Defective Neutrophil Migration in Monosomy-7

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The migration in vitro of neutrophils from six patients with monosomy-7 or partial deletion of the long arm of chromosome 7 was studied by two methods: the Millipore filter assay and the migration under agarose assay. Four of the patients had preleukemia, one had subacute myelomonocytic leukemia, and one polycythemia vera. In four patients, chemotaxis (migration towards a higher concentration of chemoattractant) and chemokinesis (stimulated migration without a gradient) were shown to be defective by both methods. In the remaining two patients, this defect could be demonstrated only by the Millipore filter assay or by the agarose assay. Under agarose, random locomotion (no chemoattractant present) of the patients' neutrophils was less than that of the control subjects in four patients, whereas no clear difference could be shown by the Millipore filter method. This study demonstrates that the previously described defect of neutrophil migration in monosomy-7 involves not only chemotaxis but all stimulated migration and, at least in some patients, random locomotion as well. Defective migration in two patients with an apparently terminal deletion of the long arm of one chromosome 7 indicates that the distal half of 7q carries genetic material important for neutrophil locomotion.

THERE IS A rapidly growing number of reports concerning diseases with defective neutrophil migration in vitro, which is frequently associated with increased susceptibility to bacterial infections.[1] The cellular structures and metabolic events involved in neutrophil migration are still largely unknown. A new approach to the study of factors regulating neutrophil migration has been made possible by the recent finding of defective chemotaxis associated with specific chromosomal disorders such as Down's syndrome.[2] We have reported defective neutrophil chemotaxis in vitro in five patients with monosomy-7 associated with various hematologic diseases.[3]

Here we extend our investigations to cover two other parameters of neutrophil migration in vitro, namely random locomotion (no chemoattractant present) and chemokinesis (chemoattractant present without a gradient), in addition to chemotaxis (migration towards a higher concentration of chemoattractant) (for definitions see Keller et al.).[4] These three parameters were studied using two different assay systems in six new patients with total or partial monosomy for chromosome 7.

MATERIALS AND METHODS

Patients

The main features of our six patients are summarized in Table 1. Four of the patients (nos. 1, 2, 4, and 5) were regarded as having preleukemia. We have discussed the problem of preleukemia previously and have given our criteria.[5] One of the patients with preleukemia had previously diagnosed multiple myeloma treated with melphalan. Melphalan treatment had been discontinued 2 mo prior to the neutrophil studies, and the bone marrow had a normal proportion of plasma cells. At the time of the neutrophil studies the amount of the paraprotein was greatly reduced from the initial level, and no peak was detectable on paper electrophoresis. All four patients with preleukemia had anemia and thrombocytopenia. Three had neutropenia with neutrophil counts between 0.6 and 1.8 $\times 10^9$/liter, most of the time over 1.0 $\times 10^9$/liter. All had normo- or hypercellular bone marrow with morphological abnormalities in at least two cell lines. There were less than 5% blast cells in the bone marrow. No other hematologic disease could be discovered in careful investigation. Deficiency of vitamin B_{12}, folate, or iron was excluded.

Patient 6 always had normal neutrophil counts. Patient 3 showed gradually decreasing numbers of neutrophils ranging from 1.8 to 0.4 $\times 10^9$/liter. The proportion of band neutrophils out of all neutrophils was less than 20% at the time of neutrophil studies in five patients. In patient 2, band neutrophils constituted about 45% of all neutrophils at the time of neutrophil studies.

The shortest interval between cytostatic therapy or radiotherapy and subsequent neutrophil studies was 2 mo. No blood transfusions were given within 1 wk prior to the neutrophil studies. Care was taken that the patients did not show any sign of infection within 2 wk prior to the neutrophil studies.

Cell Preparation

Most of the erythrocytes were removed from fresh heparinized blood by Bøyum's method.[6] Cells separated from leukocyte-rich plasma by centrifugation were washed once with Hanks' solution containing 1% human serum albumin and were suspended in Hanks' solution containing casein (Merck, Darmstadt, W. Germany), human serum albumin (Kabi, Stockholm, Sweden), human serum albumin plus N-formylmethionyl-leucyl-phenylalanine (fMLP, Sigma Chemical Company, St. Louis, Mo.), or zymosan (Sigma)-activated serum as indicated (pH 7.2–7.4).

Neutrophil Migration

Millipore method. The method of Zigmond and Hirsch[7] was used as previously described.[5] The cell concentration was adjusted to

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Table 1. Main Clinical Features of Patients

Patient	Sex	Age	Previous Illnesses	Previous Cytotoxic Therapy or Radiotherapy	Clinical Diagnosis at the Time of Study	Follow-up After the Initial Neutrophil Studies		
						Time	Clinical Course	Infections
1	M	63	—	—	Preleukemia	42 mo	Progressive thrombocytopenia after 30 mo of stable course. Died of pulmonary hemorrhage. No overt leukemia	After 30 mo Klebsiella sepsis* and two septicemias*
2	M	60	Basocellular skin cancer 1965 Intraepidermal skin cancer 1973 Lung cancer 1975	Local radiotherapy 1965 Local radiotherapy 1973 Radiotherapy, cyclophosphamide, vincristine, methotrexate and CCNU 1975-1976	Preleukemia	2 mo	No metastases or recurrence of cancer. Sudden death without an obvious clinical reason. Autopsy uninformative	None
3	F	17	—	—	Subacute myelomonocytic leukemia	7 mo	Acute myeloid leukemia. No remission with chemotherapy. Died of intracerebral hemorrhage	Two septicemias*†
4	F	70	Thyreotoxicosis Myeloma	Melphalan 1974 until August 1977	Preleukemia Myeloma	10 mo	Developed kidney failure and died of uremia	Pyelonephritis and bronchitis
5	F	54	Breast cancer, operation 1968	Local radiotherapy 1968	Preleukemia	16 mo	Acute myelomonocytic leukemia. Died of intracerebral hemorrhage	Lung tuberculosis and septicemia*†
6	F	63	—	4 × radioactive phosphorus 1972-1976 Busulphan 1977 and December 1978	Polycythemia vera	24 mo	No progression	None

*No significant neutropenia (< 1.0×10^9/liter) preceding the episode.
†Spiking fever with negative blood cultures and a good response to broad-spectrum antibiotics.

10^6 mature neutrophils/ml. The cells were allowed to migrate into 3-μm Millipore filters (Millipore Corp., Bedford, Mass.) in modified Boyden chambers for 55 min for quantitation of chemotaxis and chemokinesis and for 90 min for testing of random locomotion. Casein (5 mg/ml) was employed as the standard chemoattractant. The same batch of casein dissolved in Hanks' solution was used throughout the experiments. In some experiments, fMLP or zymosan-activated serum was used as attractant (incubation time 45 min in these experiments). fMLP was dissolved in dimethylsulfoxide at 10^{-2} *M* concentration and appropriately diluted with Hanks' solution. Pooled human serum was incubated 30 min at 37°C with zymosan to activate complement, and diluted to the final concentra-

Table 2. Chromosome Findings in Patients

Patient	Time of Testing	Bone Marrow		
		Abnormal Clonal* Karyotype	No. of Banded Mitoses Studied	Percentage of Karyotypically Abnormal Clone
1	160277	45, XY, −7	27	85
	140477		8	100
	180877		10	80
	301177		15	93
	110178		18	100
2	190179	45, XY, −7	7	100
3	140279	45, XX, −7	24	100
	130379		18	94
	260479		15	73
4	190977	45, XX, −7	30	40
	181177		5	20
	040178		12	66
	050578		21	95
	230878		100	45
5	220977	46, XX, del (7) (q22)	19	100
	231177		16	100
	290978		1	100
6	050179	46, XX, del (7) (q22) del (20) (q11)	20	95

*A clone is judged to be present if at least two mitoses with the same extra chromosome or structural rearrangement or at least three mitoses with the same missing chromosome are found.[21]

tion of 12.5 vol%. The distance that the leading front of the cells had migrated was determined in five fields of each of six filters.

Agarose assay. This assay for neutrophil migration was performed as described.[8] Bacterial culture filtrate (BCF) prepared from *E. coli* was stored in 1-ml portions at −20°C. Aliquots of the same BCF lot were used throughout the study. In some experiments fMLP or zymosan-activated serum was used as chemoattractant. Pairs of wells were cut in agarose gel, and BCF, zymosan-activated serum, fMLP, or Hanks' solution was applied to one well simultaneously with the application of 2.5×10^5 mature neutrophils in Hanks' solution to the other well. After incubation for 4 hr, the distances of migration toward the attractant (chemotaxis) or Hanks' solution (random locomotion) were determined using a projection microscope (magnification 28×). Under this magnification, individual cells at the border of the migration pattern were distinct, and the edge of the migration area was determined according to the cells advanced farthest. In most instances the edge of the migration was clear-cut, without scattered cells proceeding beyond. To study chemokinesis, BCF was appropriately mixed with the agarose medium before gel formation. After 4-hr incubation, the distance of migration was determined. Each assay was performed in quadruplicate.

Neutrophil Adhesion

To study adhesion of the neutrophils to the surface of a disposable tissue culture dish (Falcon) we used the method of Crowley et al.[9]

Chromosomal Analysis

Our methods for chromosome work have been described in detail previously.[10]

Statistical Analysis

Student's t test was employed for statistical calculations. Differences of p values less than 0.01 were regarded as significant.

RESULTS

The bone marrow karyotype of patient 1 showed consistent monosomy for chromosome 7 in a large

Table 3. Migration of Neutrophils of Patients With Monosomy-7 in Millipore Assay

Patient	Date of Testing	Cells‡	Migration (μm)* Random Locomotion	Chemotaxis†	Chemokinesis†
1	6-1-77	NC	35.5 ± 1.0	108.4 ± 2.0	62.7 ± 1.4
		PC	37.0 ± 0.6	68.4 ± 1.4¶	50.7 ± 1.0¶
	6-9-77	NC	32.7 ± 0.5	110.8 ± 2.1	65.4 ± 1.6
		PC	36.8 ± 0.8§	65.1 ± 1.2¶	45.1 ± 1.2¶
	8-22-77	NC	31.9 ± 0.6	113.5 ± 2.8	ND
		PC	32.5 ± 1.0	56.7 ± 1.9¶	ND
	2-28-78	NC	37.5 ± 0.6	107.5 ± 3.0	83.9 ± 2.1
		PC	35.5 ± 0.8	53.8 ± 1.9¶	34.5 ± 2.4¶
2	2-20-79	NC	29.7 ± 0.6	114.6 ± 1.7	73.3 ± 2.4
		PC	24.3 ± 0.6¶	73.4 ± 1.6¶	52.8 ± 1.5¶
3	2-20-79	NC	29.7 ± 0.6	114.6 ± 1.7	73.3 ± 2.4
		PC	40.0 ± 0.8¶	109.4 ± 1.9	60.6 ± 2.3§
	3-13-79	NC	29.4 ± 0.5	112.7 ± 2.0	44.5 ± 1.1
		PC	32.4 ± 0.7§	100.2 ± 1.9¶	72.3 ± 1.5¶
4	10-18-77	NC	32.8 ± 0.6	84.6 ± 2.0	56.7 ± 1.1
		PC	30.4 ± 0.7	89.8 ± 1.5	57.3 ± 1.0
	1-4-78	NC	37.2 ± 0.7	128.9 ± 1.4	82.5 ± 1.5
		PC	34.6 ± 0.8	86.0 ± 2.7¶	67.2 ± 1.3¶
5	11-24-77	NC	34.2 ± 0.5	103.6 ± 1.5	65.2 ± 1.8
		PC	30.3 ± 0.8§	66.7 ± 1.7¶	48.0 ± 0.9¶
	1-12-78	NC	33.1 ± 1.0	106.0 ± 4.5	78.9 ± 3.5
		PC	31.8 ± 0.8	75.9 ± 1.9¶	58.6 ± 1.7¶
6	3-6-79	NC	34.5 ± 0.6	132.6 ± 1.7	91.9 ± 2.5
		PC	28.2 ± 0.9¶	93.0 ± 2.4¶	55.3 ± 1.6¶
	3-20-79	NC	29.8 ± 0.5	101.7 ± 2.7	62.2 ± 1.6
		PC	25.4 ± 0.8¶	55.7 ± 1.8¶	46.2 ± 1.4¶

*Mean ± SE of 6 determinations.

†Casein as the chemoattractant.

‡NC, normal cells; PC patient cells.

Level of significance of the difference between patient and control cells: §$p < 0.01$; ¶$p < 0.001$.

ND, Not done.

Table 4. Migration of Neutrophils of Patients With Monosomy-7 in Agarose Assay

Patient	Date of Testing	Cells	Migration (mm)* Random Locomotion	Chemotaxis†	Chemokinesis†
1	6-1-77	NC	1.1 ± 0.03	1.7 ± 0.03	ND
		PC	0.4 ± 0.02§	0.9 ± 0.04§	ND
	6-9-77	NC	0.9 ± 0.02	2.0 ± 0.03	ND
		PC	0.4 ± 0.08§	0.9 ± 0.05§	ND
	2-28-78	NC	0.9 ± 0.02	1.9 ± 0.03	1.7 ± 0.02
		PC	0.4 ± 0.02§	0.8 ± 0.03§	0.6 ± 0.05§
2	2-20-79	NC	0.8 ± 0.04	1.5 ± 0.06	1.4 ± 0.06
		PC	0.5 ± 0.03‡	0.9 ± 0.03§	0.8 ± 0.05§
3	2-20-79	NC	0.8 ± 0.04	1.5 ± 0.06	1.4 ± 0.06
		PC	0.6 ± 0.03‡	0.8 ± 0.04§	0.8 ± 0.06§
	3-13-79	NC	0.8 ± 0.03	1.4 ± 0.06	1.1 ± 0.06
		PC	0.6 ± 0.02§	1.0 ± 0.02§	1.0 ± 0.05
4	10-18-77	NC	0.9 ± 0.01	1.4 ± 0.03	1.2 ± 0.03
		PC	0.8 ± 0.05	1.3 ± 0.08	1.2 ± 0.03
	1-4-78	NC	1.4 ± 0.08	1.8 ± 0.04	ND
		PC	1.0 ± 0.05	1.1 ± 0.04§	ND
5	11-24-77	NC	1.0 ± 0.03	1.7 ± 0.01	ND
		PC	0.9 ± 0.02	1.1 ± 0.03§	ND
	1-12-78	NC	0.7 ± 0.02	1.5 ± 0.02	1.6 ± 0.03
		PC	0.8 ± 0.03	1.2 ± 0.04§	1.0 ± 0.03§
6	3-6-79	NC	0.8 ± 0.04	1.4 ± 0.05	1.9 ± 0.06
		PC	1.1 ± 0.08	1.9 ± 0.08‡	1.8 ± 0.05
	3-20-79	NC	0.7 ± 0.07	1.1 ± 0.10	1.2 ± 0.05
		PC	0.4 ± 0.05	1.0 ± 0.07	1.0 ± 0.05

*Mean ± SE of 4 determinations.

†Bacterial culture filtrate as the chemoattractant.

Level of significance of the difference between patient and control cells: ‡$p < 0.01$; §$p < 0.001$.

majority of the cells (Table 2). The bone marrow of patient 2 was studied once and all the cells studied showed monosomy-7. The neutrophils from both patients showed poor chemotaxis and chemokinesis both in the Millipore filter (Table 3) and under agarose (Table 4). Random locomotion of these patients' neutrophils was grossly impaired under agarose.

When the chemotactically active peptide N-formyl-methionyl-leucyl-phenylalanine became available, the cells from patient 1 (the only patient with complete monosomy-7 alive at that time) were retested in September 1980, employing both the filter and the agarose assays, with the peptide and zymosan-activated serum as attractants (Table 5). Both methods exhibited a clearcut defect in chemotaxis, and the filter method showed a defect in chemokinesis as well. The result was similar with both attractants.

Almost all of the mitoses of patient 3 showed monosomy-7 at the time of neutrophil studies, but 2 mo later 27% of the mitoses were normal. The migration of her neutrophils was similar to that of control cells in the Millipore filter on two occasions. Under agarose, however, random locomotion, chemotaxis, and chemokinesis were all less than those of control cells.

In patient 4, monosomy-7 occurred in 40% of cells in September 1977, 4 wk before the neutrophil studies, and showed a decline to 20% (1 of 5 cells) at 4 wk after the first neutrophil studies. The proportion of abnormal karyotypes increased to 66% by January 1978, when the neutrophil studies were repeated. Her neutrophils migrated normally in both assays in October 1977. In January 1978, chemotaxis was clearly inferior to that of the simultaneous control cells in both assays. The Millipore method also demonstrated depressed chemokinesis and the agarose method showed subnormal random locomotion.

In patient 5 there was an apparent terminal deletion involving half of the long arm of one chromosome 7 in

Table 5. Migration of Neutrophils From Patient 1 Tested With Zymosan-Activated Serum and N-Formyl-Methionyl-Leucyl-Phenylalanine

		Patient	Control 1	Control 2
Millipore assay				
Chemokinesis in				
ZAS*		34.8 ± 1.3†	57.5 ± 2.1‡	59.1 ± 2.0‡
HSA§		36.7 ± 1.7	63.0 ± 2.0‡	74.7 ± 1.4‡
HSA + fMLP¶	$1 \times 10^{-8} M$	42.6 ± 1.4	69.7 ± 1.6‡	67.2 ± 1.6‡
HSA + fMLP	$1 \times 10^{-9} M$	48.5 ± 1.6	89.1 ± 3.4‡	69.1 ± 2.4‡
Chemotaxis towards				
ZAS		35.0 ± 0.8	69.5 ± 1.4‡	79.7 ± 1.8‡
HSA + fMLP	$1 \times 10^{-8} M$	66.5 ± 2.4	101.8 ± 4.0‡	95.7 ± 4.2‡
HSA + fMLP	$1 \times 10^{-9} M$	56.7 ± 1.4	108.5 ± 2.8‡	95.7 ± 1.8‡
Agarose assay				
Chemokinesis in HSA		0.6 ± 0.03‖	0.8 ± 0.05	0.6 ± 0.03
Chemotaxis towards				
ZAS		0.7 ± 0.03	1.5 ± 0.06‡	ND
HSA + fMLP	$1 \times 10^{-7} M$	1.3 ± 0.08	2.6 ± 0.09‡	2.3 ± 0.11‡

*Zymosan-activated serum, 12.5 vol %.

†μm, mean ± SE of 6 determinations.

‡Level of significance of the difference between patient and control cells: $p < 0.001$.

§Human serum albumin, 1 mg/ml.

¶N-formyl-methionyl-leucyl-phenylalanine.

‖mm, mean ± SE of 4 determinations.

all cells studied on three different occasions. Her neutrophils repeatedly showed depressed chemokinetic and chemotactic migration in the Millipore filter. Both chemokinesis and chemotaxis were also depressed under agarose.

In almost all of the bone marrow cells from patient 6, half of the long arm of one chromosome 7 and most of the long arm of one chromosome 20 were deleted. In the Millipore filter, her neutrophils exhibited clearly depressed chemokinesis and chemotaxis. Random locomotion was also slightly less than that of control cells. The agarose method demonstrated no clear abnormality in the migration of the neutrophils.

Cells of patient 1 were tested for neutrophil adhesion to plastic surfaces. No difference from control cells could be seen.

The constitutional karyotype was normal in all six patients, as judged by the study of phytohemagglutin-in-stimulated lymphocytes from the peripheral blood.

To define the specific role of monosomy-7, it is important to find out whether defective neutrophil migration is found in patients with other abnormal karyotypes or in general in patients with diseases similar to those in our study. We have studied neutrophil migration by the Millipore assay in 34 patients with preleukemia who did not have monosomy-7 (published in part previously, ref. 5). Sixteen of these patients had karyotype abnormalities. Defective migration was demonstrated in only one, a patient with trisomy-8 and a high proportion of band neutrophils,[5] but a further patient with trisomy-8 had normal migration. In 9 patients, one abnormal clone was seen in more than 60% of mitoses studied. These karyotypes, associated with normal neutrophil migration, are listed in Table 6. In addition, we studied random locomotion, chemokinesis, and chemotaxis of neutrophils from 6 patients with subacute myelomonocytic leukemia, 3 patients with multiple myeloma, and 3 patients with polycythemia vera. The cells from one of the patients with subacute myelomonocytic leukemia without monosomy-7 exhibited slightly depressed chemotaxis and chemokinesis. The cells from the other patients with myelomonocytic leukemia, myeloma, or polycythemia vera migrated normally.

DISCUSSION

We have previously reported defective in vitro neutrophil chemotaxis associated with monosomy-7.[3]

Table 6. Bone Marrow Karyotypes* Associated With Normal Neutrophil Migration

46, XY, −17, +i(17q)
47, XX, +8
46, XX, t(1;3;11)(p1;q2;?q)
46, XX, del(5)(q13q31), del(22)(q11)
46, XX, del(13)(q12q14)
47, XX, del(9)(q21), +21
47, XY, +19
46, XY, t(1;16)(p3;p1)
47, XXY (constitutional)

*In over 60% of the mitoses studied.

In vivo testing would be desirable, but normal controls for leukopenic patients cannot be found for studies with skin windows. Since it is possible that none of the in vitro methods for quantitation of neutrophil migration ideally simulates the conditions prevailing in vivo, we chose to test in vitro migration employing in parallel two methods in which the conditions for migration are different.

Our data obtained by the Millipore filter method confirm the previously reported association of depressed in vitro neutrophil chemotaxis with monosomy-7.[3] In addition to depressed chemotaxis, the patients' neutrophils also exhibited depressed chemokinesis. In the Millipore filter test, the random locomotion of patient neutrophils did not significantly differ from that of control cells. However, the agarose method, well suited for the in vitro assessment of neutrophil random locomotion,[11,12] showed depressed random locomotion in the four patients with complete monosomy-7. Furthermore, the agarose method demonstrated for patient 3 a defect in chemotaxis and chemokinesis not shown by the filter method. The chemotaxis and chemokinesis of cells from patient 6, defective in the filter, were normal under agarose. The observed differences emphasize the need of using parallel methods for the in vitro determination of neutrophil migration. Both the physical environment and some of the chemoattractants are different in the two methods, and this may be one reason for the differences. Other reasons, still poorly understood, may also play a role. The finding of depressed neutrophil random locomotion along with defective stimulated migration in a large proportion of patients with monosomy-7 suggests that the defect in locomotion may be due to a defect in the inherent capacity of the cells to migrate rather than in their ability to sense and respond to chemotactically active agents.

We have previously shown that sera from patients with monosomy-7 associated with depressed in vitro neutrophil migration act as good chemoattractants for normal cells.[3] Therefore, it is improbable that an inhibitory factor in patient sera would be the cause of the observed difference.

In patient 4, the neutrophil migration, as tested by both methods, deteriorated simultaneously with an increase in the proportion of mitoses with monosomy-7. In the rest of the patients with the migration defect, only minor fluctuations in the proportion of abnormal mitoses in the bone marrow occurred, and so changes in migration properties were neither expected nor found.

We have studied neutrophil migration in 11 patients with total or partial monosomy-7, out of these 6 with preleukemia, 2 with subacute myelomonocytic leukemia, 2 with acute myeloid leukemia, and 1 with polycythemia vera (ref. 3 and present results). A defect was demonstrated in 10 patients, and the result was marginal in the eleventh case. Thus, the association between monosomy-7 and defective migration is strong. In the Millipore assay, defective migration was found in 9 of 11 patients with monosomy-7, but in only 2 of 46 other patients with similar diseases (preleukemia, subacute myelomonocytic leukemia, myeloma, or polycythemia vera) with or without other karyotype abnormalities. Thus, the defect seems to be specifically associated with monosomy-7.

Three of the six patients had received cytotoxic chemotherapy during their disease prior to the neutrophil studies. However, the shortest interval between cytotoxic therapy and neutrophil testing was 2 mo, excluding an immediate drug effect depressing the neutrophil function in vitro. Long-term effects on the metabolism and behavior of the cells cannot, of course, be excluded.

Defects of neutrophil function in vitro are frequently associated with increased susceptibility to bacterial infections.[1] Among our six patients, four had major infections that either definitely or most likely (a clinically septic state with negative blood cultures and good response to antibiotics) were caused by bacteria. Under agarose, depressed chemotaxis was exhibited by cells from all these four patients. In the filter test, one of these four showed normal chemotaxis. Patient 1 with the most prominent in vitro migration defect had no infection problems during the first 30 mo of follow-up, but subsequently developed three septicemias within a period of 5 mo without any change in the numbers of peripheral blood neutrophils. Leukemic patients with monosomy-7 are known to have an exceptionally poor prognosis,[13,14] and infection is a major cause of death in acute myeloid leukemia.[15] Infection is also a prominent feature in preleukemia.[16,17] The occurrence of severe infections in the absence of marked neutropenia (peripheral blood neutrophils $\geq 10^9$/liter) in a number of our patients suggests a role for defective neutrophil migration as one cause of depressed resistance for infection.

Our present findings reinforce the suggestion that monosomy for a gene or genes on chromosome 7 leads to impairment of granulocyte locomotor function, which may in turn be related to a concomitant decrease in the major high molecular weight surface glycoprotein (GP 130).[18] This is consistent with the provisional assignment to chromosome 7 of a gene coding for protein GP 130.[19] That the decrease in this protein is responsible for the defective locomotion remains unproven, but the expression of GP 130 in a promyelocytic leukemia cell line is associated with

simultaneous appearance of phagocytic and possibly chemotactic capacity.[20] Several lines of research are in progress for further study of this question. The existence of the defect in two patients with a deletion of the long arm of one of the chromosomes no. 7 suggests that genetic material associated with the migration defect is in this part of the chromosome.

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