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Rearrangement of the MLL gene confers a poor prognosis in childhood acute lymphoblastic leukemia, regardless of presenting age

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Abstract

MLL gene rearrangements are associated with an extremely poor prognosis in infants with acute lymphoblastic leukemia (ALL), but little is known about their clinical significance in older children. Therefore, we studied 45 cases of childhood ALL with abnormalities of chromosome 11q23 for rearrangement of the MLL gene to determine if this feature confers a uniformly poor prognosis. MLL gene rearrangements were detected in all 18 cases with the common t(4;11), t(9;11) or t(11;19) translocations, whereas only 5 of 12 patients with either unbalanced or uncommon balanced translocations demonstrated a rearrangement. Abnormalities of the MLL gene were not detected in any of the 15 cases with a deletion or inversion of the chromosomes 11q23 region. The presence of an MLL rearrangement was significantly associated with age less than 1 year (P < .001), leukocyte count >50 x 10(9)/L (P = .003), and the absence of leukemic cell CD10 expression (P < .001). In a stratified statistical analysis adjusted for age and treatment protocol, MLL gene rearrangement was correlated with an inferior treatment outcome (P = .028). The 4-year event-free survival estimate (+/- SE) was 10% +/- 6.5% for cases with a rearranged MLL gene and 64% +/- 19.2% for other cases. When infants were excluded from the analysis, MLL rearrangement was still significantly associated with a poor outcome (P = .02), and remained so with the exclusion of t(4;11)-positive cases (P = .05). Thus, regardless of presenting age, MLL gene rearrangement identifies a high-risk subgroup of patients who are not likely to be cured with conventional treatment.

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