CD20 Expression in Non-Myeloma Immunoproliferative Disorders

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Abstract

Background: The majority of plasma cell myelomas (PCMs) are positive for CD200, a membrane protein with immunosuppressive function. CD200 expression has also been described in non-Hodgkin B-cell lymphomas, such as chronic lymphocytic leukemia/small lymphocytic lymphoma, hairy cell leukemia, medullary large B-cell lymphoma, and lymphoplasmacytic lymphoma (LPLs). Although there is no literature data on CD200 expression in the other plasma cell dyscrasias, we studied the expression of CD200 by flow cytometry (FC) in cases of monoclonal gammopathy of undetermined significance (MGUS), LPL, and other plasmablastic lymphomas (PBL), and correlated expression with clinicopathologic parameters.

Design: 74 diagnostic bone marrow (BM) aspirates (61 MGUS, 10 LPL, and 3 PBL) were evaluated by 4-color FC with antibodies against CD5, CD10, CD19, CD20, CD38, CD45, CD56, CD117, CD200, and surface and cytoplasmic light chains. Expression of CD200 was assessed in plasma cells (PCs) based on an isotype control tube containing CD200. CD200 expression status in patients with MGUS was then correlated with clinicopathologic parameters, including CBC data, immunophenotype, BM morphology, and cytogenetics. For comparison, we evaluated CD200 expression in 74 newly diagnosed PCMs BM aspirates.

Results: 33/61 (54.1%) MGUS, 2/10 (20.0%) LPLs, and 3/30 (10%) PBLs were CD200(−). CD200 expression was found in 32/56 (57.1%) PCs of MGUS, 21/29 (72.4%) LPLs, and 27/28 (96.4%) PBLs. Comparison of clinicopathologic parameters for all MGUS cases, based on CD200 expression status, showed no differences between the two groups. 74% (57/74) of newly diagnosed PCLs were CD200(−). The proportion of CD200(+) new PCMs in our series was significantly higher than in the MGUS cohort (p=0.030) and LPLs (p=0.002). Conclusion: 54% of MGUS in our series are CD200(−), which is significantly lower than the proportion of CD200(+) new PCMs reported in our study (73%) and in the literature. Although we also demonstrated undetermined expression of CD200 in a limited number of LPLs and PBLs, respectively, the proportion of CD200(+) LPLs (8/10, 80%) reported in a recent immunohistochemistry study.

Introduction

CD200 is a member of the type-I immunoglobulin superfamily that is highly expressed in the central nervous system, dendritic cells, and lymphocytes. CD200 is functionally involved in an immunosuppressive signaling pathway, via interaction with its receptor, CD200R, with downstream effects of macrophage inhibition, induction of regulatory T cells, and inhibition of tumor-specific T cells. Besides being expressed in normal tissues, CD200 has also been demonstrated in solid tumors and hematologic malignancies, such as acute leukemias, chronic lymphocytic leukemia / small lymphocytic lymphoma, hairy cell leukemia, medullary large B-cell lymphoma, classical Hodgkin lymphoma, and angioimmunoblastic T-cell lymphomas. In addition, CD200(+) neoplastic plasma cells frequently upregulate CD200 expression, as demonstrated by the large proportion of CD200(+) plasma cell myeloma (PCM) cases (approximately 70%) found by gene expression profiling (GEP) and flow cytometry (FC). In contrast, normal plasma cells are CD200(−).

Although CD200 expression and stability have been studied in PCM, there are no FC literature data on CD200 expression in other, non-PCM immunoproliferative disorders, such as monoclonal gammopathy of undetermined significance (MGUS), LPL, and other plasmablastic lymphomas (PBL), and correlated expression with clinicopathologic parameters. We also compared CD200 expression in the neoplastic plasma cells in these conditions, with CD200 expression in newly diagnosed PCM cases.

Materials and Methods

74 patients with MGUS, LPL or PBL, and 74 patients with PCM that had FC data available were included in the study.

- Four-color FC was performed with antibodies against CD5, CD10, CD19, CD20, CD38, CD45, CD56, CD117, CD200, and light chains.

- CD200 expression was found in 32/56 (57.1%) PCs of MGUS, 21/29 (72.4%) LPLs, and 27/28 (96.4%) PBLs. All and MGUSs contained an isotype-matched control tube containing CD200 to establish the positive staining threshold for plasma cells. Positivity for an antigen was defined as at least 20% of events beyond a 2% isotype control threshold.

- Clinical and laboratory data was available from chart review.

Results

- CD200 expression was present in plasma cells of 72.9% of PCMs; 54.1% of MGUSs, 20% of LPLs, and 33% of PBLs (Figures 1 and 2).

- The proportion of CD200(+) PCM cases was significantly higher than in CD200(+) MGUSs (p=0.030) and LPLs (p=0.002).

- CD200 expression was found in 32/56 (57.1%) non-IgM MGUSs (IgG or IgA) and 1/5 (20%) IgM MGUSs.

- Comparative clinical and laboratory findings in CD200(+) and CD200(−) MGUS patients are summarized in Table 1 and show no significant differences.

- The median percentage of neoplastic plasma cells exceeding the isotype control threshold was 90% (range, 29-190%) in CD200(+) PCM cases, which was also higher than in CD200(+) MGUS cases (p<0.001).

- There was no difference in the frequency of cases with CD200(+) plasma cells when comparing patients with MGUS vs. LPL (p=0.085).

Conclusions

- CD200 expression was present in plasma cells of 54.1% MGUSs, 20% LPLs, and 33% PBLs by flow cytometric analysis.

- The proportion of cases with CD200(+) plasma cells was significantly higher in PCM than in MGUS and LPL.

- In addition, the larger proportion of CD200(+) plasma cells that exceeded the isotype control threshold in positive cases indicates a higher density of CD200 antigen in PCM plasma cells, compared to MGUS.

- Our findings demonstrate a predominance of CD200(+) cases in a limited number of LPLs, which is in contrast to the high percentage of CD200(+ LPLs (8/10, 80%) reported in a recent immunohistochemistry study. It is likely that CD200 expression was estimated in the B cells, since no specific reference was made to plasma cells in that particular publication.