

The Role of Morphology, Cytochemistry and Immunohistochemistry in the Diagnosis of Lymphoproliferative Disorders

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Abstract

The bone marrow examination is a valuable procedure in the diagnosis and management of patients who have NHL. Posttherapy bone marrow examination is useful for assessing a patient's response to chemotherapy and for monitoring previously treated patients for evidence of recurrent disease. The bone marrow examination should include trephine biopsy section, trephine imprints, aspiration smears, clot sections and blood smears and all of these preparations should be studied by the same pathologist. In addition to the morphologic evaluation, the aspirated marrow is the best material for several important supplemental studies for characterization of NHLs, including immunophenotyping by flow cytometry, cytogenetics, most molecular studies, and microbiologic cultures. Flow cytometric immunophenotyping studies to determine lineage, clonality of B-cell processes, and approximate stage of neoplastic infiltrates are the most useful adjuvant to morphologic assessment for NHLs. This review concentrates on the characteristic morphology, cytochemistry, immunohistochemical assessment and immunophenotyping of each clinical entity according to WHO classification. For the differential diagnosis, reactive lymphoid lesions, including lymphocytic aggregates, reactive polymorphous lymphohistiocytic lesions, benign follicles with germinal centers and polyclonal immunoblastic proliferations will be discussed.

1. Presented Cases

1.1. Case 1

A 68-year-old woman with complaints of weight loss and night sweat presented with extensive cervical and abdominal lymphadenopathy. Histological examination of the excised cervical lymph node revealed a malignant lymphoma, diffuse large B cell. White blood cell count was $9.8 \times 10^9/l$ with 5% circulating lymphoma cells. Bone marrow involvement was noted with 9.6% of neoplastic lymphoid cells which were positive for CD20 and CD79a, but negative for CD3 on immunohistochemistry.

1.2. Case 2

A 52-year old man presented with submandibular

mass. Histological examination of the salivary gland revealed low grade mucosa associated lymphoid tissue (MALT)-lymphoma. Immunohistochemical stain of this tumor was positive for CD79a and CD23 and negative for CD3. White blood cell count was $3.1 \times 10^9/l$ with 1% circulating atypical cell. Bone marrow aspirate revealed 94.6% of neoplastic lymphoid cells, including 16.4% of large cells and 78.2% of small lymphoid cells.

1.3. Case 3

A 68-year-old-man presented with multiple lymphadenopathy. Histological examination of the cervical lymph node revealed mantle cell lymphoma. Immunohistochemical stain of this tumor was positive for CD5 and negative for CD10 and CD23, but noncontributory for cyclin D1. White blood cell count was $3.9 \times 10^9/l$ with 2% circulating lymphoma cells. Bone marrow aspirate re-

vealed 49.0% of small to medium sized, round neoplastic lymphoid cells. Flow cytometry of these cells was positive for CD19, CD20, CD5, Sm IgM, Sm lambda and FMC 7, but negative for CD10, CD3 and CD7.

1.4. Case 4

A 64-year-old woman with complaints of fever, chill and night sweat presented multiple lymphadenopathy and hepatosplenomegaly. Histological examination of neck lymph node revealed peripheral T cell lymphoma, unspecified, pleomorphic large cells. Immunohistochemical stain of this tumor was positive for CD3, CD4, UCHL-1, TIA and Ki67, but negative for CD79a, CD10, CD8, CD30, bcl-6 and CD56. White blood cell count was $1.8 \times 10^9/l$ with 1% circulating atypical lymphocyte. Bone marrow aspirate revealed clustered or scattered individual neoplastic lymphoid cells and mild increase of hemophagocytic histiocytes.

1.5. Case 5

A 31-year-old man with complaints of fever, chill and sweating presented splenomegaly and multiple lymphadenopathy at both axillae. White blood cell count was 1.7

$\times 10^9/l$ without evidence of circulating lymphoma cells. Bone marrow aspirate revealed small number of large-sized neoplastic lymphoid cells, having irregular nuclei and moderate amount of cytoplasm in the small lymphocytic background. Immunohistochemical staining of large, neoplastic lymphoid cells were positive for CD20 and CD79a, but negative for CD3, CD15 and CD30. On the contrary, surrounding small lymphoid cells were positive for CD3.

1.6. Case 6

A 14-year-old girl with a history of kidney transplantation due to severe crescentic rapidly progressive glomerulonephritis on September, 1998 admitted with abdominal pain and nausea. White blood cell count was $28.4 \times 10^9/l$ with 13% circulating lymphoma cells. Bone marrow aspirate revealed 92.8% of neoplastic lymphoid cells. Flow cytometry of these cells was positive for CD19, CD22, CD20, FMC7, Sm IgM and Sm kappa, but negative for CD2, CD3, CD5 and CD7. In situ hybridization and PCR for EBV were negative. Histological examination of the kidney revealed no evidence of acute and chronic rejection.