Soluble Intercellular Adhesion Molecule-1 Correlates With Markers of Disease Activity in B-Cell Chronic Lymphocytic Leukemia

To the Editor:

We were delighted to read the recent article by Christiansen et al.1 dealing with correlation between soluble intercellular adhesion molecule-1 (sICAM-1) and tumor mass in B-cell chronic lymphocytic leukemia (CLL) because we have independently made identical observations.2 Indeed, in 95 previously untreated CD5+ B-cell CLL patients studied with a sandwich enzyme immunoassay (CELLFREE ICAM-1 test Kit; T-Cell Diagnostic, Inc, Cambridge, MA) sICAM-1 levels were found to be significantly increased (606.0 ± 275.9 ng/mL) in comparison to 25 healthy controls (352 ± 162 ng/mL; P < .001).

sICAM-1 levels tended to increase as a function of tumor load. In other words, the more advanced the clinical stage the higher sICAM-1 concentrations (stage A, 505.7 ± 238.2 ng/mL; stage B, 613 ± 210.3; stage C, 817.5 ± 328.4; P < .01 in the analysis of variance). The same applied when patients were analyzed according to the histopathologic pattern of bone marrow (BM) involvement (nondiffuse BM, sICAM-1 = 500.3 ± 211.9 ng/mL; diffuse BM, sICAM-1 = 775 ± 299.5 ng/mL; P < .001).

It is not clear whether the increased sICAM-1 levels result from shedding by normal host cells or by tumor cells. Leukemic cells of CLL patients may express ICAM-1,3 with such a finding being poorly correlated with sICAM-1 levels (r = .244; P = not significant).3 On the other hand, the lack of correlation between sICAM-1 levels and peripheral blood lymphocytosis (r = .107; P = not significant) support the view that sICAM-1 is likely to reflect tumor mass as defined by BM involvement and clinical stage of disease rather than the absolute number of leukemic cells.

The correlation between sICAM-1 and lymphocyte doubling time (LDT) reported by Christiansen et al.1 is not surprising if we look at the functional role of cellular and soluble form of ICAM-1 in patients with malignancy. Cellular expression of ICAM-1 by tumor cells may initially enhance immune recognition and thereby facilitate tumor cytolysis.5 If tumor cells survive this phase, active growth may lead to shedding of sICAM-1, which retains its capacity to bind to LFA-1 and to block LFA sites on T, NK, and LAK cells.6 As a consequence of impaired host antitumor immunity, a more rapid spread of neoplastic cells, reflected in a short LDT, may occur. In our series, sICAM-1 discriminated patients with different LDT value with respect to the whole patient population (Table 1). The same applied when other serum and cellular markers of disease activity (ie, sCD23, thymidine kinase, Ki67 on BM lymphocytes) were taken into account. Finally, patients fulfilling the criteria of Montserrat et al.6 of "smoldering" CLL had sICAM-1 levels significantly lower (443.6 ± 141.8 ng/mL) than those with "active" stage A (569 ± 189 ng/mL; P < .02).

Table 1. Correlation Between LDT and Serum Markers

<table>
<thead>
<tr>
<th>LDT</th>
<th>sICAM-1 (ng/mL)</th>
<th>sCD23 (U/mL)</th>
<th>TK (U/L)</th>
<th>Ki67 (% of BM positive lymphocytes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12 mo</td>
<td>453.6 ± 172.7 (n = 44)</td>
<td>1,486 ± 1,085.3 (n = 44)</td>
<td>10.4 ± 3.1 (n = 17)</td>
<td>0.5 ± 0.12 (n = 17)</td>
</tr>
<tr>
<td>12 mo</td>
<td>770 ± 325.0 (n = 34)</td>
<td>4,240.5 ± 3,098 (n = 34)</td>
<td>33.2 ± 16 (n = 26)</td>
<td>7.9 ± 6.2 (n = 26)</td>
</tr>
</tbody>
</table>

| P Value | <.0005 | <.0005 | <.0005 | <.0005 |

Stage distribution of 43 patients in whom TK and Ki67 were studied was as follows: stage A, 18; stage B, 18; stage C, 7.

Abbreviations: TK, thymidine kinase.
In conclusion, these results show that sICAM-1 concentrations correlate with the progression of disease in CLL, thus providing an additional tool for monitoring the clinical course of patients with early CLL.

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REFERENCES

Soluble intercellular adhesion molecule-1 correlates with markers of disease activity in B-cell chronic lymphocytic leukemia [letter; comment]

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