Case Reports

Near-Triploid Acute Lymphoblastic Leukemia with TEL/AML1 Translocation

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An 11-year-old girl was diagnosed as B-precursor acute lymphoblastic leukemia (ALL) with co-expression of myeloid antigens. Cytogenetic analysis revealed a near-triploid (75-82 chromosomes/cell) abnormal chromosomal complement. Fluroscent in situ hybridization studies indicated presence of TEL/AML1 fusion genes. We discuss the prognostic relevance of TEL/AML1 in this rare near-triploid subtype of ALL.

Keywords: *Leukemia, Triploidy.*

Cytogenetic techniques have contributed significantly towards risk stratification of childhood leukemias. Using newer methods of chromosomal analysis, abnormalities are detected in nearly 90% of cases of acute lymphoblastic leukemia (ALL). Abnormalities exist in chromosomal number (ploidy) and structure. However, there are still rare cytogenetic abnormalities related to ploidy whose prognosis is unknown especially when complicated by structural chromosomal abnormalities. We report a child with near-triploid ALL with TEL/AML1 translocation, and discuss its prognostic implication.

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Case Report

An 11-year-old girl presented with back and extremity pain for one week, associated with fatigue. There was no fever, weight loss or bleeding manifestations. Her past medical history and family history were not significant. Her physical examination revealed tachycardia and conjunctival pallor. There were no petechiae, lymphadenopathy or hepatosplenomegaly. Initial hemogram revealed hemoglobin 7 g/dL with a mean corpuscular volume of 78.2 fl; white blood cell count 1,100/cu mm; platelets 85,000/cu mm. Peripheral smear showed normocytic, normochromic red blood cells with decreased platelets. There was a predominance of lymphocytes with occasional atypical lymphocytes. Bone marrow examination revealed large blasts with scanty cytoplasm; clumped chromatin; and partially and completely indented nucleus (Rieder cells). On cytochemistry, the blasts were negative for Sudan Black and myeloperoxidase. Immunophenotyping showed CD34 negative blasts with 98% blasts expressing CD19, CD22 and CD10, 84% expressing CD9 and CD40, and 100% blasts positive for HLA-DR; 95% blasts showed positive expression of myeloid antigens CD13 and CD33. Significantly, there was no expression of cytoplasmic myeloperoxidase. In view of the

cytochemistry and immunophenotyping, the final diagnosis was B-precursor ALL with co-expression of myeloid antigens. Cytogenetic analysis revealed a near triploid (75-82 chromosomes/cell) abnormal chromosomal complement. The DNA index was 1.72. Fluorescent in situ hybridization (FISH) studies indicated presence of TEL/AML1 fusion genes. The patient was treated with 4-drug induction chemotherapy comprising prednisone, vincristine, daunomycin and L-asparaginase. Subsequently, she was managed with consolidation chemotherapy comprising high dose methotrexate at 1 g/m^2. Patient is presently in maintenance phase of chemotherapy (6-mercaptopurine and oral methotrexate) and in clinical remission.

Discussion

The above case highlights an interesting subtype of ALL based on morphology, immunophenotyping and cytogenetics involving both numerical and structural changes in the chromosomal complement of the leukemic cells. According to the European Group of Immunological classification of leukemias scoring system for immunophenotype of leukemia, our patient was classified as having B-precursor ALL with myeloid coexpression and not biphenotypic leukemia; myeloperoxidase by cytochemistry as well as cytoplasmic myeloperoxidase by flow-cytometry which is a major component of myeloid lineage was negative in our case(1,2). Myeloid antigen co-expression may be seen in about 1/3rd of cases of childhood ALL. Even though myeloid antigen co-expression shows significant association with specific genetic abnormalities such as involvement of mixed lineage leukemia gene on chromosome 11q23 and Philadelphia chromosome, it lacks prognostic significance in childhood ALL(3).

The international system for human cytogenetics nomenclature (ISCN) 1995 defines near triploidy as chromosome number 58-80 and near tetraploidy as 81-103 chromosomes. In our case the majority of the chromosome number (varying from 75-82 in different metaphases) were in the range of near triploidy. The large size and peculiar nuclear features of the lymphoblasts are an attempt to accommodate the extra DNA content of the near-triploid cells.

Cytogenetic abnormalities in chromosome number and structure appear to have prognostic significance for ALL. Patients with hyperdiploidy tend to have a relatively favorable prognosis; hypodiploidy and pseudodiploidy are associated with a poor outcome, and those with near-haploid have the worst prognosis(4). DNA index of 1.16-1.6 which corresponds to a chromosomal number of >52 chromosomes is one of the strongest prognostic factors for improved survival in childhood ALL(4). An exception to the general rule of hyperdiploid cases having a good prognosis is the relatively rare group of near-tetraploid subtype of ALL which is found in approximately 1% of cases of childhood ALL(5). The near-tetraploid group of ALL patients is associated with an older age of onset, T-cell immunophenotype and a poorer prognosis(5). Near-triploidy is even rarer and is found in <0.5% of patients with ALL; the near-triploid cases of ALL were similar to the general ALL population in clinical features and outcome(5).

TEL/AML1 translocation t(12; 21) (p13; q22) is a cryptic abnormality, detected by FISH or polymerase chain reaction, which results in the fusion of the coding regions of two transcription factors (TEL on chromosome 12p13 and AML1 on chromosome 21q22). This cryptic translocation is observed in approximately 27% of children with ALL in the west and is associated with a favorable

prognosis(6), although it is observed in <1% in childhood ALL from India(7). In a series of 169 patients of childhood ALL with TEL/AML translocation(8), the blast cells were pseudodiploid (45.6%), hyperdiploid with 47 to 51 chromosomes (24.3%), hypodiploid with 44 to 45 chromosomes (10%), near triploid (0.6%), or near tetraploid (5.9%). Further studies are needed to determine prognostic relevance of TEL/AML1 in this rare near-triploid subtype of ALL.

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