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Retrospective evaluation of the clinical and laboratory data from 300 patients of various hematological malignancies with chromosome 3 abnormalities

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This retrospective study was designed to evaluate the clinical and laboratory behaviors of chromosome 3 abnormalities by analyzing the morphological, cytogenetic, and follow-up data from 300 patients of various hematological malignancies with chromosome 3 abnormalities. From the results, trisomy 3, translocation (3q), and del(3) were the abnormal types most frequently observed (>10%) among the chromosome 3 abnormalities. In hematological malignancies, chromosome 3 abnormalities were most frequently seen in the patients with acute myeloid leukemia (AML) (24.7%) and myelodysplastic syndrome (MDS) (16%), followed by those with acute lymphocytic leukemia (ALL) (13.7%) and multiple myeloma (MM) (12.7%). In this series, genomic losses were the most frequent genetic abnormalities in AML, ALL, and hybrid acute leukemia (HAL) patients, whereas structural rearrangements were frequently seen in chronic myeloid leukemia (CML) and MDS patients, and genomic gains in MM, lymphoma and chronic lymphocytic leukemia (CLL) patients. Chromosome 3 abnormalities mainly occurred as a component of a complex abnormality (251/300) rather than a sole one (14/300). Survival analysis demonstrated a statistical difference between the patients with trisomy 3, who had a better prognosis, and patients with del(3), who had a worse prognosis in this series ($P < 0.05$). Abnormalities in chromosome 3 may imply an unfavorable outcome in CML and ALL.

Keywords Chromosome 3 abnormality, cytogenetics, EVI1, hematological malignancies, t(3;3)/inv(3)

In patients with hematologic malignancies, chromosome 3 abnormalities are observed less often than abnormalities involving chromosomes 5, 7, or 8. However, the abnormalities on chromosome 3 have been increasingly highlighted in recent years, after the t(3;3)/inv(3) was defined as a reproducible abnormality in the World Health Organization (WHO) 2008 classification criteria (1). Therefore, we performed a retrospective analysis of 300 first-visit patients with chromosome 3 abnormalities from a patient database that includes over 45,000 patients with hematological malignancies who were treated from 1985 to 2011 in our center. This analysis was conducted to clarify the distributions and characteristics of each subtype of chromosome 3 abnormalities in hematological malignancies and the possible relationships among these conditions.

Materials and methods

The clinical and laboratory data regarding the age, gender, diagnosis, and outcome of 300 patients with hematological malignancies and chromosome 3 abnormalities who were treated in our center from 1985 to 2011 were retrospectively analyzed. For the analysis, the occurring pattern and distribution of the chromosome 3 abnormalities in the

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Table 1 Distributions and characteristics of chromosome 3 abnormalities in the hematological malignancies in this series (n = 300)

	Chromosome loss or gain		Genomic loss or gain of a region of chromosome 3			
	Trisomy 3	del(3)	add(3q)	del(3q)	add(3p)	del(3p)
Cases, n (%)	64 (21.3)	38 (12.7)	18 (6.0)	22 (7.3)	9 (3.0)	15 (5.0)
Age, y, median (range)	48.5 (14–83)	54 (15–79)	42.5 (17–77)	33 (11–75)	50 (26–72)	25 (17–76)
Gender, male:female	1.56:1	1.53:1	3.5:1	1:1	1.25:1	1.5:1

[a] Includes ins(3), idic(3), etc.
[b] Defined as two or more abnormalities concurrently seen on chromosome 3 in one patient.

hematological malignancies and the incidence of these abnormalities in various hematological disorders were summarized. Additionally, a survival analysis was performed for 96 of these patients, who had full follow-up data. In order to compare the prognosis of hematological malignancy patients with chromosome 3 abnormalities to that of those without chromosome 3 abnormalities, the patients in the control group included 73 chronic myeloid leukemia (CML) cases (34 with t(9;22) abnormalities alone and 39 with abnormal karyotypes other than in chromosome 3), 60 acute lymphocytic leukemia (ALL) cases (25 with normal karyotypes and 35 with abnormal karyotypes other than in chromosome 3), and 21 multiple myeloma (MM) cases with normal karyotypes.

Cytogenetic analysis was performed on bone marrow (BM) cells using direct method or 24-hour cultures. An R-banding assay was used for karyotypic analysis. Clonal karyotypic abnormalities were described according to the International System for Human Cytogenetic Nomenclature 2013 (2). For the patients with abnormalities in the long arm of chromosome 3 (3q) regions whose bone marrow cells were available, *EVI1* rearrangements were examined by fluorescence in situ hybridization (FISH).

Statistical analysis was performed using Statistical Package for Social Science (SPSS) 16.0 software (IBM, Armonk, NY). The survival analysis was performed by Kaplan–Meier analysis; $P < 0.05$ was considered statistically significant.

Results

Full clinical and laboratory data from 300 patients with hematological malignancies and chromosome 3 abnormalities were obtained from a patient database that included 45,000 patients with chromosomal identification results. The patients in the study were aged from 11 to 87 years (median 47 y), with a male/female ratio of 1.73:1. As shown in Table 1, the chromosome 3 abnormalities could be categorized as a chromosome loss or gain (del(3), trisomy 3), genomic loss or gain of a region of chromosome 3, structural rearrangement, or other abnormalities in chromosome 3, all of which are more commonly observed in men than women, with the exception of del(3q). Among these types of abnormalities, chromosome loss and gain were the most frequently

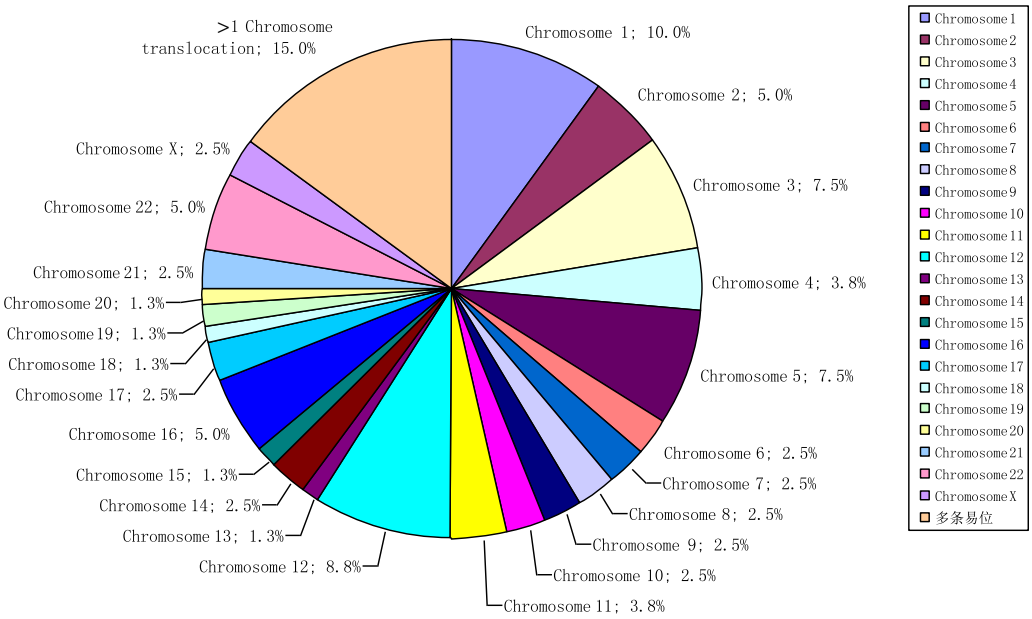

Figure 1 Frequency of the chromosomes that participated in the formation of translocation t(3;V): Chromosome 3 can interact with any of the chromosomes (chromosomes 1–22) within the genome to form a translocation t(3;V), particularly involving chromosomes 1, 12, 3, 5, 2, 16, and 22 (≥5.0%).