Near Haploid Cell Line in Lymphoid Blast Crisis of Ph1-positive Chronic Myeloid Leukemia

Allégria Kessous, Pierre Colombies, Jacques Pris, and Danielle Clement

Unite INSERM U.100 [A. K], Service d'Hématologie et Génétique [P. C] and Service d'Hématologie, Clinique Dieupafy [J. P], Centre Hospitalier Universitaire, Purpan, Toulouse, France

ABSTRACT

This report describes a case of lymphoid blast crisis of a chronic myelocytic leukemia with the occurrence of a double chromosomal population carrying a Philadelphia chromosome. Fifty-five % of the cells have 28 chromosomes, and 36% show the exact duplicate of the near haploid chromosome complement. The similarities between this near haploid cell line and those previously reported, as well as the presence of such clones in acute lymphoblastic leukemia, are discussed. In the leukemic lymphoblasts, the association of the Philadelphia chromosome with a near haploid karyotype described so far in acute lymphoblastic leukemia provides further support for the concept of a pluripotent Philadelphia chromosome-positive stem cell common to both lymphoid and myeloid lines.

INTRODUCTION

The close association of the Ph1 chromosome with CML is well established and documented. This chromosome abnormality is usually observed in cells of myelocytic origin although it may be found in precursors of erythrocytes, monocytes, and megakaryocytes (6, 30). As PHA-stimulated lymphocytes of CML patients failed to show the Ph1 chromosome marker, it was believed that CML originates from stem cell common to myelocytes, erythrocytes, monocytes, and megakaryocytes. Recently, several investigators reported the presence of the Ph1 chromosome either in ALL or in the lymphoblastic conversion of CML. In all these Ph1-positive ALL, the Ph1 chromosome was found either alone (1, 3, 7, 8, 12, 26, 29) or with additional chromosomal abnormalities (11, 16, 20, 23, 25). These findings have raised questions about the origin of the myelocytic and lymphocytic lines which could be a pluripotent stem cell common to these 2 cell types (4, 13, 14). We wish to report here a new case of lymphoblastic crisis in Ph1 chromosome-positive CML with the occurrence of a near haploid cell line found in the patient's bone marrow.

A 61-year-old female was admitted to the hospital in May, 1972, with clinical and hematological diagnosis of CML, which was confirmed by cytogenetic and cytochemical findings. The patient underwent a complete remission with Misulban. A second chromosome examination was carried out while the patient was pancytopenic. The Ph1 chromosome was found either alone (1, 3, 7, 8, 12, 26, 29) or with additional chromosomal abnormalities (11, 16, 20, 23, 25). These findings raise questions about the origin of the myelocytic and lymphocytic lines which could be a pluripotent stem cell common to these 2 cell types (4, 13, 14). We wish to report here a new case of lymphoblastic crisis in Ph1 chromosome-positive CML with the occurrence of a near haploid cell line found in the patient's bone marrow.

RESULTS

The first karyotype study performed at the onset of the disease and prior to any treatment revealed the presence of the Ph1 chromosome in all the scored metaphases of the bone marrow and in 7 metaphases from PHA-stimulated blood culture. No other abnormalities were found either in the 13 karyotyped cells of the bone marrow or in the 12 analyzed metaphases from blood culture. A second chromosome examination was carried out while the patient was pancytopenic. The Ph1 chromosome was found in the bone marrow cells but not in blood cultures. No other consistent modifications were observed. A third cytogenetic study was performed at the time of relapse prior to any new therapy. In the bone marrow aspirates, all cells were Ph1 chromosome-positive with 2 modal chromosomal numbers. Fifty-five % of the cells had 28 chromosomes, and 36% had 56 chromosomes. Only 9% of the cells showed 46 chromosomes (Table 1). Karyotype analysis by R-banding technique revealed the following observations. In the cells with 28 chromosomes (Fig. 1, A and B), only 4 pairs were found normal, i.e., Numbers 13, 14, 18, and 21. The G22 pair, also present, included one Ph1 chromosome. The C6 pair was totally absent, and one chromosome of the C11 pair was structurally modified (the short arm was deleted, and a segment was translocated to the deleted end). Due to the absence of almost one-half of a chromosome complement, it was difficult to establish whether this translocated segment corresponded to a fragment of a C6 chromosome long arm. All the other pairs including the X group were haploid. The metaphases with 56 chromosomes showed the exact duplicate of the chromosome...
Near Haploid Cell Line in a Human Leukemia

The near haploid cell line described in this paper is the fourth one reported. The first observation of such a hypodiploid clone has been described by our group in an ALL case (15). More recently, 2 other cases have been reported (18, 22). The clinical, cytological, and cytogenetic characteristics of these 4 cases showed several similarities although some differences in the chromosome distribution were observed.

The previously published clones (15, 18, 22) were all described in children who presented with ALL where hyperdiploidy is more commonly observed (7, 10, 19, 30, 31). It is noteworthy to point out that, in our present study, the 28-chromosome cell line was observed during the lymphoid blast crisis of CML diagnosed 5 years ago in an adult patient. Thus, this near haploidy might have some close relationship with the ALL type and with its reported poor prognosis (15, 18).

In both our cases and the patient of Oshimura et al. (18), 2 cell lines were observed, one with a near haploid set of chromosomes and the other showing an exact duplicate of the near haploid chromosome complement. Two blast cell populations, small and large lymphoblasts, were reported in these patients. This double blast population might reflect the presence of 2 chromosomal populations. This fact is supported by the case of Prieto et al. (22) who found only the near haploid clone and one lymphoblast population.

In all the clones, each chromosome pair was at least represented by one normal chromosome with the following exceptions. In the case of Oshimura et al. (18), the Number 7 chromosome was involved in a translocation with apparently a very limited chromosomal material loss. In our patient, the C6 pain was partly, if not totally, missing.

The comparison of the karyotype analysis of all such clones revealed several similarities in spite of some differences in the chromosome distribution (Table 2). In all cases, the A and B groups are represented by one chromosome of each pair. In the C group, all the pairs were haploid except for the No. 10 pair which was normal in 2 cases (15, 18), the No. 11 pair which is partly normal in the present study, and finally, the total or partial loss of the No. 6 pair discussed above. In the D-group chromosomes, 3 cases, if not all, showed a single No. 15 chromosome, and in the E group, the No. 18 pair was found normal, at least in 3 patients. The F pairs were haploid in all cases. The No. 21 pair is normal in 3, if not all, patients, and in the case described in this report, we observed two 22 chromosomes, one of them being the Ph1 chromosome. For the X and Y chromosomes, one X at least was retained in all cases. In this comparative analysis, the similarities are too numerous among the 4 clones and thus appear to be nonrandom. In addition to these observations, the cytogenetic data reported in these cases also raise questions as to the significance of the near haploid clones in ALL occurrence.

The association of 3 factors, namely, Ph1 chromosome, lymphoid blast crisis, and presence of a near haploid clone thus far reported in ALL, raised questions about the origin of
the primary target cell in this CML. Several cases of Ph+ chromosome-positive ALL have been reported in the literature (1, 3, 7, 8, 11, 12, 16, 20, 23, 25, 26, 27, 29). Since in a minority of CML patients the blast crisis was described as having a lymphoblastic appearance (2, 4, 5, 13, 17), the Ph+ chromosome-positive ALL’s were interpreted by Beard et al. (2) as blast crises either of clinically nonexpressed CML or of CML with a very short chronic phase. However, the hypothesis of the pattern proposed by Janossy et al. (14) concerning the cell origin of some CML’s. Several cases of Ph’ chromosome-positive stem cell (common to lymphoid and myeloid lines) as target cell in some CML’s was suggested by Boggs (4) who observed the ALL conversion of CML in 3 patients. This hypothesis was supported by Janossy et al. (13) on the basis of surface marker analysis of blasts and more recently by the observation of Prchal et al. (21). The patient we described here developed at first a CML which converted in acute lymphoblastic form 5 years later. The Ph+ chromosome was found throughout the course of the disease. Thus, this acute lymphoblastic phase might be considered as a CML blast crisis of lymphoid morphology. However, the cytological and cytochemical characteristics of the leukemic blast cells, as well as the presence of a near haploid clone which so far has been found in ALL, raise the possibility of a pluripotent Ph+ chromosome-positive stem cell (common to both lymphoid and myeloid lines) as cell origin in this leukemia. If so, this observation would help to support the hypothesis of Boggs (4) and the pattern proposed by Janossy et al. (14) concerning the cell origin of some CML’s.

ACKNOWLEDGMENTS

We thank B. Szirth and L. Allaire for their technical and secretarial assistance.

REFERENCES


Fig. 1. Karyotypes established from R-banded metaphases with 28 chromosomes.
Near Haploid Cell Line in Lymphoid Blast Crisis of Ph¹-positive Chronic Myeloid Leukemia

Allégria Kessous, Pierre Colombies, Jacques Pris, et al.


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/40/4/1354

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.