Clinical and Laboratory Characteristics of Acute Leukemia with the 4;11 Translocation

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This report describes the clinical and laboratory features of seven cases of acute leukemia associated with the 4;11 chromosomal translocation. All seven children had acute lymphoblastic leukemia by standard morphologic and cytochemical criteria. Leukemic blasts from six of seven patients were terminal deoxynucleotidyl transferase-positive. Immunologic phenotyping suggested the leukemias were of B cell origin; blasts from five patients expressed HLA-DR and p24 (CD-9 antibody), blasts from three patients expressed B4 (CD-19), and blasts from two patients expressed the common acute lymphoblastic leukemia antigen (CD-10). One patient's leukemic blasts contained cytoplasmic immunoglobulin. Analysis of DNA from four of five patients demonstrated additional evidence of B cell differentiation with heavy-chain immunoglobulin gene rearrangement. When DNA from the four patients with heavy-chain immunoglobulin gene rearrangement was analyzed, one patient's DNA demonstrated light-chain immunoglobulin gene rearrangement. However, flow cytometric analysis of blasts from three patients showed the simultaneous expression of the lymphoid-associated antigen B4 (CD-19) and the myeloid-associated antigen My-1 (X-Hapten). Electron microscopic examination of blasts from one patient that expressed both lymphoid- and myeloid-associated antigens demonstrated ultrastructural characteristics of both lineages. These findings suggest that acute leukemia with the t(4;11) abnormality has mixed lineage characteristics as a result of leukemogenesis in a multipotential progenitor cell or aberrant gene expression later in differentiation. Furthermore, serial analysis of karyotype, immunophenotype, and heavy-chain immunoglobulin genes revealed changes in these biologic markers over time, suggesting continued chromosome rearrangement and gene modulation after the leukemogenic event in cells with the t(4;11).

THE ASSOCIATION of the chromosomal translocation t(4;11) with acute leukemia characterized by hyperleukocytosis, a young age, and a poor prognosis has been described.[1-4] This translocation was first reported to be associated with acute lymphocytic leukemia (ALL). Further studies have suggested that the leukemogenic process involves either (1) a precursor cell with the capacity to differentiate along either myeloid or lymphoid lineages or (2) a myeloid progenitor cell.[5,6] We, therefore, analyzed the clinical and laboratory characteristics of seven patients with the t(4;11) in an effort to clarify the lineage of this abnormality. Our studies indicate that this translocation is usually associated with a lymphoid morphology and heavy-chain immunoglobulin gene rearrangement. Although the majority of blasts expressed lymphoid-associated surface antigens, careful flow cytometric analysis of cell surface antigens demonstrated the simultaneous expression of lymphoid- and myeloid-associated antigens on individual blasts from all three patients studied. Ultrastructural study in one patient confirmed dual lineage characteristics within individual leukemic cells. The expression of mixed lineage characteristics[7-11] supports the idea that either a multipotential precursor cell is involved[5,12,13] or aberrant gene expression occurs in leukemias with t(4;11).[14] Our findings are consistent with the descriptions of this translocation in both lymphoid[4] and myeloid[5,6] leukemia and in a cell line with characteristics of both lineages.[15] Furthermore, serial studies of karyotypes, immunophenotypes, and heavy-chain immunoglobulin gene rearrangements at diagnosis and relapse in our patients suggests that such biologic characteristics undergo modification in leukemic cells with this translocation.

MATERIALS AND METHODS

Patients. From Sept 1979 to Feb 1984, 329 of 413 newly diagnosed children with acute leukemia seen at St Jude Children's Research Hospital had adequate mitoses for bone marrow chromosome analysis. Six of these patients were found to have the t(4;11). From Oct 1981 to Oct 1983, 11 of 12 newly diagnosed children with acute leukemia seen at the Tom Baker Cancer Centre had adequate mitoses for bone marrow chromosome analysis, and patient 7 is from that institution. None of the patients in this series had a history of hematologic disorders. All patients were treated with modern, intensive, combination chemotherapy and CNS prophylactic therapy.[16-18] The blasts of all patients were included in leukemia cell profile studies approved by the institutions' clinical trials committees. Informed consent was obtained in each instance.

Morphologic and cytochemical studies. Bone marrow smears were stained with Wright-Giemsa, periodic-acid Schiff (PAS), myeloperoxidase (MPO), Sudan black B (SBB), chloroacetate esterase (CAE), and alphanapthyl butyrate (ANB).[19] Morphologic classification followed conventions of the French-American-British (FAB) cooperative group.[20]

Ultrastructural study. Electron microscopic studies were performed on previously frozen bone marrow cells from patient 7. Ultrastructural localization of peroxidase was performed by the method of Breton-Gorius et al.[21] The cryoprotectant was removed by washing, and the cells were fixed for one hour at 4 °C in 0.5% glutaraldehyde with 2% paraformaldehyde and 1% tannic acid. After washing, the cells were incubated in the dark at room temperature in diaminobenzidine/hydrogen peroxide for one hour.

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Submitted March 4, 1985; accepted Sept 18, 1985.

Supported in part by Grants H-128 and H-129 from the Alberta Heritage Trust Fund; Applied Research Cancer, MA-4655 from Medical Research Council of Canada, Grants CA-20180 and CA-21765 from the National Cancer Institute, and by the American Lebanese Syrian Associated Charities. Dr Mirro is the recipient of a Clinical Oncology Career Development Award from the American Cancer Society. Dr Lauzon is a fellow of the Alberta Heritage Foundation for Medical Research.

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0006-4971/86/6703-0021$03.00/0