Correspondence

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The greater volume and complexity of laboratory data being produced would seem to suggest a larger role for pathologists as interpreters of these data. Yet, many clinicians seem less receptive to this role for pathologists, preferring instead to regard the laboratory merely as the source of test results. Despite the laudable efforts of pathology societies to advance the role of pathologists as clinical consultants, it is becoming increasingly difficult to remain optimistic about the future of our specialty. As the authors note, the commoditization of laboratory testing shifts the emphasis toward maximizing productivity rather than promoting appropriate use of laboratory testing. This mentality undermines the clinical-laboratory interface and cost-effective patient care.

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Patient testing. One consequence of the changing laboratory-clinical interface cited by the authors is that physicians have less exposure to laboratory medicine during their training and, therefore, have little or no understanding of what actually goes on in a clinical laboratory. Evidence of this deficiency is experienced directly by laboratory technologists, who are confronted by irate physicians who demand platelet counts on clotted CBC samples or tests for sexually transmitted diseases on unlabeled samples or who fail to understand that hemolyzed blood samples cause erroneous K+ measurements.

Table 1

Improperly Collected Samples That Are Not Rejected for Point-of-Care Testing

<table>
<thead>
<tr>
<th>Sample Type</th>
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</thead>
<tbody>
<tr>
<td>Unlabeled samples</td>
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<tr>
<td>Unmixed samples</td>
</tr>
<tr>
<td>Clotted samples</td>
</tr>
<tr>
<td>Hemolyzed samples</td>
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<tr>
<td>Intravenous contaminated samples</td>
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<tr>
<td>Improperly performed finger-stick samples</td>
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</tbody>
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To the Editor

We read with interest the article “Diagnostic Usefulness and Prognostic Impact of CD200 Expression in Lymphoid Malignancies and Plasma Cell Myeloma” by Alapat et al.1 The authors presented as one of their findings flow cytometric data on CD200 expression in 52 cases of plasma cell myeloma (PCM), and the proportion of CD200+ cases (71%) was similar to that previously reported by our group (in a cohort of 76 patients)2 and by other authors.3 In addition, the authors correlated CD200 immunophenotypic expression findings with gene expression profiling (GEP) information; of 27 patients with serial GEP analyses, 5 (19%) had a change in CD200 gene expression, and this change (particularly loss of CD200 expression) may have occurred during disease progression.3 However, no serial evaluation of CD200 expression by flow cytometry (FC) was available in their cohort.

The authors incorrectly state that there are no literature data on the FC stability of CD200 in PCM. In our previous article, we reported the stable expression of CD200 in 19 patients with PCM who had serial FC analyses.2 Because there are no additional data reported on the stability of CD200 expression in PCM, we chose to expand and detail our findings in a cohort of 32 PCM bone marrow biopsy specimens (from 21 newly diagnosed cases and 11 treated patients with residual disease). We serially studied the CD200 expression patterns in neoplastic plasma cells by using 4-color FC with antibodies against the following antigens: CD19, CD20, CD38, CD45, CD56, CD117, CD200, and surface and cytoplasmic light chains. Immunophenotypic analysis was performed according to previously reported methods.4 Antigen expression in plasma cells (including CD200) was assessed based on an isotype control tube containing CD38. Positivity for an antigen was defined as at least 20% plasma cells exceeding the isotype control threshold. We defined a change in CD200 expression as loss (switch from positive to negative) or gain (switch from negative to positive) of antigen expression, based on the isotype control.

Our patient group included 24 men and 8 women, with a median age at diagnosis of 61 years (range, 35-76 years). Based on the International Staging System, 27% patients were stage I, 44% were stage II, and 30% were stage III. Of 32 PCMs, 20 (63%) were found to be CD200+. The median percentage of neoplastic plasma cells exceeding the isotype control threshold was 88% (range, 60%-100%) in CD200+ cases compared with 2% (range, 0%-6%) in CD200− cases. When comparing the CD200+ PCMs with CD200 PCMs, we found no differences in the frequency of cases with IgA heavy chain isotype, elevated β2-microglobulin level, low albumin level, elevated C-reactive protein level, lactate dehydrogenase, or cytogenetic abnormalities (data not shown).
Additional immunophenotypic findings at baseline included the following: CD19+, 97% of cases; CD56+, 69%; CD20+, 28%; CD45+, 53%; and CD117+, 31%; 22/32 (69%) showed cytoplasmic κ light chain restriction. These findings are similar to previously published data.2,5 Of the 20 CD200+ PCMs, 13 were newly diagnosed cases and 7 were in treated patients and had a total of 26 follow-up FC analyses. Of the 12 CD200– PCMs, 8 were newly diagnosed and 4 were in treated patients and had 14 follow-up FC analyses. The median time from baseline (diagnosis or first encounter) to follow-up FC was 6 months (range, 1–17 months); 8 patients had 2 follow-up analyses, while the remainder had 1 follow-up FC analysis. In addition to standard chemotherapy regimens, 22 of 32 patients were treated with melphalan-based high-dose chemotherapy, followed by autologous stem cell transplantation (SCT), while 3 of 32 had allogeneic SCT.

None of the 12 patients with CD200– PCM had a gain of CD200 expression at follow-up, including 2 with 2 follow-up FC analyses. Similarly, 17 (85%) of 20 patients with CD200+ PCM had no changes in CD200 expression at follow-up; this corresponded to 22 (85%) of 26 follow-up FC analyses in this group. In 11 patients, follow-up FC demonstrated persistent disease after autologous SCT (at approximately day 100); 1 patient had follow-up FC positive for persistent PCM post–autologous SCT; the remaining 8 patients in the CD200+ PCR group had follow-up analyses after chemotherapy, with the majority (11/20) undergoing a pre–autologous SCT evaluation. Of 6 patients with CD200+ PCM with 2 follow-up analyses, 5 demonstrated preserved CD200 expression in both instances—before and after autologous SCT.

In contrast, 3 (15%) of 20 patients with CD200+ PCM had a switch to a CD200– immunophenotype; this corresponded to 4 (15%) of 26 follow-up FC analyses in this patient group. One of the patients was CD200+ at diagnosis and became CD200– at his day 100 post–autologous SCT evaluation, which demonstrated low-level persistent PCM. The second patient switched from a CD200+ immunophenotype at diagnosis to CD200– plasma cells in 2 instances, following chemotherapy and during his pre–autologous SCT evaluation, respectively. The third patient had already been treated when he was evaluated at our institution, was CD200+ at his first FC analysis, and became CD200– 6 months later at his pre–autologous SCT evaluation. The initial level of CD200 expression in these 3 patients was strong and similar, in terms of proportion of CD200+ plasma cells exceeding the isotype control threshold, to the remainder of the cohort (median, 95% vs 88%). When compared with their baseline immunophenotype, 2 of 3 patients with loss of CD200 had otherwise similar immunophenotypic findings at follow-up, while the third patient had a change in CD19 expression (from negative to positive) in one analysis and in CD56 expression (from positive to negative) in the second analysis. The remainder of the cases that did not show a change in CD200 expression showed variations in CD56 expression (from positive to negative, 1 case), CD20 expression (from positive to negative, 1 case), CD45 expression (from negative to positive, 6 cases), and CD117 expression (from positive to negative, 4 cases).

Our findings indicate that CD200 expression in PCM determined by FC is relatively stable over time and during the course of chemotherapy. Only 3 (9%) of 32 patients demonstrated a change in expression, from CD200+ to CD200–, and none of the CD200– cases showed the reverse finding. These numbers are similar to those generated by microarray analysis by Alapat et al,1 who found that 4 (18%) of 22 patients with serial GEP analyses showed significant down-regulation of the MOX2 gene, which encodes CD200. It has been demonstrated that CD200 expression established by GEP and FC shows a good, though not perfect, correlation,1,3 and our FC findings of CD200 stability support this finding when compared with the GEP stability results from the latter study. Because Alapat et al1 hypothesize that loss of CD200 expression may serve as a marker for disease progression in PCM, the availability of FC for examining this marker offers a practical alternative to GEP for the detection of this potential prognostic indicator in PCM.

We demonstrated a temporal variation in CD200 expression by FC in a subset of CD200+ PCMs. We confirmed the findings of Alapat et al1 and showed that CD200 expression in PCM may be useful pursuing not only at diagnosis but also in follow-up analyses as a potential prognostic marker. While further study of a larger number of cases is needed to validate these findings, identification of loss of CD200 in PCM may support a new role for FC in providing additional prognostic information.

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References