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Acute Myeloid Leukemia

Tetraploidy or near-tetraploidy clones with double 8;21 translocation: a non-random additional anomaly of acute myeloid leukemia with t(8;21)(q22;q22)

We report on 6 patients with tetraploidy or near-tetraploidy acute myeloid leukemia (AML) with double t(8;21)(q22;q22) and review the literature on cases with the same cytogenetic abnormalities. Some common features were revealed by this analysis.

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The cytogenetic abnormality of tetraploidy or near-tetraploidy is a rare finding in acute myeloid leukemia (AML). Lemez *et al*.[1] divided near-tetraploidy AML into 2 categories: primary and secondary according to its origin. It is known that patients with primary near-tetraploidy AML manifest some common features: (i) near-tetraploidy karyotypes in most of the bone marrow metaphases examined at diagnosis of AML; (ii) the presence of giant myeloid blasts and dysplastic morphology in erythroid and/or megakaryocytic lineages in the bone marrow, pointing to the origin from pluripotent myeloid progenitor cells; (iii) expression of CD34 antigen; (iv) low yields of granulocyte- macrophage colony-forming units (GM-CFU) in culture; (v) a preceding preleukemic phase before the onset of the disease, and (vi) a poor prognosis. So far secondary tetraploidy or near-tetralpoidy AML has been associated with multiple structural chromosomal aberrations. There have been seven cases of AML with clearly secondary tetraploidy or near-tetraploidy metaphases with duplication of t(8;21)(q22;q22) at diagnosis or during the course of leukemia reported in the literature[2-6] (Table 1). We report here another six such cases.

Between January 1990 and December 2003, 216 cases of t(8;21) (q22;q22) AML were diagnosed in our institute, and all of them were AML-M2 subtype according to the FAB criteria. The patients' ages ranged 3–65 years with a median of 28 years; 125 were male and 91 female. Seventy-three patients(33.8%) presented with coexistence of normal and abnormal karyotypes, an additional chromosome aberration occurred in 146/216 (67.6%) of the patients and 53 (24.5%) had a complex karyotype (≥3 chromosomal abnormalities). The most frequent additional abnormalities were loss of a sex chromosome (41.2%), partial deletion of the long arm of chromosome 9 (23 cases, 10.6%) and less often, deletion or partial deletion of the long arm of chromosome 7 (6 cases, 2.85%). Other additional structural anomalities included

Table 1. Clinical and genetic features of the 13 cases of tetraploidy or near-tetraploidy AML with double t(8;21)(q22;q22).

Case	*Sex/age(years)*	*Karyotype*	*Survival (months)*	*Reference*
1	M/28	90,XX,-Y,-Y, t(8;21)(q22;q22)?2[5]/46,XY,-1, t(8;21)(q22;q22), +der(1), t(1;?) (p36;?) [2] /46,XY[4]	23	Testa[2]
2	M/53	46,XY/90,XX,-Y?2,-11, t(8;21)(q22;q22)?2,+mar[92.5%]	12+	Abe[3]
3	M/31	46,XY, t(8;21)(q22;q22)[2]/46,XY,add(7)(q31) t(8;21)(q22;q22)[6]/ 92,XXYY, add(7) (q31)?2, t(8;21)(q22;q22)?2[70]/46,XY[10]	4	Xue[4]
4	F/8	46,XX, t(8;21)(q22;q22)[13]/ 46,XX,+4 t(8;21)(q22;q22)[45]/ 92,XXXX,+4?2, t(8;21)(q22;q22)?2[38]/46,XX[1]	6	Xue[4]
5	F/10	46,XX, t(8;21)(q22;q22)[6]/110-117,XXX,-X,-X,-1,+4,+4,-7,add(7)(q31)?3, t(8;21)(q22;q22)?2,+der(21) t(8;21)(q22;q22),+22[272] / 92,XXXX,add(7) (q31)?2, t(8;21)(q22;q22)?2[21]/46,XX[7]	8	Xue[5]
6	M/7	45,X,-Y, t(8;21)(q22;q22)[6]/90,XX,-Y,-Y, t(8;21)(q22;q22)?2[32]/46,XY[2]	20+	Xue[5]
7	F/61	45,X,-X, t(8;21)(q22;q22)[1]/90,XXX,-X, t(8;21)(q22;q22)?2,-9[7]/46, XX[12]	3	Yamamoto[6]
8	F/6	46,XX,t(8;21)(q22;q22)[13]/92,XXXX,t(8;21)?2[2]	12	Present case[1]
9	M/48	41-44,X,-Y,-15,-17,t(8;21)(q22;q22),9q+,11q-,+Mar[cp2]/92,xxyy,der(22) t(4;22) (q10;q10)?2,t(8;21)?2,9q+?2,-11,-20,+Mar[cp15]	9	Present case[2]
10	F/9	46,XX,t(8;21)(q22;q22)[7]/92,XXXX,t(8;21)?2[8]	11	Present case[3]
11	M/35	46,XY,t(8;21)(q22;q22),-10,+11[1]/45,X,-Y,t(8;21)(q22;q22)[3]/46,XY,t(8;21)[1] /92, XXYY, t(8;21)?2[4]/46,XY[7]	3	Present case[4]
12	F/11	46,XX, t(8;21)(q22;q22)[10]/88-96, XXXX, t(8;21)(q22;q22) ?2 [cp15]	4	Present case[5]
13	F/12	46,XX,t(8;21)(q22;q22)[5]/92,XXXX,t(8;21)(q22;q22) ?2 [7]/46,XX[2]	6	Present case[6]

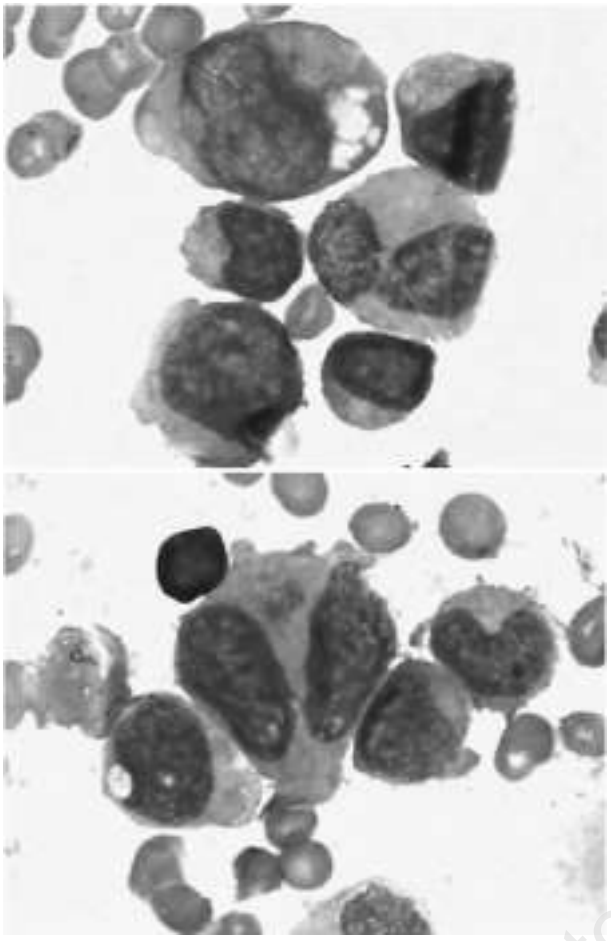

Figure 1. Leukemic cells in bone marrow smears are large (A) and bizarre (B) (Wright-Giemsa stain, ×1,000).

t(1;6)(p32;p10), t(1;7)(q10;p10), t(1;11)(q23;p15), t(3;11)(q23;p15), t(3;21)(q21;q21), t(4;22)(q10;q10), t(11;17)(p10;q10), inv(16)(p12p21) and t(18;20)(p11;q12), each in one case.

Six cases (2.85%) of near-tetraploidy or tetraploidy with double t(8;21) (q22;q22) AML were found in this series. There have been seven other t(8;21) AML with the same chromosome abnormality reported in the literature.[2-6] An analysis of all 13 cases (Table 1) was made to reveal any clinical and genetic features in common. The patients were aged from 6 to 61 years with a median of 12 years, six cases were male and 7 female. There were some common features, as follows: (i) the patients were mainly East-Asians (11/13 cases); (ii) there were giant and bizarre myeloblasts in the bone marrow smear (Figure 1); (iii) the immunophenotypes of the tetraploidy or near-tetraploidy cells were different from those in typical t(8;21)-AML despite a secondary genetic change originating from a diploid clone with t(8;21), the expression of CD2 or CD7 may be associated with clonal evolution to near-tetraploidy; and (iv) the prognosis was poor, the survival from diagnosis being less than one year. Cell fusion, endoreduplication and successive non-disjunction of the whole complement of chromosomes have been suggested as the possible mechanisms for the generation of leukemic tetraploidy cells.[7] Clonal karyotypic evolution has been followed in some tetraploidy or near-tetraploidy AML patients with double t(8;21) (q22;q22). In these patients the initial chromosome changes were only t(8;21) cells without double t(8;21) (q22;q22); the latter emerged during the course of the disease, suggesting that the tetraploidy or near-tetraploidy clone was the consequence of a clonal evolution.

In conclusion, a tetraploidy or near-tetraploidy clone with double 8;21 translocation is a non-random additional anomaly in some cases of t(8;21)(q22;q22) AML and predicts a poor prognosis.

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Acute Lymphoblastic Leukemia

The t(12:21) is underrepresented in childhood B-lineage acute lymphoblastic leukemia in Kerala, Southern India

t(12;21) (*TEL/AML1*) is the most common genetic event in childhood B-cell acute lymphoblastic leukemia (B-ALL) in Western countries. Samples from 42 children with ALL in Kerala were tested by reverse transcription polymerase chain reaction for *TEL/AML1*, t(1;19) and t(4;11). Only 2 out of 42 (4.8%) cases were positive for the *TEL/AML1*, and t(1;19) and t(4;11) were not detected. We conclude that the incidence of *TEL/AML1* is lower in the Indian population.