Translocation t(10;17)(p13;q12) in Two Cases of Acute Nonlymphocytic Leukemia with Phagocytic Activity of Blasts

A New Cytogenetic Entity?

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ABSTRACT: *We report two cases of translocation t(10;17)(p13;q12) found in a series of 278 cytogenetically studied acute nonlymphocytic leukemia cases. Blast cells, in both cases, were undifferentiated and had phagocytic properties. These patients might represent cases of a new cytogenetic entity.*

INTRODUCTION

In the past few years, several chromosome rearrangements have been correlated with particular cytologic features in acute nonlymphocytic leukemias (ANLL). These rearrangements include t(8;21)(q22;q22) [1, 2], t(15;17)(q22;q12-21) [3], inv(16)(p13q22) [4], inv(3)(q21q26) [5], and t(8;16)(p11;p13) [6, 7]. Some of these cytogenetic entities are restricted to one FAB subtype of ANLL, whereas others are not.

Since 1981, we have performed cytogenetic analysis in 278 cases of ANLL. In two cases, we found a t(10;17)(p13;q12). The blasts of both patients had similar cytologic features and appeared morphologically undifferentiated. Diagnosis of ANLL was made after cell surface marker analysis. These two patients may be the first reported cases of a new cytogenetic subgroup of ANLL.

MATERIAL AND METHODS

Cytogenetics

Cytogenetic analysis was performed on bone marrow cells after a 24-hour culture. Chromosomes were analyzed using R and G banding and classified according to the ISCN [8].

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Cytomorphology

Blood and bone marrow smears were stained according to standard procedures, including May Grunwald Giemsa, peroxidase [9], periodic acid-Schiff (PAS) [10], acid phosphatase [11], nonspecific esterase [naphthyl ASD acetate esterase (NASDA) and α-naphthyl butyrate esterase (αNB)], and chloracetate esterase (CAE) [12].

Immunologic Markers

Mononuclear cells were isolated from heparinized bone marrow on Ficoll MSL (Eurobio) and studied by indirect immunofluorescence (flow cytometry on FACS-Star, Becton Dickinson). Controls were carried out with irrelevant monoclonal antibody (Mo Ab).

RESULTS

Clinical and Hematologic Findings

Case 1. A 25-year-old female patient was hospitalized in March 1987 because acute leukemia was suspected. She had no previous medical history. Symptoms of anemia had appeared a few weeks earlier.

On admission, clinical findings were unremarkable and no organomegaly was found. A diagnosis of acute leukemia was made on blood count and marrow aspirate (Table 1). Blasts appeared undifferentiated with light microscopic examination and cytochemical stains (Table 2), but immunologic findings allowed the diagnosis of ANLL, with a probable megakaryoblastic component (Table 2). The bone marrow trephine biopsy showed massive leukemic infiltration without myelofibrosis. No coagulopathy was found. The patient was treated by combination chemotherapy of rubidazone and cytosine arabinoside (ara-C) and reached complete remission (CR). She received consolidation and maintenance chemotherapy, as no allograft was possible. She remains in CR in August 1988.

Case 2. A female patient, aged 81, was referred to our hospital unit in January 1988 for pancytopenia. Hysterectomy followed by pelvic radiotherapy had been performed 14 years earlier for carcinoma of the endometrium. She remained well afterward, until August 1987, when macrocytic anemia was discovered and pancytopenia subsequently developed.

On admission, she had symptoms of anemia. No organomegaly was found. The blood count and marrow aspirate (Table 1) led to the diagnosis of undifferentiated acute leukemia possibly secondary to previous radiotherapy. Immunologic studies (Table 2) favored a diagnosis of ANLL with a probable megakaryoblastic component,

Table 1 Hematologic data of the two patients at diagnosis

	Blood				Bone marrow aspirate	
Case	WBC ($\times 10^9$/L)	Blasts (%)	Hemoglobin (g/L)	Platelets ($\times 10^9$/L)	Density	Blasts (%)
1	6.1	22	7.5	105	++	75
2	1.6	9	8.6	123	+	44

Table 2 Cytochemistry and immunologic data of bone marrow blasts (% positive cells)

	Cytochemistry							Immunophenotype[a]									
Case	Myelo-peroxidase	PAS	Acid phosphatase	NASDA	NASDA + NaF	αNB	CAE	CD2	CD7	HLA DR	CD10	CD19	CD14	CD13	CD33	Anti-VWF	Anti-GP IIb IIIa
1	—	8	12[b]	+	Partially inhibited	ND	ND	ND	9	12	11	ND	15	46	45	31	ND
2	—	3	66[c]	+	Not inhibited	—	—	28	ND	56	45	27	42	48	ND	ND	38

Abbreviation: ND, not done.

[a] The population was considered positive when more than 30% of the cells were reactive.

[b] Weak positivity.

[c] Strong positivity in 21%.

but biphenotypic myeloid–lymphoid acute leukemia could not be excluded. Therapy with low dose ara-C (10 mg/m^2/12 hours) was started but without success, and the patient died in June 1988.

Cell Morphology and Cytochemical Findings

The morphology of the blast cells (Fig. 1) was similar in cases 1 and 2: the cell size was heterogenous (15–35 μm). The larger cells were often multinucleated. The light-blue cytoplasm was scanty in the smaller blasts, more abundant in the larger cells, without granules, but prominent and confluent vacuoles were seen here and there. The cytoplasm was often rugged and budding. The nucleus was oval, with finely reticular chromatin and one or several inconspicuous nucleoli. Blast cells showed phagocytosis of platelets, red cells, erythroblasts, granulocytes, or even blasts. The phagocytic activity was moderate in case 1 (0.3% of blasts) but more intense in case 2 (3%). Small numbers of micromegakaryocytes were seen in both patients. There was no dysgranulopoiesis or dyserythropoiesis. Cytochemical studies on blast cells (Table 2) showed no evidence of differentiation.

Cell Surface Markers

Case 1 reacted with myeloid Mo Ab (CD13:46%; C33:45%) and for von Willebrand factor (VWF) related antigen Mo Ab (31%), but was negative for all the lymphoid markers and anti HLA-DR.

Case 2 expressed HLA-DR (56%) and reacted with CD10 (anti-Calla) (45%), but not with CD2 (pan T) or CD19 (pan B). The blasts reacted with antimyeloid Mo Ab (CD14:42%; C13:48%) and antimegakaryocytic GP IIbIIIa (38%).

Cytogenetic Findings

In both cases abnormal and normal cytogenetic clones were observed (AN). In cases 1 and 2, 23 and 28 cells were analyzed, respectively. In case 1, the translocation t(10;17)(p13;q12) was observed in 20 cells (Fig. 2a,b) and three cells had a normal karyotype (46,XX).

In case 2, two cellular clones were present: normal cells (46,XX; nine metaphases) and 46,XX,t(10;17)(p13;q12 or q21) (20 metaphases) (Fig. 2c,d).

In both patients, chromosome breakpoints were situated at the 10p13 and 17q12-21 regions. This translocation was not found in any other of our 276 ANLL patients on whom cytogenetic analysis has been performed since 1981.

DISCUSSION

A t(10;17)(p13;q12) was seen in two patients with morphologically undifferentiated acute leukemia, but with immunologic markers of ANLL. To our knowledge, this translocation has not previously been reported in ANLL [13]. It appears to be a rare event, as we found it in only two of 278 karyotypes performed at diagnosis in ANLL during the last 8 years.

Our two patients had no particular clinical features in common except female sex. In case 2, the disease was preceded by a few months of macrocytic anemia and was possibly secondary to radiotherapy, although the long interval (14 years) and the absence of associated chemotherapy could not rule out simple coincidence. The bone marrow infiltration was massive in case 1 and only partial in case 2.

Cytologically, the blasts were similar in both cases and appeared undifferentiated

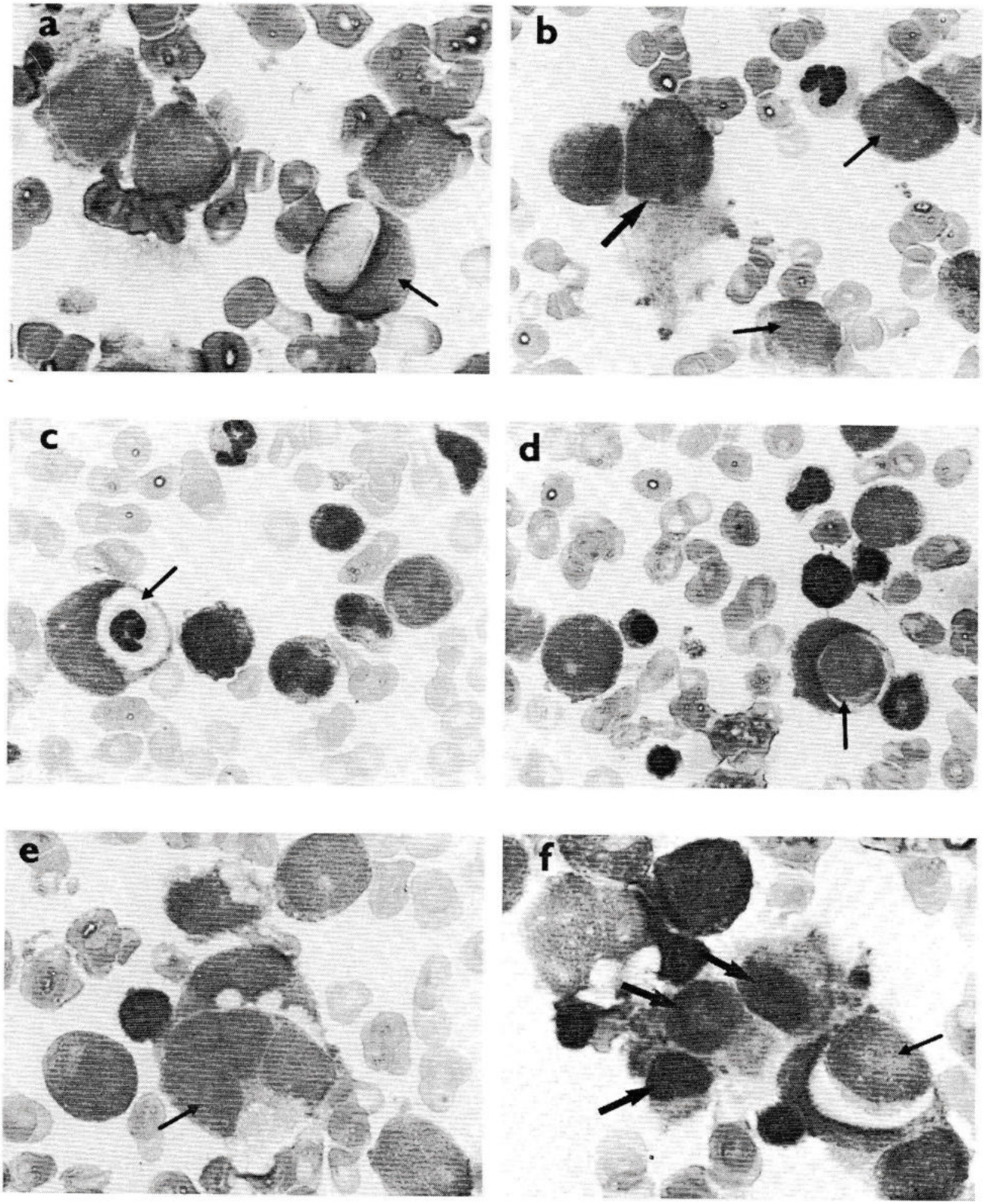

Figure 1 Morphology of blast cells in bone marrow smears. Patient 1. (a) Four blasts, one of them showing erythrophagocytosis (arrow); (b) a small megakaryocyte (thick arrow) and two blasts (thin arrow). Patient 2. Blasts showing a polymorphonuclear (c) and a blast internalization (d); (e) multinucleated and vacuolized blast; (f) three micromegacaryocytes (thick arrows) and blasts; one blast seems to ingest another blast (thin arrow).

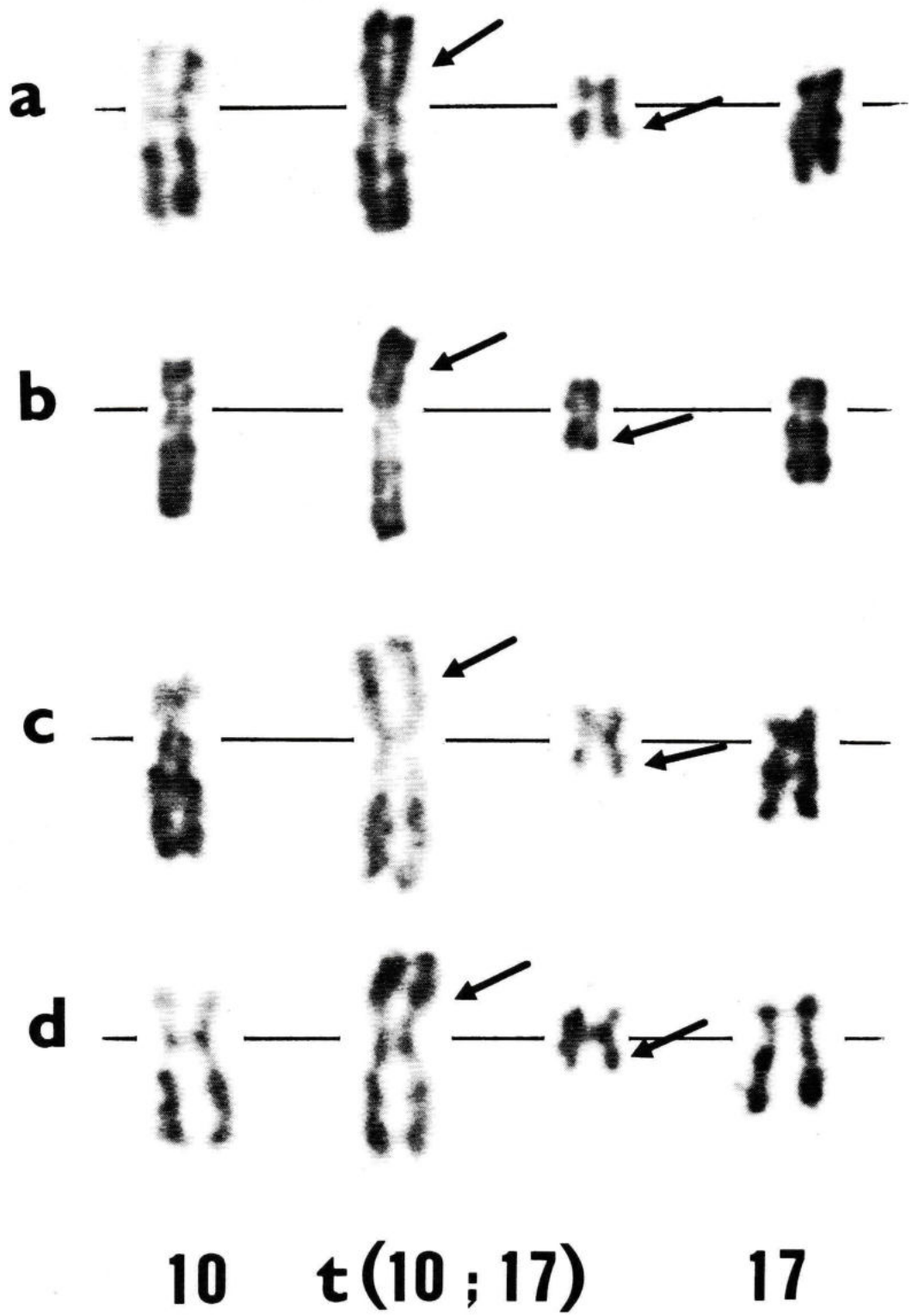

Figure 2 Partial karyotypes from case 1 (a) and (b) and case 2 (c) and (d): 46,XX, t(10;17)(p13;q12). Breakpoints are indicated by black arrows (R banding).

morphologically and with cytochemical stains. They were characterized by heterogeneity of cell size, presence of multinuclear forms, and phagocytic properties of some of the blast cells. This phagocytic activity was prominent in case 2, but less obvious in case 1. The normal blasts of healthy bone marrow do not exhibit phagocytosis [14]. Conversely phagocytosis is one of the cytologic features of acute monoblastic leukemia with t(8;16) [6, 7]. It has also been reported, although rarely, in other subtypes of ANLL [15–17] or in ALL [18].

Immunologic studies favored the diagnosis of ANLL with a megakaryoblastic

Table 3 Involvement of 17q and 10p in leukemia

Translocation	Type of leukemia	Ref.
t(15;17)(q22;q11-21)	Acute promyelocytic leukemia (M3 FAB)	[3, 19]
t(12;17)(q11;q11)	Acute lymphoblastic leukemia	[20]
t(1;17)(p11;q11)	Chronic myeloid leukemia in blastic or accelerated phase	[21, 22]
t(11;17)(q24;q21)	Acute monoblastic leukemia (M5a FAB)	[23, 24]
17q region	Secondary leukemia	[25]
t(17;19)(q11;q13)	pre-B ALL	[26]
t(10;11)(p14-15;q22-23)	ANLL (M5a FAB)	[27, 28]

component in both cases. Unfortunately, we could not perform electron microscopic study in our two patients in order to confirm the presence of platelet peroxidase. In case 2, positivity for CALLA antigen was found. This could suggest a biphenotypic myeloid–lymphoid leukemia, although CD19, another marker of early pre-B cells, was negative in the present case.

Breakpoints on chromosomes 10p and 17q were probably identical in our two patients in the 10p13 and 17q12 or 21 regions. As seen in Table 3, involvement of the long arm of chromosome 17 is often encountered in leukemia, whereas involvement of the short arm of chromosome 10 is infrequent.

No oncogene has been mapped to 10p, but protooncogenes *c-erb A* and *c-erb A2* have been located on 17q [29, 30], as well as the gene coding for myeloperoxidase, which is transferred to chromosome 15 in M3 leukemias with t(15;17) [31–33]. The contribution of these genes to leukemogenesis in humans still has to be documented.

Our two patients may represent the first two reported cases of a new cytogenetic entity, but our findings will have to be confirmed by publication of similar cases.

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