To the Editor:

In the July 15, 1990 issue, Meeker et al. described the molecular events underlying the (5;14)(q31;q32) translocation that occurs in acute lymphocytic leukemia (ALL) of B-lineage associated with eosinophilia. Observations of specific chromosomal translocations such as the t(5;14), which are associated with hematopoietic malignancies displaying a unique biologic or clinical characteristic, are important clues in dissecting the molecular events contributing to their pathogenesis. We recently observed a variant t(5;14), also involving the long arms of chromosomes 5 and 14, but with different breakpoints [t(5;14)(q34;q12)], which was associated with a preleukemic phase, a feature observed in a small subset of patients with ALL.

Our patient was a 14-month-old white boy referred for evaluation of pancytopenia and hepatosplenomegaly. Physical exam demonstrated shotty bilateral posterior cervical adenopathy and an enlarged liver and spleen. The white blood cell count was 6,300 with 95% lymphocytes and 5% atypical lymphs; the hematocrit was 18% and the platelet count 8,000.

A bone marrow aspirate demonstrated absence of myeloid precursors and a population of activated lymphocytes. Immunophenotyping studies demonstrated a mixture of T cells and polytypic B cells. Cytogenetic analysis of the bone marrow cells showed a 46 XY karyotype. A liver biopsy demonstrated portal lymphoplasmacytic infiltration, again with polyclonal immunophenotyping studies. A mesenteric lymph node biopsied at laparotomy demonstrated follicular hyperplasia and polyclonal immunophenotyping. He received transfusions of red blood cells and platelets. During the course of his hospitalization, the peripheral platelet, reticulocyte, and neutrophil counts began to recover, and he was discharged. Subsequent complete blood counts were normal, and he was well until 5 weeks later, when he presented with pallor and fever. The liver and spleen were again enlarged. The white blood cell count was 53,000, with 4% neutrophils, 1% monocytes, and 85% blasts; the hematocrit was 22% and the platelet count 28,000. A bone marrow aspirate demonstrated lymphoblasts with LI morphology. The blasts were granular PAS-positive and esterase-negative, with occasional blasts demonstrating Sudan black staining. Immunologic typing studies were positive for CD19, CD10, HLA-DR, and TdT; myelomonocytic surface markers and surface Ig were not present. Cytogenetic analysis of bone marrow cells showed a 46 XY karyotype with a reciprocal (5q34;14q12) translocation (Fig 1). He underwent remission induction therapy with vincristine, prednisone, L-asparaginase, and daunorubicin. A bone marrow exam after 4 weeks of therapy demonstrated remission.

ALL preceded by a period of aplasia (also referred to as preleukemia preceding ALL) has been well described in both children and adults but has not previously been associated with a specific chromosomal abnormality. Abnormalities involving the long arm of chromosome 5 are a common feature of preleukemic and myelodysplastic syndromes but, except for the typical t(5;14), are not often seen in childhood ALL. The 5q34 breakpoint is the location of many growth factor and growth factor receptor genes, while the 14q12 breakpoint is the location of the genes encoding the α and β chains of the T-cell receptor. It is tempting to speculate that the t(5;14) described here resulted in the juxtaposition of a growth factor-related gene and a T-cell receptor gene, which led to the preleukemic phase of this patient’s...
illness. Cytogenetic analysis and molecular studies of the TCR α chain and TCR β chain genes at 14q12, and candidate genes on the long arm of chromosome 5, in cases of ALL preceded by aplasia may identify a molecular event similar to that seen in ALL with the standard t(5;14) and eosinophilia. Such studies will be important in expanding our understanding of this leukemia and its pathogenesis.

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REFERENCES
Acute lymphocytic leukemia with variant t(5;14) and preleukemia: expanding the spectrum of the 5q- abnormality? [letter; comment]

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