Involvement of the cerebrospinal fluid cells in children with acute lymphoblastic leukemia: prognostic implications

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In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Cancela et al.[1] analyzed the incidence and the risk factors for central nervous system (CNS) relapse in children and adolescents with acute lymphoblastic leukemia (ALL) treated using the GBTLI-ALL 99 protocol and found that a leukocyte count > 50 x 10^9/L at diagnosis was the only significant factor associated with a high incidence of CNS relapse.

Leukemic infiltration of the CNS is defined as five or more leukocytes/mm^3 and blast cells in cerebrospinal fluid (CSF) or cranial nerve palsy[2]. It is a well-established prognostic factor in children with ALL[2-6]. The cumulative incidence of CNS relapse (combined or isolated) presently varies from 2.6 to 9.5%[7]. No clinical or morphological CNS involvement is evident at diagnosis in about 60% of patients who eventually develop CNS relapse[3-6,8-10].

Similar to systemic chemotherapy in the treatment of systemic ALL, there is a growing concern to identify factors associated with increased risk of leukemia infiltration of the CNS and to consequently adapt the protocol aimed at the treatment and prophylaxis of neurological involvement[11]. Several risk factors have been associated with a higher incidence of initial involvement or relapse in CNS, such as high risk genetic abnormalities [t(9;22) and mixed lineage leukemia (MLL) rearrangements], T-lineage ALL and high peripheral leukemic-cell burden[7,12].

Some studies have also demonstrated that patients with any identifiable blast cells in CSF, or CSF contamination by blastic cells during traumatic lumbar puncture, present an increased risk of CNS relapse[13-15]. Others however have not found this association[16-18]. Conventional cytological analysis has proved useful, but the analysis of cells in CSF, especially with low cell counts, is more difficult than is widely admitted and it is not always conclusive[19]. Molecular involvement detected by more sensitive and specific techniques such as PCR and direct sequencing has been shown in around 45% of pediatric patients; the prognostic impact of this molecular involvement seems to be dependent of the intensity of treatment[20,21]. It is possible that morphological involvement of the CNS would represent one of the extremes of a clinical spectrum ranging from gross to minimal residual disease involvement of the CNS and that molecular involvement could reflect biologically more aggressive disease.

The explanation for these discrepancies is probably related to the efficacy of systemic and CNS-directed therapy in different treatment regimens, suggesting that the poor prognosis associated with these variables can be overcome by more effective therapy[21].

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