A New Case of dic(9;12)(p13;p11) in Acute Lymphocytic Leukemia

Recently, Carroll et al. [1] described a new cytogenetic abnormality in childhood acute lymphocytic leukemia (ALL): a dic(9;12) observed in eight of 432 children karyotyped at diagnosis. In their patients and two other previously reported patients [2, 3] with dic(9;12), breakpoints were tentatively located in 9p11 and 12p12. Between January 1981 and May 1988, we cytogenetically studied 90 cases of childhood ALL. One of them had a dic(9;12) chromosome. Breakpoints on chromosomes 9 and 12, however, seemed different from those published by Carroll et al. [1].

A 9-year-old boy was hospitalized in April 1988 for anemia; he had hepatosplenomegaly and lymphadenopathy. There was no central nervous system (CNS) or mediastinal involvement. The blood count showed a hemoglobin level of 3.5 g/dl, leukocytes at $1.5.10^{9}$ /L, and platelets at 80.10^{9} /L. The bone marrow was hypercellular and was infiltrated by 96% of L1 blasts, which were peroxidase negative, CALLA positive (75%), HLA DR positive (67%), and T (CD2 and CD7) negative (cytoplasmic immunoglobulin was not studied). The patient was treated with combination chemotherapy and achieved complete remission (CR). He remains in CR after 12 months. Cytogenetic studies were made on bone marrow after 24-hour culture. RHG, GTG, and CBG banding were performed by heating, trypsin, and barium-SSC technique. Forty mitoses analyzed showed three cellular clones: normal cells (46,XY) (20 metaphases), 46,XY,+8,-9,-12,+dic(9;12)(p13;p11) (18 metaphases), and 45,XY,-9, -12,del(17)(p11)+dic(9;12)(p13;p11) (two metaphases).

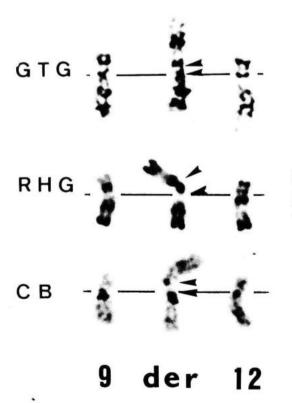


Figure 1 Partial karyotype showing the dic(9;12)(p13;p11) (GTG, RHG, and CB banding). Breakpoints are located at 9p13 and 12p11.

Rearrangements involving 9p and 12p regions are found in about 10% of cases of childhood ALL, particularly as deletions and balanced or unbalanced translocations [4-6]. In our patient, the interpretation of the karyotype with the three techniques of denaturation strongly favors a dic(9;12), with breakpoints occurring in 9p13 and 12p11 (Fig.1). The C-banded pattern shows the dicentric chromosome. The G-banded pattern is difficult to interpret, as in the report of Carroll et al. [1], but the R-banded pattern strongly suggests our interpretation. The breakpoints at 9p13 and 12p11 seen by us are different from the breakpoints at 9p11 and 12p12 previously reported in the literature in cases of dic(9;12) [1-3]. However, they are in agreement with previously published cases of childhood ALL with del (9p) in which the breakpoint was also located in p13 [4, 5]. On the other hand, a breakpoint at 12p11-12, a region to where the Kras 2 protooncogene has been mapped [7], has been reported in several hematologic malignancies including ALL [6], myelodysplastic syndromes [8] (especially chronic myelomonocytic leukemia) [9], and acute nonlymphocytic leukemia [8]. The publication of additional cases of dic(9;12) in ALL would be interesting in order to determine the possible variation of breakpoints from case to case.

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REFERENCES

- 1. Carroll AJ, Raimondi SC, Williams DL, Behm FG, Borowitz M, Castleberry RP, Harris MB, Patterson RB, Pullen DJ, Crist WM (1987): tdic(9;12): A nonrandom chromosome anomaly in childhood B-cell precursor acute lymphoblastic leukemia: A pediatric oncology group study. Blood 70:1962–1965.
- Lazarus H, Barell EF, Krishan A, Livingston DM, Harris K, Schlossman SF, Chess L (1978): Characterization of a unique cell line (LAZ 221) from human acute lymphocytic ("null" cell) leukemia. Cancer Res 38:1362–1371.
- 3. Heerema NA, Palmer CG, Baehner RL (1985): Karyotypic and clinical findings in a consecutive series of children with acute lymphocytic leukemia. Cancer Genet Cytogenet 17:165– 179.
- Kowalczyk J, Sandberg AA (1983): A possible subgroup of ALL with 9p. Cancer Genet Cytogenet 9:383.
- 5. Laī JL, Fenaux P, Pollet JP, Estienne MH, Savary JB, Huart JJ, Deminatti M (1988): Acute lymphoblastic leukemia with 9p anomalies. A report of four additional cases and review of the literature. Cancer Genet Cytogenet 33:99–109.
- Raimondi SC, Williams DL, Calli Han T, Peiper S, Rivera GK, Murphy SB (1986): Nonrandom involvement of the 12p12 breakpoint in chromosome abnormalities in childhood acute lymphoblastic leukemia. Blood 68:69-75.
- Popescu NC, Amsbaugh SC, Di Paolo JA, Tronick SR, Aaronson SA, Swan DC (1985): Chromosomal localization of three human ras genes by in situ molecular hybridization. Somatic Cell Molec Genet 11:149–155.
- 8. Berger R, Bernheim A, Leconiat M, Vecchione D, Pacot A, Daniel MT, Flandrin G (1986): Abnormalities of the short arm of chromosome 12 in acute nonlymphocytic leukemia and dysmyelopoietic syndrome. Cancer Genet Cytogenet 19:281-289.
- 9. Groupe Français de Cytogénétique Hématologique (1986): Cytogenetics of chronic myelomonocytic leukemia Cancer Genet Cytogenet 21:11, 30

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