Flow Cytometric Immunophenotyping of Plasmacytic Neoplasms

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Plasmacytic differentiation may be seen in a significant minority of B-cell non-Hodgkin lymphomas (NHLs). Lymphoplasmacytic lymphoma (LPL), a B-cell NHL whose cytologic composition includes small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells, is arguably paradigmatic of this phenomenon. In patients with LPL, plasmacytic differentiation often manifests clinically with the secretion of a monoclonal immunoglobulin (typically of IgM type) and signs and symptoms of hyperviscosity (Waldenström macroglobulinemia). However, plasmacytic differentiation in the B-cell NHLs is not limited to LPL; it is not infrequent in extranodal marginal zone B-cell lymphoma (mucosa-associated lymphoid tissue [MALT] lymphoma) and may also be seen in follicular lymphoma and B-cell chronic lymphocytic leukemia. Nor is plasmacytoid differentiation limited to the low-grade B-cell NHLs; in some cases of diffuse large B-cell lymphoma, for example, plasmacytoid immunoblastic differentiation may be prominent. Similarly, a monoclonal IgM gammopathy may accompany B-cell NHLs other than LPL.

In certain circumstances, distinction between a B-cell NHL with plasmacytic differentiation and a plasma cell neoplasm (ie, plasma cell myeloma or solitary plasmacytoma) may be diagnostically challenging. For example, the pathologist confronted with a fine-needle aspirate or needle core biopsy specimen of an extranodal lesion that comprises predominantly mature plasma cells may be unable to determine whether the patient has a MALT lymphoma or plasma cell myeloma. Indeed, some have argued that a subset of cases designated “extramedullary plasmacytoma” may, instead, represent MALT lymphomas with extreme plasmacytic differentiation. At the other end of the cytologic spectrum, a lesion that consists of large cells with plasmacytoid immunoblastic features might represent large B-cell lymphoma or plasmablastic myeloma (although some have suggested on the basis of immunohistochemical analysis that plasmablastic lymphoma may be more closely related to plasma cell myeloma than to diffuse large B-cell lymphoma). The differential diagnosis in such cases is made even more challenging when, as is often the case at the time of biopsy, the patient has not undergone a thorough staging evaluation for lymphoma or myeloma.

It is in precisely this setting that the study reported by Seegmiller and colleagues in this issue of the Journal may prove useful. The authors sought to determine whether flow cytometric immunophenotyping of neoplastic plasma cells might facilitate the distinction between B-cell NHLs with plasmacytic differentiation and myeloma or plasmacytoma. They compared the immunophenotypic features of the CD38(bright)+ plasma cells in 41 cases of B-cell NHL with plasmacytic differentiation with those of the plasma cells in 41 consecutive cases of bone marrow plasma cell myeloma. CD19, CD45, and surface membrane (as opposed to cytoplasmic) immunoglobulin were expressed more commonly by the plasma cells in B-cell NHLs with plasmacytic differentiation than those of the plasma cells in 41 consecutive cases of bone marrow plasma cell myeloma. CD19, CD45, and surface membrane (as opposed to cytoplasmic) immunoglobulin were expressed more commonly by the plasma cells in B-cell NHLs with plasmacytic differentiation than by the plasma cells in myeloma. In the case of CD56 expression, the reverse was true, whereas CD20 expression was detected with a similar frequency in B-cell NHLs with plasmacytic differentiation and myeloma. (For comparison, normal plasma cells are typically CD19+, CD20−, CD45+, and CD56− or low when evaluated by flow cytometry.) Significantly, whereas the plasma cells in 95% of cases of B-cell NHL were CD19+, this antigen was negative in 90% of cases of plasma cell myeloma. In this initial series of 82 cases, classification of a given case as B-cell NHL or myeloma solely...
on the basis of the presence or absence of CD19 on the plasma cells yielded a diagnostic accuracy of 93%. Of the 6 cases that would have been misclassified on the basis of CD19 expression alone, 3 would have been correctly assigned by incorporating CD56 expression into the diagnostic algorithm.

Next, the authors tested their immunophenotypic approach in a separate series of 13 small biopsy or fine-needle aspiration specimens, including cases of osseous lesions from patients with myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma.11 As expected, all myeloma-associated osseous lesions and solitary plasmacytomas of bone were CD19− and/or CD56(bright)+, but 2 of the 4 extramedullary plasmacytomas (both of which represented lesions of thyroid, a common site of origin for MALT lymphoma) exhibited a composite immunophenotype associated with B-cell NHLs: CD19+, CD45+, and CD56−. The latter finding prompted the authors to suggest, as has been argued previously,8 that some cases of extramedullary plasmacytoma may actually represent MALT lymphoma or other B-cell NHLs with plasmacytic differentiation. In further support of this concept are the many reports of extramedullary plasmacytoma in sites that are now recognized as typical sites of origin for MALT lymphomas, including thyroid (in association with Hashimoto thyroiditis), lung, gastrointestinal tract, breast, and skin (reviewed by Dimopoulos et al14).

Flow cytometry has been used in previous studies of the immunophenotype of neoplastic plasma cells in cases of B-cell NHL with plasmacytic differentiation15 and plasma cell myeloma.12,13,16 In general, the data from these earlier studies and the present study are concordant in that the plasma cells in cases of B-cell NHL have typically been CD19+,15 whereas those in myeloma have usually been CD19−.12,13,16 Taken together, these data suggest that flow cytometric detection of CD19 expression by neoplastic plasma cells in an individual plasmacytic neoplasm would increase the likelihood of its being a B-cell NHL, and the absence of CD19 (and/or presence of bright CD56 expression)11−13,15,16 would tend to favor myeloma or plasmacytoma. Flow cytometric immunophenotyping may, therefore, be a useful adjunct in the distinction between B-cell NHLs with plasmacytic differentiation and plasma cell myeloma or plasmacytoma.

Although not specifically addressed in the study by Seegmiller et al,11 it is reasonable to speculate that evaluation of surface or cytoplasmic immunoglobulin heavy chain expression might refine further the immunophenotypic distinction between a B-cell NHL with plasmacytic differentiation and plasma cell myeloma or plasmacytoma because IgM+ plasma cell myeloma is exceedingly rare.17 Nevertheless, as illustrated by the study by Seegmiller et al,11 immunophenotypic distinction between B-cell NHLs with plasmacytic differentiation and plasma cell myeloma or plasmacytoma is imperfect. Moreover, the plasma cell immunophenotype in myeloma may differ in association with specific clinical18 and genetic19 variables. Therefore, it would seem prudent to continue to recommend clinicopathologic correlation, including appropriate laboratory and radiographic studies, and bone marrow examination in the evaluation of lesions found to contain neoplastic plasma cells.

References


