Central nervous system involvement after follicular large cell lymphoma

The central nervous system (CNS) becomes involved after non-Hodgkin's lymphoma (NHL) in about 8 % of patients, but rarely after follicular lymphoma. Serum lactate dehydrogenase (LDH) concentrations over twice the normal, bone marrow involvement and stage IV disease are known risk factors for CNS involvement. We describe two cases of CNS involvement after follicular large cell lymphoma (FLCL) in two patients who had the above mentioned risk factors at diagnosis.

Patient #1. Follicular large cell lymphoma stage IV Bcl-2+, t(14;18) positive by polymerase chain reaction (PCR); was diagnosed in a 44-year old male. Laboratory tests at diagnosis revealed high levels of LDH (973 U/L) and β2-microglobulin (β2m) (12.6 mg/L). Two courses of adriamycin, vincristine and prednisone (APO) resulted in a partial remission. Two courses of dexamethasone, cisplatinum and aracytin (DHAP), and high doses of etoposide and methotrexate resulted in partial remission. Relapse occurred one month later with leukemization (WBC $53{,}930\times10^6$/L, with 36% of immature lymphocytes), and an LDH of 17,092 U/L. Chemotherapy with rituximab, aracytin and mitoxantrone was started followed by granulocyte colony-stimulating factor and peripheral blood progenitor cell (PBPC) harvest. A few after harvest he developed right eyelid ptosis and hemiparesis. Computed axial tomography of the brain was normal. Lumbar puncture showed a massive infiltration (940×10^6/L) of heterogeneously sized cells, from very large to medium-size, with moderately abundant basophilic cytoplasm; the nuclei were irregularly lobulated and showed slight and homogeneous chromatin condensation, with occasional poorly outlined nucleoli (Figures 1 and 2). Cells were negative to peroxidase reaction. Immunophenotyping showed positivity for CD19, CD20, CD10, κ+. The patient was submitted to intrathecal chemotherapy with aracytin, methotrexate and prednisone and achieved normalization of cerebro-spinal fluid (CSF). He underwent an autologous peripheral blood stem cell transplant but died from disease progression 3 months later.

Patient #2. Follicular lymphoma stage IV Bcl-2 +, t(14;18) positive by PCR; was diagnosed in a 56-year old male. Laboratory tests revealed high levels of LDH (801 U/L). Five courses of CHOP resulted in a good partial remission. Before the start of the 6th cycle of CHOP, the patient developed chin and lip anesthesia, and hyposthenia of the left arm. Laboratory tests revealed high LDH values (958 U/L), lumbar puncture showed a massive infiltration (540×10^6/L) of immature lymphoid cells with similar morphology to those of patient #1. Immunophenotyping showed positivity for CD10, CD19, κ+. The patient was submitted to intrathecal chemotherapy with aracytin, methotrexate and prednisone, achieving normalization of CSF, and chemotherapy with rituximab, aracytin and mitoxantrone. The patient died from disease progression 2 months later.

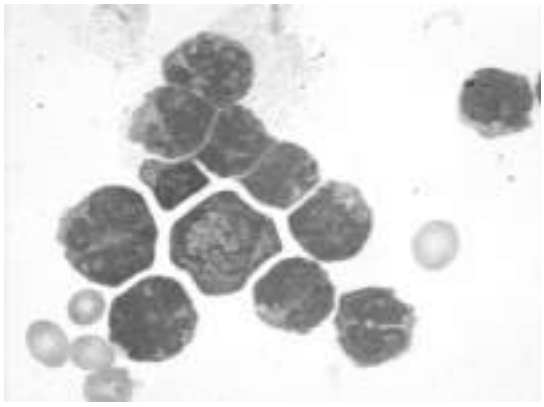

Figure 1. Lymphoma cells in cerebrospinal fluid.

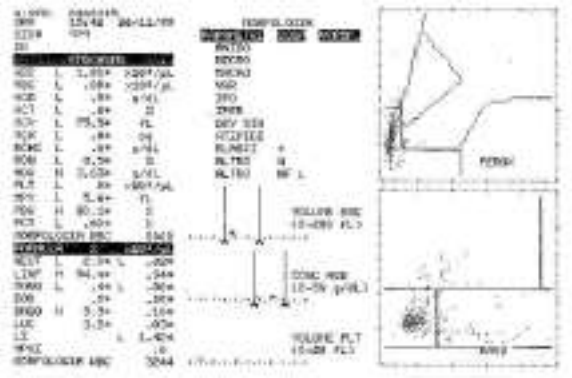

Figure 2. Automated cytochemistry in CSF in patient #1.

FLCL is an uncommon disease representing 3% to 7% of NHL.[1-2] It is distinguished from other follicular lymphomas both in the Working formulation and in the REAL classification.[3] Tomita *et al.* identified a serum LDH concentration ≥ twice normal, stage IV and bone marrow involvement, as predictive factors for CNS involvement in NHL. All of these factors were present in our patients at diagnosis.[4] CNS involvement after follicular lymphoma and FLCL is extremely rare, in fact there are only a few reports in the literature.[1,4-5] According to available literature CNS involvement after FLCL carries a poor prognosis as confirmed by our cases.[4-5] We, therefore, suggest that CNS prophylaxis should be considered for NHL patients with a serum LDH concentration ≥ twice normal at diagnosis, especially if associated with stage IV disease and bone marrow involvement.

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References

1. Rodriguez J, McLaughlin P, Hagemeister FB, et al. Follicular large cell lymphoma: an aggressive lymphoma that often presents with favorable prognostic features. Blood 1999; 93:2202-7.
2. National Cancer Institute sponsored study of classifications of non-Hodgkin's lymphomas: summary and description of a working formulation for clinical usage. The Non-Hodgkin's Lymphoma Pathologic Classification Project. Cancer 1982; 49:2112-35.
3. Harris NL, Jaffe ES, Stein H, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood 1994; 84:1361-92.
4. Tomita N, Kodama F, Sakai R, et al. Predictive factors for central nervous system involvement in non-Hodgkin's lymphoma: significance of very high serum LDH concentrations. Leuk Lymphoma 2000; 38:335-43.
5. Lasota J, Nordling S, Miettinen M. Testicular diffuse large cell lymphoma with tubule preservation-molecular genetic evidence of transformation from previous follicular lymphoma. Virchows Arch 2000; 436:276-83.