chronic lymphoproliferative disorders with morphologic features of chronic lymphocytic leukemia (CLL) and/or prolymphocytic leukemia (PLL). In addition to the characteristic expression of CD5, these patients exhibited concurrent expression of CD11c previously considered specific for hairy cell leukemia (HCL). Both reports noted that tartrate-resistant acid phosphatase (TRAP) was negative in all patients tested. We report a CLL/PLL patient with CD5 and CD11c expression who also exhibited TRAP positivity. The patient is a 65-year-old Caucasian female who presented in 1987 with shoulder pain. There was no lymphadenopathy or organomegaly. The leukocyte count was 30.5 x 10⁹/L with 90% lymphocytes. Limited immunophenotypic analysis of these lymphocytes showed CD19+, CD5+ and moderate intensity κ light chain positivity.

Over the next 4 years the patient was treated with intermittent courses of low-dose chlorambucil, prednisolone, and cyclophosphamide. In May 1991, she had developed palpable splenomegaly (4 cm below left costal margin) with no lymphadenopathy. The leukocyte count was 300 x 10⁹/L with neutrophils of 3 x 10⁹/L, smear cells 69 x 10⁹/L, and lymphocytes 228 x 10⁹/L, 27% of which had characteristic prolymphocytic morphology with a regular cytoplasmic outline. The hemoglobin was 85 g/L and the platelet count was 167 x 10⁹/L.

Bone marrow aspirate displayed normal megakaryopoiesis and markedly reduced erythropoiesis and myelopoiesis with 80% small lymphocytes and 20% prolymphocytes. The trephine was 90% cellular with a diffuse infiltration of lymphocytes. Reticulin was mildly increased.

TRAP staining of the peripheral blood and bone marrow was positive in the majority of prolymphocytes. Electron microscopy (EM) confirmed the presence of populations of mature lymphocytes and prolymphocytes (Fig 1).

Immunophenotypic analysis of peripheral blood and bone marrow displayed positivity for CD5, CD19, CD20, CD22, surface κ 59% (moderate intensity), CD11b, and CD11c with CD11/CD19 coexpression. In addition, the cells were negative for CD25 and CD10.

With light microscopy and EM, the lymphoproliferative disorder of the patient is consistent with CLL/PLL. The expression of CD5 together with the monoclonal light chain expression of moderate intensity concurs with this classification. CD11c and CD11c/19

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Fig 1. This photomicrograph (original magnification ×24,000) illustrates the electron microscopic features of the patient’s peripheral blood prolymphocytic cells.
coexpression was present, whereas CD25 was absent. Importantly, no cytoplasmic projections or ribosomal lamellar complexes characteristic of HCL were noted on EM.

What is intriguing about the current patient is her TRAP positivity. Although TRAP positivity is classically associated with HCL, 10% of HCL are TRAP-negative,3 and up to 5% of PLL patients exhibit TRAP positivity.4

Although we partly agree with Hanso et al’s proposal2 that “CD11c-positive, Leu 8, CD25 and TRAP negative B-cell malignancy constitute a spectrum of disorders... intermediate between CLL and HCL,” we do not consider TRAP negativity an absolute criterion for phenotypic inclusion into this group of chronic lymphoproliferative disorders. It will be may that a specific subgroup of these patients with CLL/PLL morphology and CD11c and CD11c/19 coexpression will, like our patient, exhibit TRAP positivity. The clinical significance of these findings remains to be determined.

REFERENCES


RESPONSE

Prince et al describe an interesting case of a CLL in apparent prolymphocytoid transformation that exhibited TRAP positivity with an immunophenotype showing expression of CD5, CD19, CD20, CD22, CD11c, and monoclonal k Ig. We appreciate their recognition that the distinction between CLL and HCL can sometimes be blurred and that a spectrum of intermediate chronic lymphoproliferative disorders probably exists. Their case brings up two points of interest worth further discussion. One of the main contentsions of our report was the problem of relying on a single laboratory test (eg, CD5, CD11c, etc) as the “gold standard” for the diagnosis of a specific disease entity, such as CLL or HCL. 3 Prince et al point out that TRAP staining is neither an absolutely specific or sensitive test for HCL, which is a well-established fact in the literature.2 Rather, HCL is a disease diagnosed on clinical findings, nuclear and cytoplasmic features of leukemic cells in blood and bone marrow smears, bone marrow histologic sections, and, finally, TRAP cytochemical staining.3 All these components are necessary in the evaluation of HCL, but are not essential for the diagnosis of HCL. The finding of TRAP positivity in this case of CLL in prolymphocytoid transformation is certainly within the known spectrum of TRAP staining, which has been reported in some cases of PLL.2

The second point relates to the biologic role of the CD11c/CD18 complex in chronic lymphoproliferative disease. CD11c is one of the α chain components of the CD11c/CD18 leukocyte adhesion complex.1 Its role in leukocyte biology involves cell-cell and cell-surface interaction. Our data and those of others suggest that this molecule, undoubtedly in association with other lymphocyte migration and adhesion complexes, may selectively promote migration/adhesion to extranodal sites, such as the spleen.2,4,5 The case described by Prince et al had many similarities to the cases described in our study, including the presence of splenomegaly without lymphadenopathy. Unfortunately, CD11c was not evaluated at the initial presentation and we cannot tell from their letter whether CD11c was expressed in the majority or a minority (ie, just the prolymphocytes) of cells. Anecdotally, we have also observed two cases of PLL with moderate to marked splenomegaly, in which the leukemic cells uniformly expressed CD11c, again raising questions as to whether this adhesion complex may mediate the splenic enlargement, which appears to be characteristic of these lymphoproliferative disorders.

REFERENCES

CD5+, CD11C+, trap-positive chronic lymphocytic leukemia/prolymphocytic leukemia [letter; comment]

HM Prince, J Bashford and MB van der Weyden