To the editor:

Conversion of CD38 and/or myeloid-associated marker expression status during the course of B-CLL: association with a change to an aggressive clinical course

We have read with great interest the papers by Ibrahim et al.\(^1\) and Hamblin et al.\(^2\) regarding conversion of CD38 expression and prognosis of B-CLL. The former described how one of their B-CLL patients showed a change of CD38 expression level from low (< 30%) to high (≥ 30%), with significant worsening in the patient’s clinical condition. The latter investigators also reported changes in CD38 expression over time in 10 of 41 CLL patients. Of these 10 patients, 2 showed a conversion from low to high levels of CD38 expression. However, the authors concluded that this conversion was not definitely associated with changes in clinical course.

Here, we describe 3 B-CLL patients who showed a conversion of CD38 expression (case #1, Table 1), CD13 expression (case #2, Table 1), or CD38 and CD15 expression (case #3, Table 1) from low level to high level during follow-up. The expression of these markers was evaluated by multicolor flow cytometry using fresh bone marrow samples. The low level or high level of expression of each marker was defined using 30% as the cutoff value as reported by previous studies.\(^1,4\) This conversion occurred at about 15, 8, and 12 years after diagnosis, respectively, and appeared to be associated with a change in clinical course from indolent to aggressive. These patients died with disease 21 months (case #1), 7 months (case #2), and 3 years (case #3) following this conversion. Of the 3 patients, 2 (cases #2 and #3) also required chemotherapy after conversion. Additionally, there was no evidence of morphologic transformation in the neoplastic cells during this conversion. Thus, the change of surface marker expression status was the only detectable sign for the conversion of clinical course. Previous studies by others and us have suggested that expression of myeloid-associated markers such as CD13, CD14, CD11c, or CD11b on neoplastic lymphocytes in B-CLL correlate with an unfavorable prognosis.\(^5-10\) The change of expression of myeloid-associated markers from low to high level and the possible relationship with clinical progression has not been described previously, to our knowledge.

Whether the levels of CD38 expression change over the course of B-CLL remains controversial. In contrast to the studies cited above, Damle et al have reported that levels of CD38 expression do not show significant change during follow-up among the B-CLL patients they studied.\(^4\) Stable CD38 expression again was noted in another recent study by Durig et al.\(^3\) The cause of this discrepancy among different studies is unclear but may be due to the differences in the length of follow-up of the patients studied, since the conversion may occur very late in the clinical course (15 years in case #1.)

In summary, the findings in our cases suggest that levels of CD38 and myeloid-associated marker expression can change over the course of disease in B-CLL patients and support the observations by Ibrahim et al.\(^1\) and Hamblin et al.\(^2\) Furthermore, the conversion from low- to high-level expression of these markers may be associated with a change from an indolent to an aggressive clinical course as observed by Ibrahim et al.\(^1\) Periodic monitoring of CD38 and, possibly, myeloid-associated markers may be necessary to fully assess the clinical/prognostic status of B-CLL patients. Also, as noted by others, additional studies are necessary to determine the most appropriate prognostic markers and methods for monitoring these patients.

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References


Table 1. Levels of CD38 and/or myeloid-associated marker expression over the course of disease in 3 B-CLL patients

<table>
<thead>
<tr>
<th>Case #1</th>
<th>Month*</th>
<th>178</th>
<th>182†</th>
<th>203</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD38 level</td>
<td>20%</td>
<td>38%†</td>
<td>57%</td>
</tr>
<tr>
<td>Case #2</td>
<td>Month</td>
<td>93</td>
<td>94</td>
<td>96†</td>
</tr>
<tr>
<td></td>
<td>CD13 level</td>
<td>2%</td>
<td>0%</td>
<td>50%†</td>
</tr>
<tr>
<td>Case 3</td>
<td>Month</td>
<td>136</td>
<td>147†</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CD38 level</td>
<td>21%</td>
<td>48%†</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CD15 level</td>
<td>13%</td>
<td>38%†</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Months after initial diagnosis.
†The time and levels at marker conversion.
NA indicates not applicable.
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