Translocations (5;17) and (7;17) in Patients with De Novo or Therapy-Related Myelodysplastic Syndromes or Acute Nonlymphocytic Leukemia

A Possible Association with Acquired Pseudo-Pelger-Huët Anomaly and Small Vacuolated Granulocytes

J. L. Laï, M. Zandecki, P. Fenaux, F. Le Baron, F. Bauters, A. Cosson, and M. Deminatti

ABSTRACT: *Twelve patients [two with de novo myelodysplastic syndrome (MDS), four with secondary MDS, five with de novo acute nonlymphocytic leukemia (ANLL), one with secondary ANLL] showed a 17p deletion resulting from translocations involving 17p: t(5;17)(p11;p11) in four cases, t(7;17)(p11;p11) in six cases, complex (5;17)(q23;p12) translocation with dicentric chromosome in one case, and t(17;?)(p11−12;?) in the remaining patient. All these structural anomalies were observed in hypodiploid clones associated with total or partial monosomy of chromosomes 5 and 7 (12 cases), monosomy 12 (five cases), monosomy 3 (four cases), and monosomy 4 (three cases). Median survival was only 3.3 months (range 3 days to 8 months). Striking features were observed in bone marrow mature granulocytes: all but one case had a pseudo-Pelger-Huët anomaly in a significant number of granulocytes, and eight patients had granulocytes with reduced size and clear cytoplasmic vacuoles. Careful cytological review of 51 patients with MDS or ANLL and various cytogenetic anomalies was performed for comparison: vacuolated granulocytes were a very uncommon finding. On the other hand, eight patients had a pseudo-Pelger-Huët anomaly, which correlated significantly with total monosomy 17 in these patients. A possible correlation between cytological anomalies and cytogenetic data is discussed, and the role of 17p in the nuclear segmentation of granulocytes is stressed.*

INTRODUCTION

Myelodysplastic syndromes (MDS) are a heterogenous group of disorders characterized by ineffective hematopoiesis leading to cytopenias and, in about 30% of all cases, to acute nonlymphocytic leukemia (ANLL) [1, 2]. Their morphological classification is based on the French-American-British (FAB) group criteria [3]. In addition to MDS

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arising de novo, the number of cases of MDS appearing after successful chemotherapy, or radiation therapy, or both for neoplasia is increasing. Forty to 85% of the patients with secondary MDS or ANLL have clonal chromosome abnormalities [4–11]. The aberrations most often associated with MDS and secondary ANLL are partial or complete deletions of chromosomes 5 or 7, trisomy 8 [12] and, less frequently, t(1;7) [13, 14], del/t(11q) [15], del/t(6p) [16], or del/t(12p) [17]. In de novo ANLL, the same type of abnormalities may occur, but the most consistent findings include rearrangements such as t(8;21), t(15;17), t(9;11), or inv(16) [18].

Morphological changes in bone marrow (BM) cells are frequent in ANLL and almost constant in MDS. A correlation between morphological changes and cytogenetic rearrangements has been well documented in the "5q− syndrome" [19] and to a lesser extent in patients with t(8;21) [20] and t(8;16) translocations [21, 22].

We report 12 patients with de novo or secondary ANLL or MDS and a rearrangement involving 17p. Eleven of them had a translocation 5;17 or 7;17. An unusual type of dysgranulopoiesis associated with a pseudo-Pelger-Huët anomaly and small vacuolated granulocytes was noted in most patients. This association was rarely found in the rest of our patients with ANLL or MDS.

PATIENTS AND METHODS

Patients

Between January 1981 and December 1988, successful cytogenetic analysis was performed at diagnosis in 330 patients with MDS (de novo or secondary) and in 300 patients with ANLL (de novo or secondary). Twelve of these patients (1.9%), with either a t(5;17) or a t(7;17) or a structural abnormality of 17p, are the subject of this report.

Morphological Analysis

Diagnosis of ANLL and MDS was made according to FAB morphological criteria [3, 23], including Morphologic, Immunologic, and Cytogenetic (MIC) group recommendations [12]. Blood and BM smears were stained with May-Grünwald-Giemsa, cytochemical tests using conventional methods [24] were performed in patients with ANLL, and myeloperoxidase (MPO) deficiency in mature granulocytes was demonstrated by the modified Hattori technique [25]. Myelodysplastic features were analyzed in blood and BM cells in each of the 12 patients. Three comparative groups of patients with ANLL or MDS diagnosed between the same period of time at our institution were also cytologically examined: group A, 30 unselected cases of ANLL or MDS without any cytogenetic anomaly; group B, 13 cases of ANLL or MDS with a cytogenetic anomaly or anomalies involving chromosomes other than 5, 7, and 17; and group C, eight cases of ANLL or MDS with cytogenetic anomalies involving complete loss of chromosome 17, excluding patients with 17p anomalies.

Cytogenetic Analysis

Cytogenetic analysis was performed on BM cells (10 patients), or on blood leukocytes isolated by the Dextran method (two patients) after a 24-hour culture without stimulation by phytohemagglutinin (PHA). Chromosomes were identified by RHG banding [26] and classified according to the International System for Human Cytogenetic Nomenclature [27].

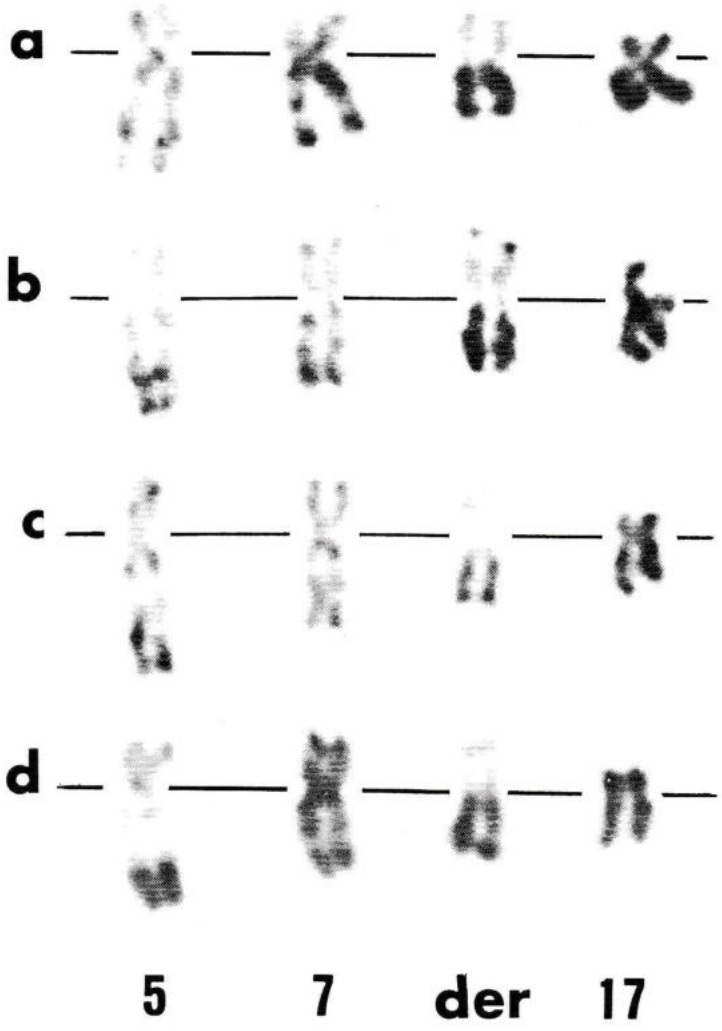

Figure 1 Partial karyotype showing (a,b) der 17 t(7;17)(p11;p11) (patients 1 and 2) (c,d) der 17 t(5;17)(p11;p11) (patients 5 and 7) (RHG bands).

RESULTS

Clinical and Hematologic Findings

Tables 1 and 2 show the clinical and hematologic findings of the 12 patients: two with de novo MDS, four with secondary MDS, five with de novo ANLL (four of which were classified as M2) and one with secondary ANLL. Because the patients were elderly or had secondary myeloid disorders, most of them received either supportive care or low-dose cytosine arabinoside (Ara-C). No response to low-dose Ara-C was observed. Only two patients received combination chemotherapy. One of them achieved a short complete remission (5 months). Median survival was only 3.3 months (range, 3 days to 8 months).

Cytogenetic Findings

Cytogenetic analysis was successful in all 12 patients. Results are shown in Table 3. In 11 patients chromosomes 5, 7, and 17 were implicated in chromosomal rearrangements. A translocation 7;17 was present in six cases (patients 1–4, 10, 11), a t(5;17) was present in four cases (patients 5–7, 12), and a translocation involving 17p was present in one case (patient 9); in patient 8, a complex (5;17)(q23;p12) translocation led to formation of a dicentric chromosome. In t(5;17) and t(7;17) the breakpoints were situated near the centromere on the short arm of the two chromosomes implicated (5 or 7 and 17) (Fig. 1). Thus, in 10 patients the translocations were located in 5p11,

Table 1 Clinical findings in 12 patients

Patient	Age/Sex	Exposure to carcinogens	Organomegaly	Diagnosis (and evolution)	Treatment	Treatment outcome	Survival (mo)
1	67/F	Yes	No	RAEB (RAEB-T after 4 mo)	Supportive care	—	8
2	82/M	No	No	M2-ANLL	Low-dose Ara-C	Death in aplasia	1
3	65/M	No	No	M2-ANLL	Supportive care	—	3
4	69/M	No	No	M2-ANLL	Low-dose Ara-C	Failure	2
5	60/F	No	Splenomegaly	M6-ANLL	Anthracyclin–Ara-C combination	Complete remission (5 mo)	6.5
6	63/M	Yes[a]	No	RA (RAEB after 1 mo)	Supportive care	—	5
7	40/M	No	No	RAEB-T	Anthracyclin–Ara-C combination	Death in aplasia	1
8	67/F	No	Splenomegaly	M2-ANLL	No therapy	—	3 days
9	53/M	Yes[a]	No	RA (RAEB after 1 mo)	Low-dose Ara-C	Failure	3
10	72/F	Yes[b]	No	RAEB	Low-dose Ara-C	Failure	6
11	30/F	Yes[c]	No	RAEB (M2-ANLL after 6 mo)	Supportive care	—	8
12	68/M	No	No	CMMoL	Supportive care	—	0.5

Abbreviations: RA, refractory anemia; RAEB, refractory anemia with excess of blasts; RAEB-T, RAEB in transformation; CMMoL, chronic myelomonocytic leukemia; M2-ANLL, acute myeloid leukemia type 2.

[a] Multiple myeloma treated by melphalan.

[b] Polycythemia vera treated by radiophosphorus and busulfan.

[c] Hodgkin's disease treated by 6 MOPP, 6 ABVD, and radiotherapy.

Table 2 Main hematological data in 12 patients

	Blood				Bone Marrow							
						Megakaryocytes					Abnormal neutrophils[b]	
Case no.	WBC 10^9/L	Neutrophils 10^9/L	Blasts %	Plts 10^9/L	Cellularity	Density	Morphology	Blasts %	Mature granulocytes %	MPO deficiency[a]	Pseudo-Pelger	Vacuolated granulocytes
1	3.7	1.3	0	398	N	N	ABN	6	7	ND	+ + +	+ + +
2	4.2	0.5	48	58	DIM	N	±ABN	37	14	Yes	+ + +	+ + +
3	0.8	0.4	2	68	N	DIM	±ABN	57	2	Yes	+ +	+ + +
4	2.5	1.0	2	229	DIM	DIM	±ABN	48	5	No	—	—
5	9.9	0.7	24	49	DIM	N	N	32	11	No	+ + +	—
6	1.8	0.9	2	88	DIM	N	ABN	4	20	Yes	+ + +	+ + +
7	1.9	0.5[c]	3	73	N	N	±ABN	25	15	Yes	+ + +	+
8	550	1.6	84	90	N	DIM	N	78	3	Yes	+ + +	+ + +
9	2	0.8	0	40	DIM	DIM	±ABN	2	3	ND	+ +	+
10	1.1	0.3	16	42	ND	ND	ND	ND	ND	ND	ND	ND
11	4.4	1.3	5	50	N	N	ABN	20	8	No	+	+
12	5.6	1.4	0	96	DIM	DIM	N	3	24	ND	+ +	—

Abbreviations: N, normal or increased; DIM, diminished; ABN, abnormal; ±ABN, some degree of dysmegakaryocytopoiesis.

[a] Yes, partial myeloperoxidase deficiency in mature granulocytes; No, no deficiency.

[b] (—) no abnormal mature neutrophils; (+) 5–10% mature granulocytes affected; (+ +) 11–25% mature granulocytes affected; (+ + +) more than 25% mature granulocytes affected.

[c] Some mature granulocytes with pseudo-Pelger-Huët morphology.

Table 3 Summary of cytogenetic results of 12 patients with MDS and ANLL

Patient	Material analyzed (24 hours)	Nb metaphases: Normal cells	Nb metaphases: Abnormal cells	Karyotype
1	BM	2	11	44,XX,−5,−7,−17,+der(17)t(7;17)(p11;p11)
2	BM	1	12	43,XY,−5,−7,−12,−16,−17,+der(17)t(7;17)(p11;p11) +min,+mar
3	BM	2	19	42/43,X(−Y),−4,−7,−17,del(4)(q24)t(19;?)(p13;?)t(11;?) (p11;?),+der(17)t(7;17)(p11;p11), with variation
4	BM	12	16	45,XY,−3,−4,−5,−7,−12,+11,−17,+der(17)t(7;17) (p11;p11),+3mar
5	Blood	—	14	43,X(−X),−5,−7,−17,t(12;?)(p13;?),+der(17)t(5;17) (p11;p11)
6	BM	2	18	44,XY,−5,−7,−12,−17,t(1;?)(q42;?),+der(17)t(5;17) (?p11;?p11),+mar
7	BM	4	22	42,XY,−3,−4,−5,−7,−11,−12,−16,−17,−20, +der(17)t(5;17)(p11;p11),+4mar
8	BM	1	17	43,XX,−3,−5,−7,−17,del(2)(p13)del(5)(q11q23),del(6) (p21),del(15)(q15),dic(5;17)(q23;p12),t(9;?)(p13;?), t(12;?)(p11;?)
9	BM	2	15	45,XY/44,X(−Y),−5,−7,−10,−17,−18,der13, +der(17)t(17;?)(p11−12;?),t(11;?)(q13;?),+3mar
10	Blood	1	14	43,XX,−5,−7,−12,−17,+der(17)t(7;17)(p12;p11) with variation
11	BM	—	23	45,XX,−7,−17,del(5)(q12q32),+der(17)t(7;17) (p11;p11)/44,X(−X),−7,−17,del(4)(q26),del(5)(q12q32), t(3;?)(p13;?),+der(17)t(7;17)(p11;p11) with variation
12	BM	—	11	46,XY,−1,−3,−5,−7,−13,−17,−18,+der(17)t(5;17) (p11;p11),+min,+r,+4mar

BM, bone marrow; MDS, myelodysplastic syndrome; ANLL, acute nonlymphocytic leukemia.

7p11, and 17p11. These particular structural anomalies lead to 5q or 7q and 17p deletions.

In 11 patients these structural anomalies were associated with a hypodiploid clone (42 to 45 chromosomes): total or partial monosomy of chromosome 5, 7, and 17 was observed in all patients, monosomy of chromosome 12 was observed in five cases, monosomy of chromosome 3 was observed in four cases, and monosomy of chromosome 4 was observed in three cases (Figure 3). In three of these patients (patients 3, 10, and 11), the karyotype was complex with a major clone (Table 3) and variation with minor numeric and/or structural anomalies. In patient 12 t(5;17) was observed in a diploid clone, in association with ring, markers, and minute chromosomes. Nine patients had both normal and abnormal cells; in three patients no normal cells were observed (patients 5, 11, and 12).

Cytological Findings

The main cytological findings are shown in Table 2.

Bone marrow. Eleven patients had BM smears for cytological examination. The morphology of megakaryocytes was abnormal in three patients (patients 1, 6, and 11): some large cells with small nonlobulated nuclei (i.e., the cytological anomaly encoun-

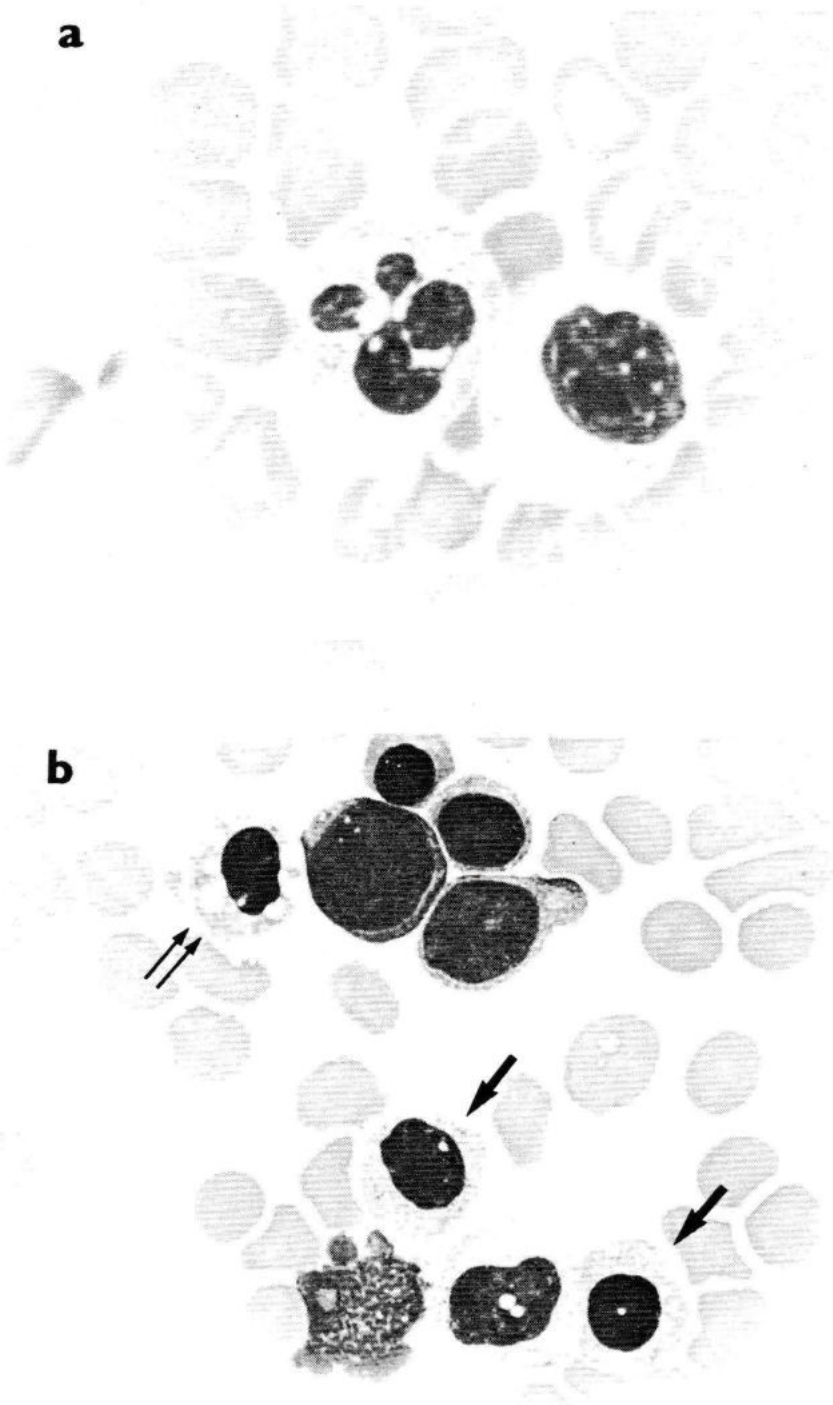

Figure 2 (a) A plurisegmented neutrophil is near another one with nonsegmented nucleus and well-clumped chromatin, i.e. the pseudo-Pelger-Huët anomaly (patient 2). (b) Mature granulocytes with round or oval nucleus contour (arrows) and another one with numerous cytoplasmic vacuoles (double arrow) (patient 1).

tered in patients with the 5q − syndrome) intermixed with micro and normal-appearing megakaryocytes. The other patients had either a few abnormal cells or no anomaly.

Erythroblasts were always present in the 11 patients, with variable dyserythropoietic changes (caryorrhexis, intermediate megaloblasts, stippled cytoplasm) (data not shown). Immature and mature granulocytes were observed in variable percentages (see Table 2) in all patients. In all but one case (patient 4) a variable percentage of polymorphonuclear granulocytes had dysgranulopoietic changes.

Ten of the 11 patients with dysgranulopoiesis had a pseudo-Pelger-Huët anomaly,

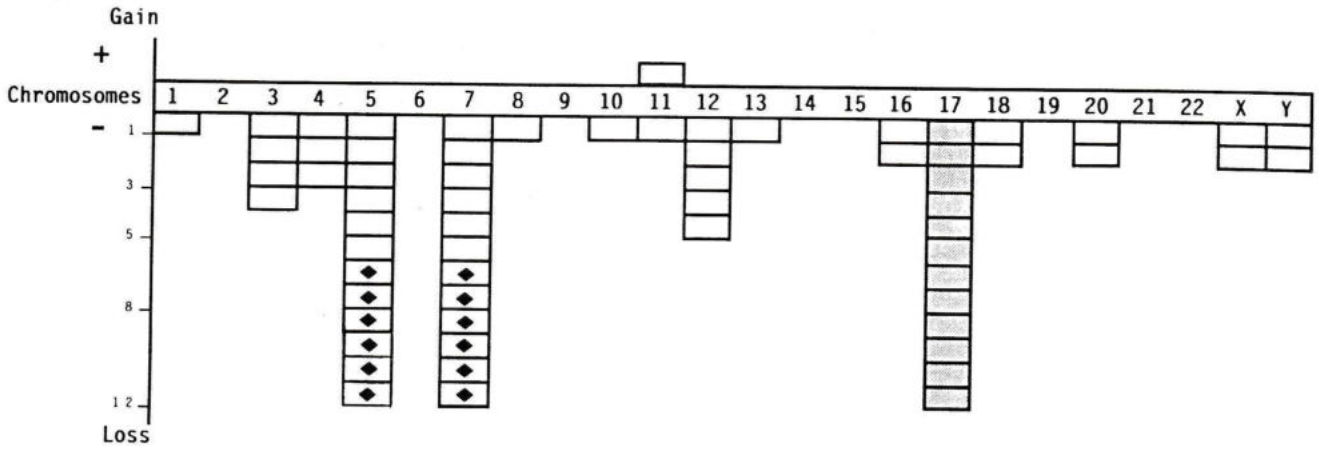

Figure 3 Histogram showing the gain or loss of chromosomes for the 12 patients: der 17 t(5;17) or t(7;17) (hatched bars); partial monosomy (bars with solid diamond).

which was prominent in nine patients (more than 10% affected granulocytes) and was less frequent in another patient (patient 11): most of the affected cells had an oval or round small nucleus with well-clumped chromatin and/or the so-called "pince-nez" bilobated picture (Fig. 2).

Eight patients (see Table 2) had another morphological abnormality of granulocytes: the overall size was diminished with a centrocellular nucleus and a reduced cytoplasm containing vacuoles in variable numbers; granules were scarce and the nucleus had either the pseudo-Pelger-Huët anomaly or was hyperchromatic with a homogeneous pattern (Fig. 2). The latter pattern of granulopoiesis was conspicuous in five patients (patients 1–3, 6, and 8) and less marked in three (patients 7, 9, and 11). Careful analysis of the comparative groups (A, B, and C) showed a significant pseudo–Pelger-Huët anomaly (more than 5% of mature granulocytes affected) in five of the eight patients with multiple chromosomal anomalies and loss of chromosome 17 (group C). When chromosome 17 was not involved, the pseudo-Pelger-Huët anomaly was infrequent: 0 of 13 patients with cytological anomalies other than 5, 7, and 17 (group B) and 3 of 30 patients ($p < 0.0001$) without any cytogenetic anomalies (group A). Vacuolated mature granulocytes were a rare finding: 0 of 30 patients in group A, and occasional (1–5%) of the mature granulocytes in 1 of 13 patients in group B and two of eight patients in group C.

Partial MPO deficiency was evident in five of the eight tested cases (patients 2, 3, and 6–8). Neutrophils with normal MPO content coexisted with partially or totally deficient granulocytes in all five cases; MPO deficiency was observed in pluriseg-mented cells and in most but not all of the pseudo-Pelger-Huët and/or small vacuolated granulocytes.

Blood. Eleven of the 12 patients had absolute neutropenia ($<1.5 \times 10^9$/L); careful search for the abovementioned anomalies was negative, except in patient 7 who had some pseudo-Pelger-Huët circulating granulocytes.

DISCUSSION

Although an involvement of chromosomes 5, 7, and 17 is frequently reported in MDS and secondary ANLL (and to a lesser extent in de novo ANLL), translocations between these chromosomes have been found in only a limited number of patients: among 34 ANLL patients with aberrations of #17 [excluding cases of t(15;17)] reported by the Fourth International Workshop on Chromosomes in Leukemia [28], 2 had a t(5;17); a few other single cases of t(5;17) or t(7;17) have been reported in de novo MDS [6, 29],

de novo ANLL [30], secondary MDS [8, 31] and secondary ANLL [29, 32, 33]. These two translocations were not observed in several large series of de novo or secondary MDS and ANLL, however [4, 7, 9, 34]. A t(5;17) or t(7;17), in our experience, was found in 2.9% of ANLL patients and 5.8% of MDS patients with chromosomal anomalies. In our 12 patients these translocations led to partial or total monosomies of 5/5q or 7/7q and 17p (17p→pter). Such findings could have led to interprete the karyotype as −5 (or −7), −17, +mar or 17p+ [18], thus underestimating the frequency of t(5;17) and t(7;17).

Most of our patients had an unusual form of dysgranulopoiesis, which was associated with a pseudo-Pelger-Huët abnormality in 10 and with the presence of small vacuolated granulocytes in eight. Pseudo-Pelger-Huët anomaly is found in MDS [12, 23, 35], ANLL [23, 36], and chronic myeloid leukemia (CML) [37]. Kuriyama et al. [36] observed this anomaly in the BM of 38 of 50 cases (76%) of primary MDS, but only two patients had more than 5% of their granulocytes affected; in ANLL [36] pseudo-Pelger-Huët anomaly was present in six of 22 cases, which were all FAB M2. In our patients this anomaly was restricted to BM and (with the exception of patient 7) was not observed in circulating granulocytes. Pseudo-Pelger-Huët anomaly was almost constant in our patients with translocations 5;17 or 7;17 and was also demonstrable in five of eight patients with variable cytogenetic anomalies associated with total monosomy 17. In contrast, it was found in only three of 43 cases of ANLL or MDS patients without rearrangement or loss of chromosomes 5, 7, and 17. Sessarego and Ajmar [37] reported a possible correlation between pseudo-Pelger-Huët anomaly in circulating granulocytes and involvement of 17p11→pter region in the blastic phase of CML associated with an isochromosome 17q: thus, a link between 17p and nuclear segmentation of granulocytes may exist. In the other series reporting a high incidence of pseudo-Pelger-Huët anomaly in MDS or ANLL, no cytogenetic results were available [35, 36].

Small vacuolated granulocytes were noted in eight of our 12 patients and in only three of the 51 patients of the comparative groups. To our knowledge, no correlation between small vacuolated granulocytes and cytogenetic rearrangements of chromosome 5, 7, or 17 has been reported previously.

Survival was short in our patients irrespective of the novo or secondary nature of their MDS or ANLL. A very poor prognosis has also been reported in patients with de novo or secondary ANLL or MDS and complex abnormalities of chromosomes 5, 7, and 17 [32, 38] or with many complex karyotypic anomalies [11].

The gene of nuclear protein p53 has been mapped to the short arm of chromosome 17 [39, 40]. Rearrangements of this chromosomal region may alter the normal process of cell duplication, thus leading to nuclear abnormalities. Further studies in molecular biology, however, are clearly needed to understand the genomic basis of the morphological abnormalities of myeloid cells that occur in MDS and ANLL.

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REFERENCES

1. Linman JW, Bagby GC (1978): The preleukemic syndrome (hemopoietic dysplasia). Cancer 42:854–864.
2. Rosenthal DS, Moloney WC (1984): Refractory dysmyelopoietic anemia and acute leukemia. Blood 63:314–318.
3. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnick HR, Sultan C (1982): Proposals for the classification of the myelodysplastic syndromes. Br J Haematol 51:189–199.

4. Ayraud N, Donzeau M, Raynaud S, Lambert JC (1983): Cytogenetic study of 88 cases of refractory anemia. Cancer Genet Cytogenet 8:243–248.
5. Smadja N, Krulik M, Audebert AA, Brissaud P, Debray J (1983): Etude hematologique et cytogénétique de sept cas d'état préleucémique ou de leucémie aiguë secondaire au traitement d'une première affection maligne. Semin Hop Paris 23:1729–1735.
6. Knapp RH, Dewald GW, Pierre RV (1985): Cytogenetic studies in 174 consecutive patients with preleukemic or myelodysplastic syndromes. Mayo Clin Proc 60:507–516.
7. Yunis JJ, Rydell RE, Oken MM, Arnesen MA, Mayer MG, Lobell M (1989): Refined chromosome analysis as an independent prognostic indicator in de novo myelodysplastic syndromes. Blood 67:1721–1730.
8. Le Beau MM, Albain KS, Larson RA, Vardiman JW, Davis EM, Blough RR, Golomb HM, Rowley JD (1986): Clinical and cytogenetic correlations in 63 patients with therapy-related myelodysplastic syndromes and acute nonlymphocytic leukemia: Further evidence for characteristic abnormalities of chromosome no. 5 and 7. J Clin Oncol 4:325–345.
9. Jacobs RH, Cornbleet MA, Vardiman JW, Larson RA, Le Beau M, Rowley JD (1986): Prognostic implications of morphology and karyotype in primary myelodysplastic syndromes. Blood 67:1765–1772.
10. Whang-Peng J, Young RC, Lee EC, Longo DL, Schechter GP, De Vita VT (1988): Cytogenetic studies in patients with secondary leukemia/dysmyelopoietic syndrome after different treatment modalities. Blood 71:403–414.
11. Yunis JJ, Lobell M, Arnesin MA, Oken MM, Mayer MG, Rydell RE, Brunning RD (1988): Refined chromosome study helps define prognostic subgroups in most patients with primary myelodysplastic syndrome and acute myelogenous leukaemia. Br J Haematol 68:189–194.
12. Third MIC Cooperative Study group (1988): Recommendations for a morphologic immunologic and cytogenetic (MIC) working classification of the primary and therapy. Cancer Genet Cytogenet 32:1–10.
13. Scheres JMJC, Hustinx TWJ, Haldrinet RSG, Geraedts JPM, Hagemeijer A, Vander Blij Philipsen M (1984): Translocation 1:7 in dyshematopoiesis: Possibly induced with a non random geographic distribution. Cancer Genet Cytogenet 12:283–294.
14. Lai JL, Fenaux P, Savary JB, Jouet JP, Le Pelley P, Bauters F, Deminatti M (1987): Translocation (1;7) in a case of secondary chronic myelomonocytic leukemia. Cancer Genet Cytogenet 24:355–357.
15. Mecucci C, Van Orshoven A, Vermaelen K, Michaux JL, Tricot G, Louwagie A, Delannoy A, Van den Berghe H (1987): 11q− chromosome is associated with abnormal iron stores in myelodysplastic syndromes. Cancer Genet Cytogenet 27:39–44.
16. Mecucci C, Michaux JL, Louwagie A, Boogaerts M, Van den Berghe H (1988): The short arm of chromosome 6 is nonrandomly rearranged in secondary myelodysplastic syndromes. Cancer Genet Cytogenet 31:147–155.
17. Berger R, Bernheim A, Le Coniat M, Vecchione D, Pacot D, Daniel MT, Flandrin G (1986): Abnormalities of the short arm of chromosome 12 in acute nonlymphocytic leukemia and dysmyelopoietic syndromes. Cancer Genet Cytogenet 19:281–289.
18. Mitelman F (1988): Catalog of Chromosome Aberrations in Cancer, 3rd Ed., Alan R. Liss, New York.
19. Van den Berghe H, Vermaelen K, Mecucci C, Barbieri C, Tricot G (1985): The 5q− anomaly. Cancer Genet Cytogenet 17:189–225.
20. Sakurai M, Oshimura M, Kakati S, Sandberg AA (1974): 8-21 Translocation and missing sex chromosomes in acute leukemia. Lancet 2:227–228.
21. Lai JL, Zandecki M, Jouet JP, Savary JB, Lambiliotte A, Bauters F, Cosson A, Deminatti M (1987): Three cases of translocation (8;16)(p11;p13) observed in acute myelomonocytic leukemia: A new specific subgroup? Cancer Genet Cytogenet 27:101–109.
22. Heim S, Avanzi GC, Billström R, Kristoffersson U, Mandahl N, Bekassy AN, Garwicz S, Wiebe T, Pegoraro L, Falda M, Resegotti L, Mitelman F (1987): A new specific chromosomal rearrangement t(8;16)(p11;p13) in acute monocytic leukemia. Br J Haematol 66:323–326.
23. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Sultan C (1976): Proposals for the classification of the acute leukemias. French-British Cooperative Group. Br J Haematol 33:451–458.
24. Flandrin G, Daniel MT (1981): Cytochemistry in the classification of leukemias. In: The Leukemic Cell, D Catovsky, ed. Churchill Livingstone, Edinburgh, p. 29.

25. Hattori (1958): An improved method of peroxidase reaction combined with Giemsa's stain for blood cells. J Lab Clin Med 51:829–834.
26. Dutrillaux B, Lejeune J (1971): Sur une nouvelle technique d'analyse du caryotype humain. CR Acad Sci (Paris) 272:2638–2640.
27. ISCN (1985): An International System for Human Cytogenetic Nomenclature, Harnden DG and Klinger HE (eds.); published in collaboration with Cytogenet Cell Genet (Karger, Basel, 1985); also in Birth Defects: Original Article Series,Vol. 21, No 1 (March of Dimes Birth Defects Foundation, New York, 1985).
28. Fourth International Workshop on Chromosomes in Leukemia 1982 (1984): Abnormalities of chromosome 17. Cancer Genet Cytogenet 11:314–315.
29. Borgström GH, Vuopio P, De La Chapelle A (1982): Abnormalities of chromosome no. 17 in myeloproliferative disorders. Cancer Genet Cytogenet 5:123–135.
30. Misawa S, Hogge DE, Oguma N, Wiernik PH, Testa JR (1986): Detection of clonal karyotypic abnormalities in most patients with acute nonlymphocytic leukemia examined using short-term culture techniques. Cancer Genet Cytogenet 22:239–251.
31. Wilmoth D, Feder M, Finan J, Nowell P (1985): Preleukemia and leukemia with 12p− and 19q+ chromosome alterations following alkeran therapy. Cancer Genet Cytogenet 15:95–98.
32. Groupe Français de Cytogénétique Hématologique (1984): Chromosome analysis of 63 cases of secondary nonlymphoid blood disorders: A cooperative study. Cancer Genet Cytogenet 12:95–104.
33. Rowley JD, Golomb HM, Vardiman JW (1981): Nonrandom chromosome abnormalities in acute leukemia and dysmyelopoietic syndromes in patients with previously treated malignant disease. Blood 58:759–767.
34. Horiike S, Taniwaki M, Misawa S, Abe T (1988): Chromosome abnormalities and karyotype evolution in 83 patients with myelodysplastic syndrome and predictive value for prognosis. Cancer 62:1129–1138.
35. Varela BL, Chuang C, Woll JE, Bennett (1985): Modifications in the classification of primary myelodysplastic syndromes: The addition of a scoring system. Hematol Oncol 3:55–63.
36. Kuriyama K, Tomonoga M, Matsuo T, Ginnai I, Ichimaru M (1986): Diagnostic significance of detecting pseudo-Pelger-Huët anomalies and micromegakaryocytes in myelodysplastic syndrome. Br J Haematol 63:665.
37. Sessarego M, Ajmar F (1987): Correlation between acquired pseudo–Pelger-Huët anomaly and involvement of chromosome 17 in chronic myeloid leukemia. Cancer Genet Cytogenet 25:265–270.
38. Milton JM, Garson OM, Paton CM, Hurley TF (1984): A complicated but nonrandom karyotype in preleukemia. Cancer Genet Cytogenet 13:37–41.
39. Miller C, Mohandas T, Wolf D, Prokoamer M, Rotter V, Phillip Koeffler H (1986): Human p53 gene localized to short arm of chromosome 17. Nature 319:783–784.
40. Isobe M, Emanuel BS, Girvol D, Gren M, Croce CM (1986): Localization of gene for human p53 tumour antigen to band 17p13. Nature 320:84–85.