REARRANGEMENT OF RETINOIC ACID RECEPTOR α AND PML IN PROMYELOCYTIC BLAST CRISIS OF Ph1 CHROMOSOME POSITIVE CHRONIC MYELOCYTIC LEUKEMIA WITH NORMAL COPIES OF CHROMOSOME 15

To the Editor:

In the transformation of chronic myelocytic leukemia (CML), myeloblastic and lymphoid blast crisis are most common. However, a few cases of promyelocytic blast crisis have been reported, in some of which the specific chromosome abnormality of both t(15;17) and (9;22) were detected in the transformed cells. We report here a case of CML with promyelocytic transformation that showed the

Fig 1. G-banded karyotype: 51, XY, +der(1)t(1;17) (p11;q11), +7, +8, +8 t(9;22) (q34;q11), 22q−. Arrows indicate morphologically abnormal chromosomes.
The present case; lane 2, a typical APL carrying t(15;17); lane 3, normal control. In lanes 1 and 2, amplified products derived from PML-RARα fusion transcripts are clearly visible as etidium-stained bands. Slightly different sizes of the two are presumably explained by differences in breakpoints of chromosome 15 and/or alternative splicing of the PML gene.2 Numbers at left indicate marker length.

![Image](298bp 220bp)

**Fig 2.** Detection of PML/RARα fusion gene by RT-PCR. Amplified RT-PCR products were detected on a 1.5% agarose gel: Lane 1, the present case; lane 2, a typical APL carrying t(15;17); lane 3, normal control. In lanes 1 and 2, amplified products derived from PML-RARα fusion transcripts are clearly visible as etidium-stained bands. Slightly different sizes of the two are presumably explained by differences in breakpoints of chromosome 15 and/or alternative splicing of the PML gene.2 Numbers at left indicate marker length.

The translocation t(1;17)(p11;q11) translocation with normal copies of chromosomes 15 and showed to have a retinoic acid receptor α (RARα) and PML chimera gene.

A 27-year-old man was diagnosed as having CML and treated with natural interferon-α (HLBI) in the chronic phase for almost 4 years. Then transformation to an acute promyelocytic leukemia occurred. The blast cells had irregular nucleus and abundant cytoplasm with gross azurophilic granules. They showed positive immunophenotypes of CD13 and 33, and the modal karyotype was 47, XY, +der(1)t(1;17)(p11;q11), +7, +8, +t(9;22)(q34;q11), +22q—(Fig 1). Careful inspection of the banding pattern on a pair of chromosomes 15 did not disclose any morphologic abnormalities. We have analyzed RARα-PML messenger RNA by cDNA reverse transcription-polymerase chain reaction (RT-PCR),8 the amplified products derived from PML-RARα fusion transcripts were detected in the present case as well as in a patient with the typical t(15:17) translocation (Fig 2, arrow).

This observation suggests that both RARα gene on chromosome 17 and PML gene on chromosome 15 may be involved in APL cases with variant translocations such as t(1:17) and so on in the reported cases.10

Furthermore, RARα-PML chimera gene was found in leukemic cells with normal karyotype in all of six APL cases studied.11 Therefore, the fusion of RARα with PML gene might be an essential event for APL and promyelocytic blast crisis of CML, even in cases without showing morphologic abnormality on chromosomes 15 and/or 17.

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Rearrangement of retinoic acid receptor alpha and PML in promyelocytic blast crisis of Ph1 chromosome positive chronic myelocytic leukemia with normal copies of chromosome 15

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