CEREBROSPINAL FLUID PLEOCYTOSIS IN ACUTE LYMPHOBLASTIC LEUKEMIA WITHOUT CENTRAL NERVOUS SYSTEM RELAPSE*

A Report of Three Cases

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Three patients with acute lymphoblastic leukemia (ALL) developed mononuclear cells in the cerebrospinal fluid (CSF) after a flu-like histroy during maintenance treatment. None of the patients showed evidence of central nervous system (CNS) involvement by either clinical or laboratory follow-up. Although the presence of > 5 mononuclear cells/μl in the CSF is important, it may not necessarily indicate CNS disease. Clinical findings, history and cell morphology must be evaluated before deciding on further treatment.

Key words: acute lymphoblastic leukemia, central nervous system involvement, pleocytosis.

Meningeal relapse (MR) in patients with acute lymphoblastic leukemia (ALL) is defined as the presence of at least 5 mononuclear cells/μl of cerebrospinal fluid (CSF) with leukemic blasts apparent on cytocentrifuged sample[1]. However, cytomorphological evaluation and diagnosis of MR have remained controversial in patients with low CSF counts[1-6]. Flow cytometric analysis may help in the diagnosis, if there is an adequate number of cells in the CSF[2,3,7]. We report herein three patients with ALL from Hacettepe University İhsan Doğramacı Children's Hospital, who were noted to have mononuclear cells (MNC) in routine CSF samples obtained during maintenance phase intrathechal (IT) treatments on St Jude total XI protocol and who remained free of meningeal relapse.

Case Reports

Case 1

Twenty mononuclear cells/μl were detected in the routine CSF sample (20 mg/dl protein) obtained from a 12-year-old male with ALL during the first year of maintenance therapy. There was a history of a flu-like illness with headache three weeks earlier. Based on the mature morphology of the cells,

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maintenance therapy was continued according to the protocol without additional treatment. Follow-up CSF findings performed three times every two months were all within normal range.

Case 2

A 12-year-old male was diagnosed as ALL. The analysis of the CSF obtained at routine IT treatment at tenth month of maintenance therapy revealed 20 cells/μl and 32 mg/dl protein. No additional treatment was initiated because of the presence of morphologically mature MNC and absence of blasts in CSF cytology. This patient also had a history of an upper respiratory infection one week prior to this finding. Cerebrospinal fluid cytology was normal at two weeks and eight months follow-up.

Case 3

Cerebrospinal fluid pleocytosis was detected at ninth month of maintenance treatment in a 12-year-old male with ALL. Cytology revealed 20 MNC/μl with no blasts and CSF protelin was 28 mg/dl. There was a history of fever, headache and aphthous stomatitis three weeks earlier. No additional treatment was administered and follow-up CSF studies at one, three and five months were within normal limits.

Discussion

All three patients were free of neurological signs and symptoms and CSF examinations revealed > 5 MNC/μl without blastic appearance. Five-to-eight month follow-up CSF samples were within normal limits in all patients.

There have been conflicting reports in the evaluation of CSF findings in patients with ALL. In the presence of blasts, some investigators consider 10 cells/μl as significant, while others suggest that even < 5 cells/μl may indicate relapse[2,6]. In one study, 12 out of 23 patients treated for CNS involvement had < 5 cells/μl and later showed pleocytosis[2,3].

A common problem in the interpretation of cells in the CSF is the differentiation of normal and blastic cells[2,5]. Cerebrospinal fluid CSF cytocentrifugation is an important tool for differential diagnosis. Cerebrospinal fluid CSF involvement with leukemia, lymphoma, histiocytosis, multiple myeloma, or primary and metastatic CNS tumors may be detected by this technique[6]. Amo et al.[7] reported a patient with ALL with > 500/μl cells in CSF with some suspected blasts characterized by flow cytometry as a nonmalignant T-cell reaction. This finding was attributed to cytomegalovirus (CMV) infection and follow-up studies were normal. In general, flow cytometric analysis necessitates at least 3×10^6 cells per sample, which restricts the number of patients studied. Several other methods have been utilized for recognition of the leukemic cell. However, in clinical practice cytology has remained the most informative[7].

Based on the benign clinical course in our three cases with CSF pleocytosis, we emphasize that increased CSF MNC counts, in the absence of blasts, with normal CSF protein and without neurological symptoms does not necessarily indicate CNS involvement. Viral agents may cause signs and symptoms of intracranial hypertension, especially in immunocompromised patients (even with less virulent strains). History, physical examination and through morphological evaluation of the cytocentrifuged cells may eliminate the need for additional treatment.

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