5. A Complex Translocation Involving Chromosomes 1, 8, and 21 in Acute Myeloblastic Leukemia

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Current chromosome banding studies have provided considerable evidence for non-random karyotypic changes in a variety of human neoplasms. In acute myeloblastic leukemia (AML) have been found certain specific chromosome changes, among which the 8;21 translocation has attracted special attention on account of certain cytogenetic features comparable to chronic myelocytic leukemia (CML) which involves the 9;22 translocation. Recently, Lindgren and Rowley (1977) reported two cases of AML with complex rearrangements which were considered as variants of the 8;21 translocation. We wish to present another case of AML which is associated with a new complex translocation involving chromosomes 1, 8 and 21.

Case report. The patient (No. 468, N.M.), a 62-year-old male, was admitted to the Sapporo National Hospital on November 1, 1976, because of general fatigue with fever and anemia. He was diagnosed as AML. Hematological examinations revealed the following: WBC, 107,200/mm³; RBC, 1,330,000/mm³; platelets, 20,000/mm³; Hb, 5.5g/dl; blasts, 96%; Sudan black B staining, positive; peroxidase reaction, 95% positive; PAS reaction, negative; azurophile granules and Auer body, positive; and nucleated cells in bone marrow, 492,000/mm³ (96.2%, leukemic cells; 1%, erythroblasts; 1.4%, lymphocytes; 1.4%, granulocytes). Complete remission was obtained after a combination chemotherapy with daunomycin, cyclocytidine, predonisolone and 6-MP. He left the hospital on March 7, 1977. When examined on June 29, relapse was seen and he died on September 12, 1977, survival being 11 months.

Cytogenetic findings. Chromosome studies were made on cells from bone marrow aspirates before therapy, November 5, 1976, by means of the direct method as well as of the three-day-culture method without phytohemagglutinin (PHA). Initial chromosome analyses with conventional Giemsa staining on 27 cells from the direct

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preparations and 24 cells from the cultured specimens showed that all metaphases had a karyotype of 46,XY,1q−,−C,+D,+E,−G. Q- and G-band analyses on 50 metaphases revealed that the above karyotype was resulted from a complex translocation, showing that the distal parts of the long arms of #1 and #8 were deleted and these deleted segments were both translocated to the long arm of #21.

Fig. 1. Q-band karyotype from a cultured bone marrow cell of the patient. Arrows indicate rearranged chromosomes.

Fig. 2. Partial G-band karyotype, showing the complex translocation involving the chromosomes 1, 8 and 21. Four distinct bands, a, b, c and d, of t(21;8;1) probably correspond to the bands 21q21, 8q23, 1q41 and 1q43, respectively.
Consequently, the rearranged #21 possessed three extra bands, the proximal one probably being corresponded to the band 8q23 and the two distal ones to the bands 1q41 and 43, respectively (Figs. 1 and 2). The karyotype was thus described as 46,XY,1q-,8q-,21q+,t(21;8;1) (q22;q22;q32). On June 22, 1977, a PHA-stimulated lymphocyte culture was prepared from the patient's peripheral blood sample. All 20 cells examined in this sample showed a normal karyotype, 46,XY.

Further chromosome examinations were done on June 29, 1977, on direct and cultured bone marrow specimens. Two out of 20 cells analysed in the direct sample showed the same type translocation as observed at the first examination, while 13 of the remaining 18 cells had a normal karyotype, leaving 5 hyperdiploid cells with 49–52 chromosomes. These hyperdiploid cells apparently contained the markers originated from the complex translocation, though not precisely analysed due to poor banding and overlapping. By contrast, in the cultured specimens, only 3 cells had a normal karyotype and 29 cells had the complex translocation as mentioned above.

Discussion. Although several karyotype abnormalities involving numerical or structural changes of chromosomes 7, 8, 9 and 21 have been reported in AML, the 8;21 translocation appears to be most frequent and specific anomaly constituting some 10 per cent of the AML cases reported. The break points relevant to this particular translocation were estimated at bands 8q22 and 21q22, i.e., t(8;21) (q22;q22). Also noticed was that this translocation was often accompanied by a missing sex chromosome, either an X or a Y. The breaks and reunion in our case occurred apparently at the same bands as described above, and in addition a distal part of the long arm of #1 was involved in this translocation, thus forming a complex type. Whether this complex translocation has taken place simultaneously in the same cell or developed through a stepwise evolution remains unexplored. However, the fact that no cells having the standard 8;21 translocation were observed in both the first and second samples may favour the former view.

Recently, Lindgren and Rowley (1977) reported two cases of AML with similar complex translocations relating to the 8;21 translocation, in which the distal part of the long arm of #8 was translocated to either #17 or #11, and the distal portion of the affected #17 or #11 was translocated to #21. Break points of #8 and #21 in these two cases were the same as those described in the standard 8;21 translocation.

Considering the existence of comparable variant translocations between AML and CML, Lindgren and Rowley (1977) emphasized the importance of chromosomal changes in leukemia. Although in-
formation on the variant 8;21 translocations in AML is still meager, we assume that the prototypic 8;21 translocation is highly specific to a certain disease type of AML, and that the breakage occurring at the band 8q22 may be the most essential event associated with malignancy, and hence the rearranged 8q— may be comparable to the ph1-chromosome in the case of CML. It is evident that the deleted distal portion of #8 in the three reported cases of complex translocation was not necessarily translocated on #21.

It has been shown that the AML patients with the standard 8;21 translocation are characterized by certain common clinical features, i.e., younger in age, longer survival time, lower activity of alkaline phosphatase and positive Auer body in leukemic cells. Despite our patient was rather old, 62 years, he responded well to a combination chemotherapy followed by a good clinical remission for a period of nearly 4 months. Auer body was clearly demonstrated in his leukemic cells, though the activity of alkaline phosphatase was not measured.

Summary. A 62-year-old male diagnosed as AML showed a new complex translocation involving chromosomes 1, 8 and 21 in his marrow cells. The Q- and G-banding analyses interpreted the karyotype as 46,XY,1q-,8q-,21q+,t (21;8;1) (q22;q22;q32).

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References