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A 14q+ CHROMOSOME IN ADULT T-CELL LEUKEMIA

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Abstract. Chromosome studies were conducted on two patients with adult T-cell leukemia. In both patients, a marker chromosome 14q+ and a structural change involving chromosome 1 with trisomy of the q arm were found in peripheral blood leukocytes. The 14q+ marker chromosome had resulted from translocation from #5p in one patient and #5q in the other patient. The present and previous studies suggest that the donor chromosomes involved in the 14q+ translocation are variable. This indicates that the 14q+ marker chromosome rather than the donor chromosome is intimately related with adult T-cell leukemia.

Key words : 14q+ marker chromosome, adult T-cell leukemia.

A 14q+ marker chromosome (14q+) has been found in a variety of B-cell lymphoid malignancies (1-10). On the contrary, the presence of 14q+ in T-cell lymphoid malignancies has been reported in only six cases (11-15). We have reported the chromosome analysis of two patients with adult T-cell leukemia (ATL), in whom 14q+ was found (16). We present here the karyotypes of another two patients with ATL who also had 14q+, and suggest the frequent association of 14q+ with T-cell lymphoid malignancies.

MATERIALS AND METHODS

Patients. Case 1: A 45-year-old male was admitted to the Department of Medicine, Kochi Prefectural Central Hospital. White blood cell (WBC) count in the peripheral blood was 12,000/mm³ with 90% of lymphocytes. The majority of the lymphocytes had an abnormal indented or lobulated nucleus (Fig. 1A), and formed E rosettes indicating T-cells. Chromosome analysis was conducted prior to therapy.

Case 2: A 29-year-old male, born in the Nagasaki Prefecture of Kyushu, was admitted to the Department of Medicine, Okayama University Hospital. WBC count was 10,300/mm³ with 32% of lymphocytes. The majority of the lymphocytes were T-cells and appeared similar to those of Case 1 (Fig. 1B). Chromosome analysis of leukemic cells was performed twice, *i.e.*, before and after combination chemotherapy consisting of prednisolone and VP-16-213 (a derivative of podophylotoxine). After combination therapy, the WBC count decreased to 2,000/mm³ with 28% of lymphocytes, the majority

of which were still abnormal.

Chromosome analysis. Ten to 15 ml of heparinized peripheral blood was used for chromosome analysis. The blood was allowed to stand at room temperature for 1-2 h to separate WBC. Cells obtained were dispersed in 10 ml RPMI 1640 medium containing 10% fetal calf serum, and cultured at 37°C for about two days in air with 5% CO₂. Cells were arrested at a mitotic stage by treating them with 0.5µg/ml Colcemid for 2-3 h. The cells were then treated with hypotonic solution consisting of 0.075 M KCl for 13 min at 37°C.

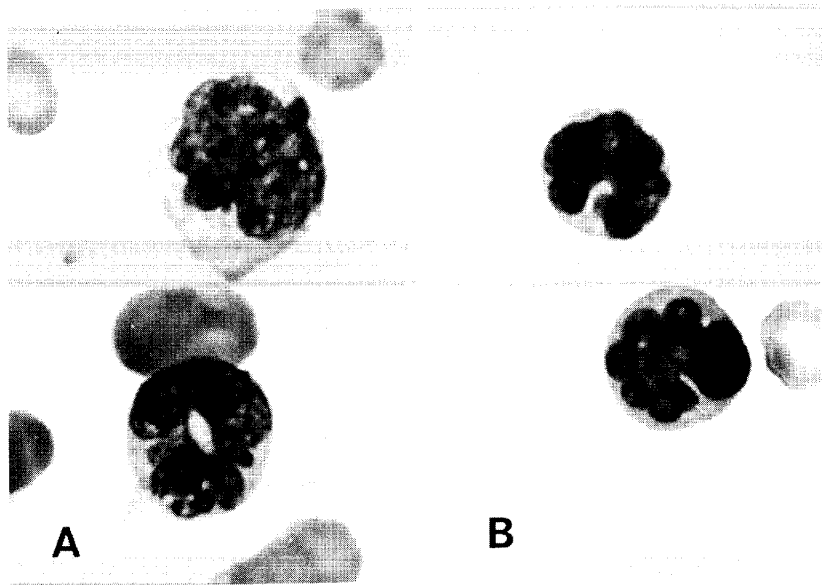


Fig. 1. Abnormal lymphocytes (from peripheral blood of case 1(A) and case 2(B)) showing indented or lobulated nuclei (May-Grünwald-Giemsa, X 1,000).

Slides were prepared according to a routine air-dry method immediately after fixation. Afterwards, 50 mitotic cells were counted in each case, and another 10 cells at least were photographed and used for banding analysis. The Q- and G-banding methods were employed, and karyotypes were expressed according to the Paris Nomenclature.

RESULTS

As shown in Table 1, 46 of 50 cells in Case 1 had 46 chromosomes whereas the remaining 4 had 45. Of another 15 cells analyzed with banding techniques, 14 showed a karyotype of 46, XY, -4, +t(1;4) (q25;p14 or 15), t(5;14) (p14;q32) (Fig. 2), and the remaining one a karyotype of 46, XY, -4, +t(1;4) (q25;p14 or 15), 4q-, 6q-, 10q+, t(5;14) (p14;q32). As to chromosome numbers analyzed

TABLE 1. CHROMOSOME DATA OF 2 PATIENTS WITH ADULT T-CELL LEUKEMIA

Case	Cells with chromosome number of					Total	Karyotype
	45	46	47	48	49		
1	4	46(15)				50(15)	46, XY, -4, +t(1;4) (q25;p14 or 15), t(5;14) (p14;q32)/46, XY, -4, +t(1;4) (q25;p14 or 15), 4q-, 6q-, 10q+, t(5;14)(p14;q32)
2-a		10(3)		40(18)		50(21)	46, XY/48, -X, Y, +1q, +3, t(5;14) (q22;q32), +mar
-b		3(1)		36(10)	11(1)	50(12)	46, XY/48, -X, Y, +1q, +3, t(5;14) (q22;q32) +mar/48, -X, Y, +3, t(5;14) (q22;q32), +2mar/48, -X, Y, +1q, +3, t(5;14) (q22;q32), +21, -22, +mar/48, -X, -Y, +1q, +3, -4, t(5;14) (q22;q32), 13p+, +3mar/48, -X, -Y, +1q, +3, 13p+, t(5;14) (q22;q32), +2mar/49, -X, Y, +1q, +3, t(5;14) (q22;q32), 18q+, +2mar

Number in parentheses, number of cells examined by banding techniques. Case 2-a, before, and 2-b, after combination chemotherapy. +mar, the marker chromosome.

prior to therapy in Case 2, 40 of 50 cells had 48 chromosomes and the remaining 10 had 46. Of another 21 cells analyzed with banding techniques, three had a normal karyotype of 46, XY while the remaining 18 had a karyotype of 48, -X, Y, +1q, +3, t(5;14) (q22;q32), +mar. The marker chromosome (+mar) appeared to have a part of the X chromosome. Chromosome analysis after combination chemotherapy showed somewhat different chromosome constitutions from those prior to the therapy; the change may have been caused by the combination chemotherapy. The chromosome numbers ranged from 46 to 49 with a modal number of 48. Of 12 cells banded, one showed a normal karyotype of 46, XY, three 48, -X, Y, +1q, +3, t(5;14) (q22;q32), +21, -22, +mar (Fig. 3), and eight a minor variation including various numbers of marker chromosomes. One of the marker chromosomes in each karyotype appeared to have a part of the X chromosome. The additional materials of 14q+ observed in the karyotypes from Cases 1 and 2 were derived from #5p and #5q, respectively.

DISCUSSION

Recently, we reported two patients with ATL having 14q+ (16); the donor chromosomes of 14q+ in these two cases were #12q and Yq. The breakpoint in chromosome 14 was at 14q32 in both the previous two and the present two cases. Ueshima *et al.* (19) described 14q+ in three patients with ATL, although the origin of the donor chromosomes of 14q+ was not mentioned. According to our

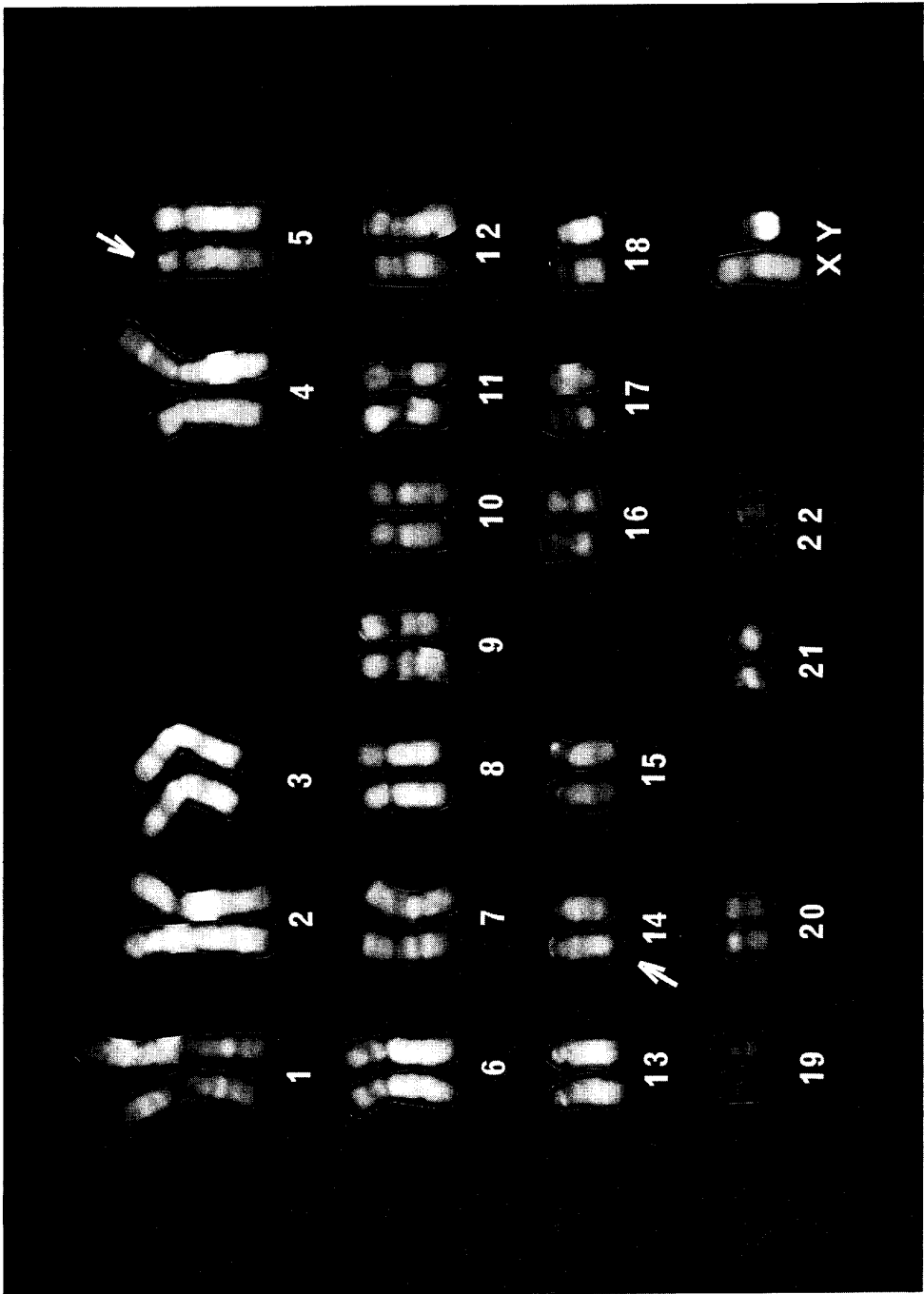


Fig. 2. Q-banding karyotype of a cell from case 1: 46, XY, -4, +t(1;4)(q25;p14 or 15), t(5;14)(p14;q32). Arrows indicate the chromosome involved in the t(5p⁻;14q⁺) translocation.

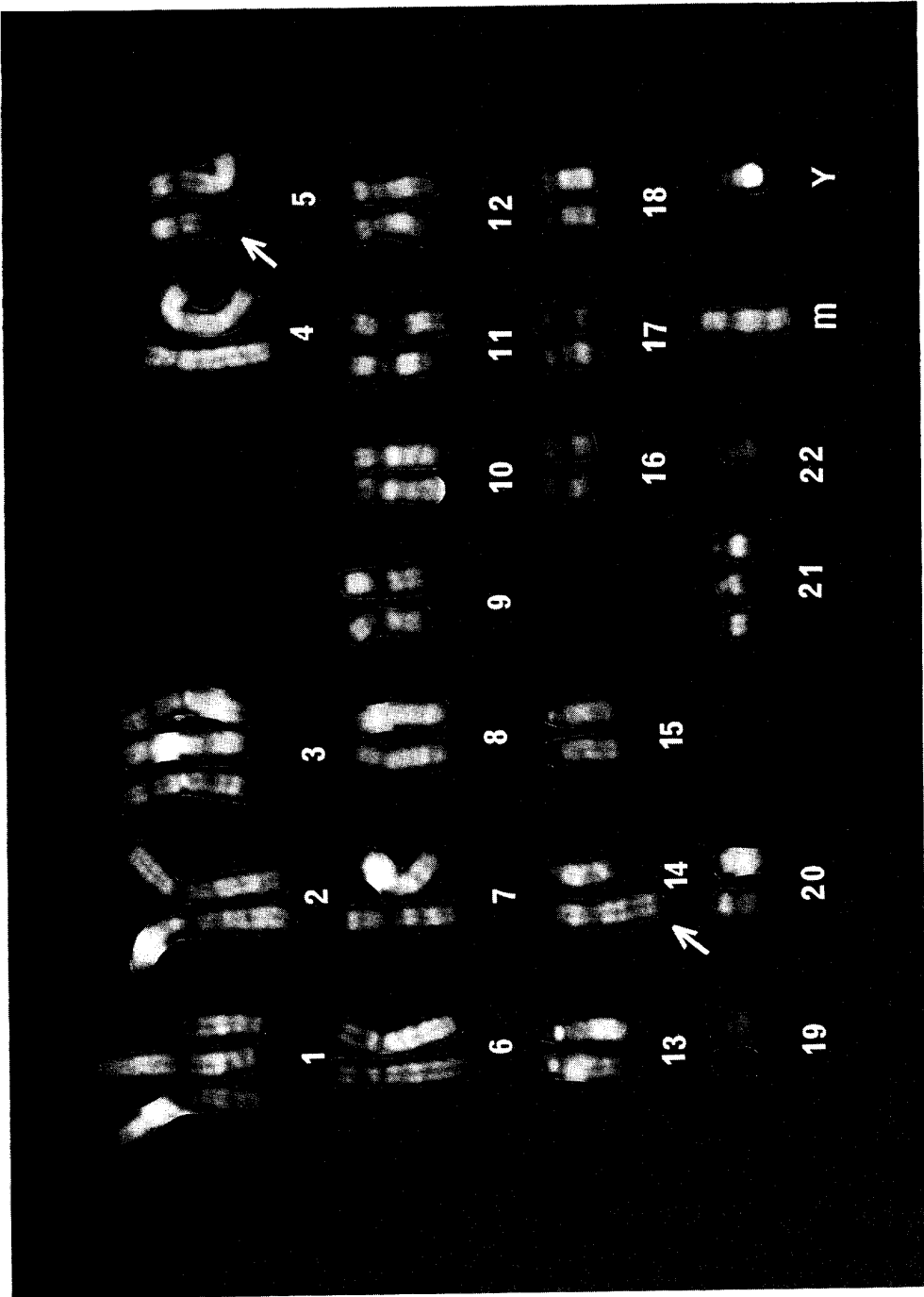


Fig. 3. Q-banding karyotype of a cell from case 2: 48, -X, Y, +1q, +3, t(5;14) (q22;q32), +21, -22, +mar. Arrows indicate the chromosome involved in the t(5q-; 14q+) translocation.

studies on 14q+, the donor chromosomes involved in the genesis of 14q+ in ATL patients were variable. This implies that 14q+ rather than the donor chromosome was intimately related to ATL.

Leukemic cells of Cases 1 and 2 had partial trisomy of the long arm of chromosome 1, which was q25-qter and q11-qter, respectively. Rowley (20) reported duplication of 1q25-1q32 in 35 patients with various hematological disorders, such as acute leukemia, polycythemia vera, and myelofibrosis. Similar chromosome changes to those of Rowley were also found in some solid tumors such as cervical and ovarian cancers (21, 22). We have also reported duplication of the long arms of chromosome 1 as well as 14q+ in a 52-year-old male with non-African Burkitt's lymphoma (6). These findings suggest that the appearance of partial trisomy of 1q and also 14q+ is intimately related to malignant change in lymphoid organs.

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