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 leukeimization (WBC 53,930×10⁶/L, with 36% of immature lymphocytes), and an LDH of 17,092 U/L. Chemotherapy with rituximab, aracytin and mitoxantrone started after the granulocyte colony-stimulating factor and peripheral blood progenitor cell (PBPC) harvest. A few months after, he developed right eyelid ptosis and hemiparesis. Computed axial tomography of the brain was normal. Lumbar puncture showed a massive infiltration (940×10⁶/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, CD79a, CD23, and negativity for CD5, CD3, CD4, CD8, BCL-2, and CD103. 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.

FLCL is an uncommon disease representing 3% to 7% of NHL. It is distinguished from other follicular lymphomas both in the Working formulation and in the REAL classification. 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. CNS involvement after follicular lymphoma and FLCL is extremely rare, in fact there are only a few reports in the literature.1-2 According to available literature CNS involvement after FLCL carries a poor prognosis as confirmed by our cases.1-2 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.

Luca Laurenti, Simona Sica, Maria Teresa Voso, Patrizia Chiusolo, Gina Zini, Giuseppe Leone
Dept. of Hematology, Catholic University, Rome, Italy

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Correspondence. Laurenti Luca, M.D., Divisione di Ematologia, Istituto di Semeiotica Medica, Università Cattolica Sacro Cuore, largo A. Gemelli, 8, 00168 Roma, Italy. Phone: international +39-06-35509353 - Fax: international +39-06-3017319 - E-mail: emacat@rm.unicatt.it

References


Figure 1. Lymphoma cells in cerebrospinal fluid.

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