Manuscript processing

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Isochromosome 17q in patients with myelodysplastic syndromes: six new cases

We report six cases of myelodysplastic syndromes (MDS) with isochromosome i(17q) as the isolated chromosome anomaly. The patients shared several features, such as severe anemia, prominent pseudo-Pelger-Hüet neutrophils, increased micromegakaryocytes and poor clinical prognosis. Our data support the concept that MDS patients with i(17q) should be considered as a new, specific subset.

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The formation of an i(17q) results in loss of the p arm and duplication of the q arm, such that the affected cell has a single copy of 17p, and three copies of 17q. So far, i(17q) as the sole structural abnormality has been reported in about 80 patients with various types of hematologic diseases.[1-8] i(17q) is a common feature of myeloid neoplasms, such as myeloproliferative and myelodysplastic syndromes (MPS and MDS), blast crisis of chronic myeloid leukemia (CML-BC), acute myeloid leukemia (AML), but is also occasionally found in acute lymphoblastic leukemia (ALL). Previous studies on isolated i(17q) have suggested that this aberration is associated with chronic myeloid abnormalities that have a high rate of progression to AML. A new clinical-pathologic entity in which i(17q) is the sole abnormality has also been reported in a mixed myeloproliferative disorder/myelodysplastic syndrome with an

Table 1. Cytogenetic and clinical features of the patients.

	Case 1	*Case 2*	*Case 3*	*Case 4*	*Case 5*	*Case 6*
Karyotype {No. of karyotype}	46,XY_i_17_q10_[8]	47, XY , i_17_q10_,+13[9]/44-46, X_i_17_q10_(6),-3, -4_,+13, -15_-16_-18_-19_2_-20_-21_2 _cp6_/45Xi_q10_(5), -Y_5_-8_-10_+13_5_-22_cp5_	44-45, _i_17_q10_(6), +X_-2_-7,+12_3_, -15_3_-16_-21_-22_ cp6_45, XY_-14[1]	46, XX_i_17 _q10_[8]	47, XX_i_17_ q10_[14]/46, XX[1]	46, XY_i_17_ q10_[6]/46, XY[1]
Sex/Age (y)	M/47	M/54	M/38	F/67	F/31	M/48
Peripheral blood						
Hb (g/L)	22	54	62	36	23	70
WBC ($\times 10^9$/L)	2.1	9.8	2.5	3.6	0.7	3.8
Platelets ($\times 10^9$/L)	10	14	179	36	29	154
Blasts (%)	0	4.0	1.0	0	0	0
Pelger-Hüet neutrophils (%)	7	9	14	5	6	11
Nucleated red blood cells	0	4	1	2	0	2
Bone marrow						
Cellularity	normal	increased	increased	increased	normal	increased
Myelopoiesis (%)	70.0	67.5	58.5	64.0	16.0	69.5
Blasts (%)	6.0	10.0	7.5	2.5	1.0	3.0
Erythropoiesis (%)	14.0	25.5	26.5	8.0	66.0	22.5
Dyserythropoiesis	No	yes	yes	yes	yes	yes
Megakaryocytes	increased	increased	increased	normal	increased	increased
Dysmegakaryocytopoiesis*						
Micromegakaryocytes	yes	yes	yes	yes	yes	yes
Large mononuclear	yes	yes	yes	no	yes	yes
Multiple small nuclei	yes	yes	yes	yes	no	yes
FAB type	RAEB	RAEB	RAEB	RA	RA	RA
Survival (months)	*	15	18	*	6+	3°

**Demonstrated by immunocytochemistry; *:lost from follow-up; °:died from myocardial infarction. RA: refractory anemia; RAEB: refractory anemia with excess blasts.*

aggressive clinical course.[4] In the present paper, we report our preliminary findings in six MDS patients with i(17q).

Between 1990 and 2000, we performed cytogenetic analysis at diagnosis in 383 cases of MDS diagnosed according to the FAB criteria. Six (1.57%) of these cases had i(17q)(Table 1), this incidence being similar to that in other series.[4] The 6 patients were aged from 31 to 68 years old; 4 were male, 2 female. All of them had moderate to severe anemia (hemoglobin 22-70g/L), a low to normal leukocyte count (0.7-9.8×10^9/L), and platelet values ranging between 10 and 179×10^9/L. Blood films showed dysgranulocytopoiesis, with pseudo Pelger-Hüet anomaly, confirming the previously reported association of Pelger-Hüet anomaly with 17p loss.[4] The predominant feature of the bone marrow smears was granulocytic hyperplasia with dysgranulocytopoiesis. Pelger-Hüet neutrophils were seen in all cases; other manifestations of neutrophil dysplasia included hypogranularity, ringed nuclei and cytoplasm containing varying numbers of small clear vacuoles. No eosinophilia, basophilia, or monocytosis was found in the bone marrow smears, which was not concordant with results reported by others.[2-4] Dysmegakaryocytopoiesis was observed in all the cases, and may be another morphologic feature of MDS patients with i(17q) (Table 1). Bone marrow biopsies from the patients did not show fibrosis in any case. Clinically, two patients had mild hepatomegaly (1.5 cm and 1.0 cm below the costal margin). Neither splenomegaly nor adenopathy was found in any of the 6 patients. An i(17q) was the only structural cytogenetic abnormality identified in all the cases. Two cases (# 2 and 3) had additional numerical abnormalities and another two (# 5 and 6) had a residual normal karyotype. As far as regards clinical outcomes, two patients (#1 and 4) were lost from follow-up, one (# 6) died from myocardial infarction 3 months later, two (# 2 and 3) developed AML 12 and 14 months later, respectively, with survivals of 15 and 18 months from diagnosis, respectively. Only one patient (# 5) is known to be alive after 6^+ months of follow-up.

In conclusion, our findings support the concept that MDS patients with i(17q) should be considered as a unique subset, accounting for about 1% of MDS; this condition is characterized by a male predominance, severe anemia, hyposegmentation of neutrophils, increased micromegakaryocytes, and a poor prognosis.

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Evaluation of leukemic contamination in peripheral blood stem cell leukaphereses vs bone marrow after consolidation therapy in acute myeloid leukemia: not a critical factor in outcome?

Evaluation of leukemic contamination in peripheral blood stem cell leukaphereses and in bone marrow after consolidation therapy in 40 patients with acute myeloid leukemia presenting cytogenetic/molecular abnormalities at diagnosis shows a close relationship between persistence of the disease-related clone, adverse karyotype and poor prognosis.

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Autologous stem cell transplantation (ASCT) is increasingly used as treatment of acute myeloid leukemia (AML); however, one unresolved issue remains the optimal source of stem cells. While the use of peripheral blood stem cells (PBSC) has significantly lowered morbidity and mortality,[1] with the potential advantage of less leukemic contamination than present in bone marrow (BM) grafts,[2-3] the large amount of reinfused cells might increase the probability of contamination and relapse.[4] Investigation of residual disease (RD) in AML is limited to patients showing cytogenetic or molecular abnormalities at diagnosis, accounting for approximately 50 % of cases.[5] Furthermore, RD detection is of varied clinical relevance as AML1/ETO transcripts may persist in long-term survivors who have AML with t(8;21),[6] while detection of PML/RARα and CBFβ/MYH11 positive cells is highly predictive of relapse in acute promyelocytic leukemia (APL) and AML with inv16, respectively.[7-8]

Between January 1994 and June 2002 we used conven-