Pattern and determinants of central nervous system relapse in childhood acute lymphoblastic leukemia in a resource-limited setting

Sir,

Despite over 80% cure rates, central nervous system (CNS) relapse is a significant hindrance in cure of childhood acute lymphoblastic leukemia (ALL). The outcome of ALL in developing nations, although improving, is far inferior, and relapse is a significant contributor. Data from developing nations concerning pattern and determinants of CNS relapse is scarce.

Hence, we analyzed 532 patients treated at our center on the modified UKALL-X and XI protocol over a period of 20 years (1990-2006, followed until 2009) to determine predictors of CNS relapse in a resource-limited setting. After three-drug induction therapy (vincristine, prednisolone and L-asparaginase), intensification (early±late) therapy consisted of (vincristine, prednisolone or dexamethasone, daunomycin and thioguanine). CNS-directed therapy consisted of cranial irradiation (18 Gy in 10 fractions) with six doses of intrathecal methotrexate. After 2001, CNS irradiation was used only in patients with a high risk or CNS disease, while three-monthly intrathecal therapy was added during maintenance therapy, which was continued till 27 months of complete remission.

One hundred and twenty-seven patients relapsed. Forty-five (8.46%) patients developed CNS relapse. Isolated and combined CNS relapse was documented in 24 (4.52%) and 21 (3.94%) cases, respectively. Mean age, platelet and total leukocyte count (TLC) at presentation were 4.93±0.9 years, 44.4±18 × 10^9/L and 39.4±28.9 × 10^9/L, respectively. The mean age at CNS relapse was 63.5±15.6 months. The mean diagnosis–relapse interval was 15.4±4.6 (1-62 months) months. There were 22, 18 and five very early, early and late CNS relapers. CNS disease at presentation and traumatic lumbar puncture were observed in two and one of these patients, respectively.

The mean age (P=0.002) and platelet count (P=0.043) at presentation of patients with CNS relapse was significantly lower compared with patients with relapse at other sites. Compared with other ALL patients in continuous–complete remission (n=236), these patients had a significantly lower platelet count (P=0.012) while the distribution of other clinic–laboratory (including age, gender, symptom diagnosis interval, mediastinal adenopathy, bulk disease, hepatosplenomegaly, TLC, L1 and L2 subtype) parameters was similar.

Earlier studies from Mumbai have reported CNS relapse in 11% and 28.5% of the relapers.[2,3] In a study on adult ALL from Mumbai, a very low rate (1.76%) of isolated CNS relapse using ITMTX and CNS irradiation as CNS-directed therapy was reported.[4]

Our study suggests that, although statistically difficult to predict, the several-fold higher rate of CNS relapse and relapse while on therapy in our center could be explained by a higher incidence of “high risk” disease, less-aggressive chemotherapy and CNS-directed therapy in high-risk cases and possible differences in the biology of leukemia in an Indian setting.

Lower age at CNS relapse could indicate inadequate therapy and non-use of irradiation in children younger than 3 years of age. Despite its clear adverse long-term neurocognitive and endocrine adverse effects, CNS irradiation might have contributed to improvement in survival outcome in a resource-limited setting.[8]

These observations indicate the need for more aggressive risk-adapted and CNS-directed therapy, use of high-dose methotrexate and exploration of triple intrathecal therapy. Cytogenetic and molecular data with assessment of response to therapy could further help in risk categorization and determination of predictors of CNS relapse in India.

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Sir,

The use of combined chemoradiotherapy in cholangiocarcinoma is very interesting. [1] Leong et al. recently reported that conformal radiotherapy and concurrent chemotherapy can be a new alternative cancer therapy for cholangiocarcinoma. We hereby would like to share an experience on the management of advanced cholangiocarcinoma, which presented its highest global prevalence in Thailand. In Thailand, most cases of cholangiocarcinoma are advanced and surgical management cannot be successful. [2] The use of chemoradiotherapy is also done but it is usually palliative. Recently, the new technique using immunotherapy is introduced. Here, the authors would like to share an experience using a standard immunotherapy, nimotuzumab therapy (400 mg weekly dosage) for the management of a case with unsectable cholangiocarcinoma who failed from previous chemoradiotherapy treatment. 1 month after giving of drug, the favorable outcome could be observed. The tumor size reduced into two-thirds of the original size and the tumor marker values also decreased for two times. This is the first world report on using this new modality for the management of advanced cholangiocarcinoma. Since cholangiocarcinoma is a tumor that can express epidermal growth factor receptor (EGFR), [3] using nimotuzumab regimen, which specifically attacks EGFR, can be a possible new alternative choice for the management of advanced cholangiocarcinoma cases.

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