SHORT COMMUNICATIONS

Promyelocytic Blast Crisis of Philadelphia-Positive Thrombocythemia with Translocations (9;22) and (15;17)

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ABSTRACT: *We report a promyelocytic blast crisis in a case of Ph-positive thrombocythemia with both t(9;22) and t(15;17). Our patient confirms the specificity of t(15;17) in malignant proliferation of promyelocytes and suggests its appearance as a second genetic event in the genesis of blast crisis occurring in a Ph-positive clone.*

INTRODUCTION

Essential thrombocythemia (ET) is a myeloproliferative disorder characterized by a platelet count consistently higher than 1000 $\times$ 10^9/L [1, 2]. Bone marrow karyotype is normal in most cases [3–5] and only a few patients develop a blast crisis [1]. In a small number of cases of thrombocythemia, however, a Philadelphia chromosome (Ph) is found [6–8] and these cases are characterized by frequent, if not constant, evolution to a blast crisis often preceded or followed (if reversal of blast crisis is obtained) by a typical picture of chronic myeloid leukemia (CML) in the chronic phase. Such Ph-positive thrombocythemias, therefore, are regarded by most investigators as CML variants [6–8].

The translocation t(15;17) is found in most cases of acute promyelocytic leukemia (APL) and is regarded to be specific of this variant of leukemia [9]. It was a constant finding in our experience of 21 cases of APL (unpublished results).

We report herein a case of APL with both t(9;22) and t(15;17), diagnosed 10 months after the discovery of extreme thrombocytosis, which we believe was a promyelocytic blast crisis of Ph-positive thrombocythemia.

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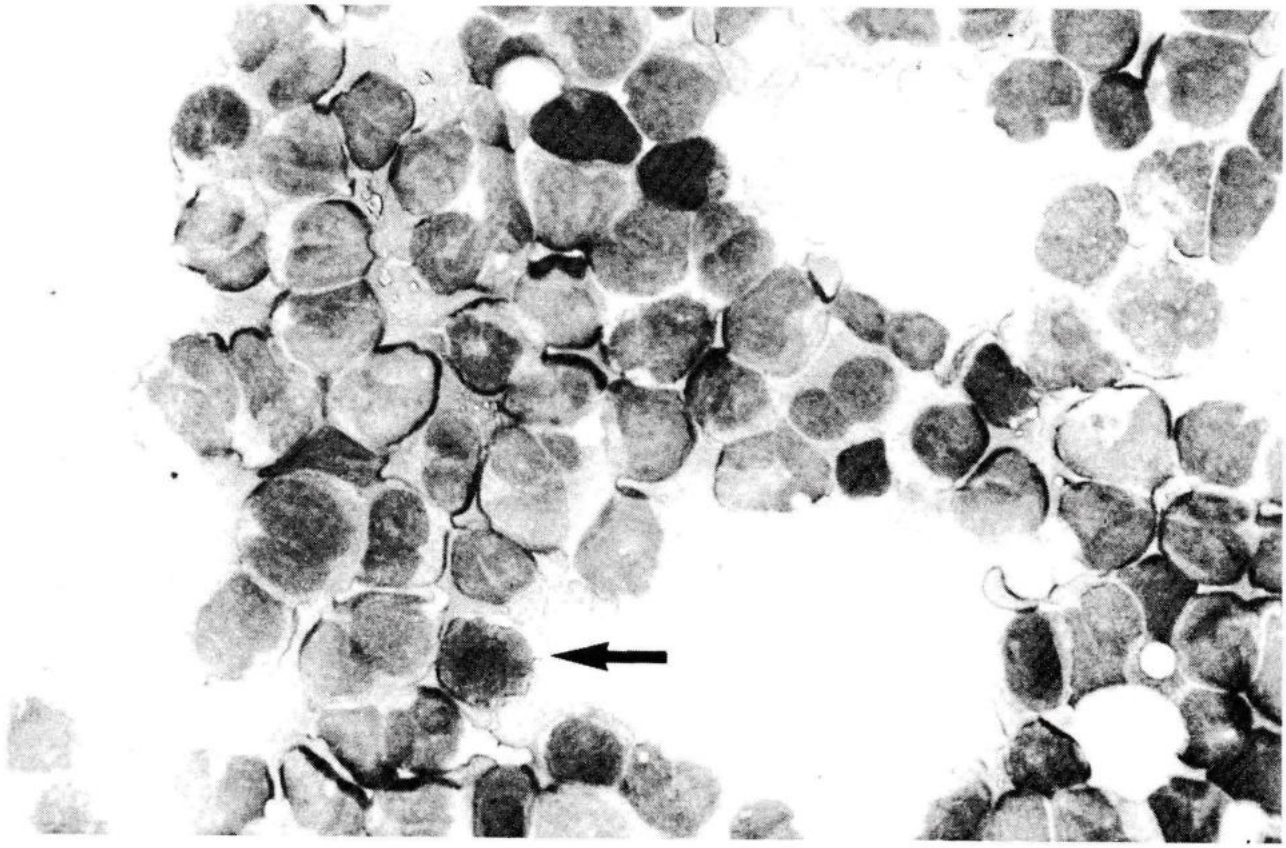
CASE REPORT

An 85-year-old female patient was referred to our hospital in October 1986 for acute leukemia. She had no previous relevant history until December 1985, when a blood count (performed because of fatigue and weight loss) showed hemoglobin 10 g/dl, WBC 10.5 $\times$ 10^9/L (neutrophils 68%, monocytes 3%, lymphocytes 28%, myelocytes 1%) and platelets 3560 $\times$ 10^9/L. Physical examination was normal. The patient refused further evaluation.

On September 15, 1986, the blood count showed hemoglobin 9.9 g/dl, WBC 6 $\times$ 10^9/L (neutrophils 65%, eosinophils 1%, lymphocytes 30%, monocytes 3%, myelocytes 1%) and platelets 1590 $\times$ 10^9/L. On October 30, 1986, when bleeding developed and blasts appeared in the peripheral blood, the patient was hospitalized. On admission, her condition was very poor and cutaneomucous bleeding was prominent. There was no organomegaly and peripheral blood findings were as follows: hemoglobin 7 g/dl, WBC 37 $\times$ 10^9/L (neutrophils 1%, lymphocytes 4%, blasts 95%), and platelets 133 $\times$ 10^9/L. Bone marrow smears showed 92% blasts, which had a morphology (as well as in peripheral blood) similar to that seen in APL microgranular form (M3 variant) [10, 11] (Fig. 1). A syndrome of disseminated intravascular coagulation was present (fibrinogen 1.4 g/L, fibrinogen degradation products 80 μg/ml, positive FS test, factor V 50%).

Because of the patient's advanced age and poor condition, no chemotherapy was started and she died 2 days later.

Figure 1 Bone marrow cells with bi- or multilobed nuclei. Cytoplasmic granules are either absent or scarce and fine. Only occasional highly granular blasts are present (arrow).



CYTOGENETIC STUDIES

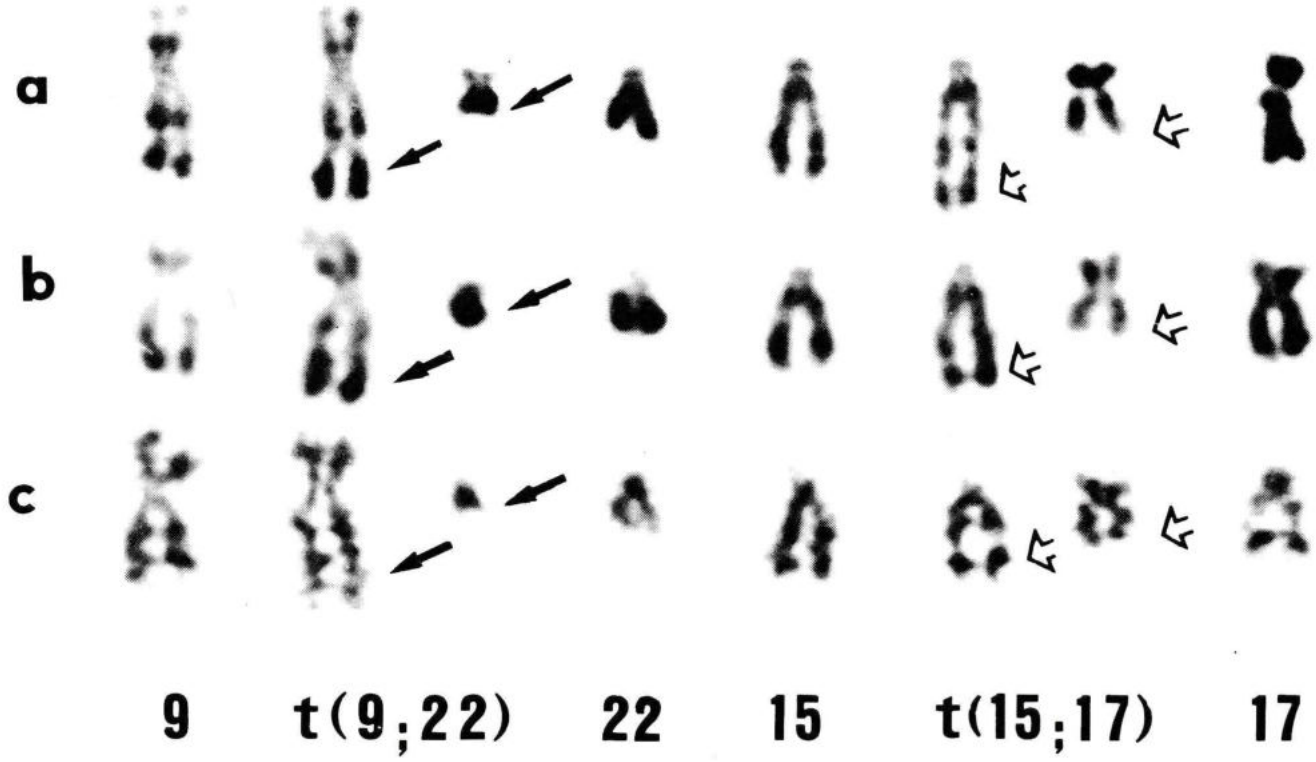
Cytogenetic study was performed on unstimulated blood culture when the patient was hospitalized in October 1986. After 24-hour culture, 35 mitoses were analyzed with banding techniques (RHG, GTG), showing a usual Ph translocation between chromosomes #9 and #22, as well as an additional t(15;17)(q22;q21) in all cells (Fig. 2).

DISCUSSION

No cytogenetic study was performed when the thrombocythemia was discovered, but we believe that the Ph chromosome was already present because the simultaneous acquisition of t(9;22) and t(15;17) has not been previously described in Ph-negative myeloproliferative disorders. Besides, although the secondary appearance of a Ph chromosome has been reported in a patient with agnogenic myeloid metaplasia [12], no such finding has been encountered in ET. Finally, no promyelocytic blast crisis has been reported, to our knowledge, in the course of ET. Most investigators regard Ph-positive thrombocythemia as a CML variant [8, 13, 14] and distinguish it from ET. Our patient could probably be included in such an entity, with subsequent development of a promyelocytic crisis.

The association of t(9;22) and t(15;17) has been documented only twice in promyelocytic blast crisis of Ph-positive CML [8, 13]; both translocations were restricted to the blast cells and dividing erythroblasts and myelocytes only had the t(9;22) [8]. Two further cases of promyelocytic blast crisis in Ph-positive CML have been reported, one completely lacking the t(15;17) [14] and the other one showing an isochromosome 17q without t(15;17) [15]. Additionally, inv(16)(p13q22) was re-

Figure 2 Partial karyotypes of chromosomes #15, #17, #9, and #22 from three blood metaphase cells during blast crisis. (a,b) RHG; (c) GTG, showing a Ph translocation accompanied by a t(15;17).



ported in association with t(15;17) in a case of acute promyelocytic transformation of acute myelomonocytic leukemia; the translocation was considered to be a secondary event [16].

This case, as well as previously reported cases of promyelocytic blast crisis of CML, reinforce the hypothesis that CML blast crisis can be the result of a second genetic event occurring in a committed cell belonging to the Ph-positive clone. Our patient also confirms the close association of t(15;17) and APL.

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