CONCISE REPORT

Chromosome Aberrations in T Lymphocytes Carrying Adult T-Cell Leukemia-Associated Antigens (ATLA) From Healthy Adults

By Shirou Fukuhara, Yorio Hinuma, Yoh-Ichi Gotoh, and Haruto Uchino

Chromosomes were studied in cultured T lymphocytes carrying adult T-cell leukemia-associated antigens (ATLA) that were obtained from five Japanese anti-ATLA seropositive healthy adults. Chromosomally abnormal cells were observed in three of the five healthy adults, and these cells were clonal in two subjects. All cells examined in one subject had rearrangements of chromosome nos. 7 and 14. Clonal cells from the second had a minute chromosome of unknown origin. A few cells in the third had nonclonal rearrangements of chromosomes. Thus, ATLA-positive T lymphocytes in some anti-ATLA seropositive healthy people have chromosome aberrations.

Japanese Adult T-Cell leukemia (ATL) has a striking geographical feature in that the patients are clustered in the southwestern part of Japan. Hinuma et al. have reported that sera from almost all patients with Japanese adult T-cell leukemia and lymphoma (ATLL) react specifically with ATL-associated antigens (ATLA) in MT-i cells of a cultured ATL cell line, in which type C virus particles are detectable. At the same time, they have described that healthy subjects with anti-ATLA sera harbor T lymphocytes carrying ATLA, which have been shown to be specific for ATL virus. We report on chromosome findings in ATLA-positive cells obtained from five healthy adults.

MATERIALS AND METHODS

Cultivation of ATLA-Positive Cells

Details of the method for cultivation of ATLA-positive cells were described elsewhere. In brief, lymphocytes of peripheral blood, obtained from five healthy Japanese adults whose sera were positive for anti-ATLA, were cultured in RPMI 1640 medium with 20% fetal calf serum and 25% T-cell growth factor (TCGF). Proliferating cells dependent on TCGF were cloned by a limiting-dilution culture method, and cultures containing approximately 50–80% ATLA-positive cells were selected for chromosome analysis (Table 1).

Chromosome Analysis

Chromosomes from these cells in each subject were prepared as described previously and analyzed using sequential photography of conventional Giemsa and quinacrine staining on the same metaphase. The abnormality was considered clonal when at least two cells from a given subject had a similar chromosome rearrangement or when 3 cells were lacking the same chromosome.

RESULTS AND DISCUSSION

Cytogenetic findings in ATLA-positive cells obtained from five anti-ATLA seropositive healthy adults are summarized in Table 1. All 50 cells examined in each of two subjects (cases 1 and 2) had a normal male karyotype, and the other three (cases 3–5) had abnormal cells in the diploid range that showed various chromosome aberrations. These aberrations were structural rearrangements, including translocations, deletions, breaks, and gaps. All of the 36 cells in case 3 showed evidence of a clonal origin, since they had two structurally rearranged chromosomes, 7q- and 14p+. We report on chromosome findings in ATLA-positive cells obtained from five healthy adults.
Table 1. Chromosome Findings in T Lymphocytes Carrying Adult T-Cell Leukemia-Associated Antigens (ATLA) From Five Healthy Adults

<table>
<thead>
<tr>
<th>Case No. (Name)</th>
<th>Sex/Age</th>
<th>Titer of Anti-ATLA*</th>
<th>Percent Positive Cells†</th>
<th>No. of Abnormal Cells‡</th>
<th>Karyotype of Clonal Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (As)</td>
<td>M/21</td>
<td>40</td>
<td>78</td>
<td>90</td>
<td>0 (50)</td>
</tr>
<tr>
<td>2 (Ke)</td>
<td>M/23</td>
<td>80</td>
<td>49</td>
<td>72</td>
<td>0 (50)</td>
</tr>
<tr>
<td>3 (Mo)</td>
<td>M/29</td>
<td>40</td>
<td>77</td>
<td>87</td>
<td>36 (36) 46,XY,t(7;14)(p15;q13) 3 cells: 46,XY,del(6)(q13q21),t(7;14)</td>
</tr>
<tr>
<td>4 (Su)</td>
<td>M/22</td>
<td>40</td>
<td>70</td>
<td>91</td>
<td>5 (28) 47,XY,+ minute 1 cell: 47,XY,del(12)(p11), + minute</td>
</tr>
<tr>
<td>5 (Te)</td>
<td>M/22</td>
<td>20</td>
<td>73</td>
<td>81</td>
<td>5 (48) (Nonclonal rearrangements)</td>
</tr>
</tbody>
</table>

*The antibody in serum was titrated by an indirect immunofluorescence method with MT-1.²
†ATLA-positive cells reported previously³ were used in this study.
‡Number in parentheses is the total no. of cells studied with banding analysis.

Fig. 1. Partial karyotype showing two structurally rearranged chromosomes, 7q- and 14p+, in T lymphocytes carrying ATLA in case 3. The rearranged chromosomes are the result of a reciprocal translocation between nos. 7 and 14 [t(7;14)(7pter → 7p15::14q13 → 14pter; 7qter → 7p15::14q13 → 14qter)]. A karyotype of 47, XY, del(12)(p11), + minute is from case 4.
14q1(1–3) translocation involving a proximal band in 14q, such as a 14q13 translocation in case 3, have been occasionally observed in various types of lymphoid malignancy, including T-cell lymphoma.5–11 These clonal cells were consistently present in peripheral T lymphocytes in ataxia telangiectasia,8 a primary immunodeficiency that predisposes to lymphoid malignancy.12 The minute chromosome noted in case 4 may be comparable to that observed in a cultured cell line (HUT 102) positive for type C retrovirus particles;13 this cell line was derived from tumor cells of a black patient with adult T-cell lymphoma-leukemia that was indistinguishable from Japanese ATLL.14 Type C virus particles have been also detected in the extracellular space of ATLA-positive cells3 used in this study; these cells had a normal karyotype in case 2 and a karyotype of 46,XY,t(7;14) in case 3.

The present results suggest that some anti-ATLA seropositive healthy people have clones of T lymphocytes with chromosome aberrations in their peripheral blood, possibly associated with ATLL. Identification of the clonal abnormalities in the peripheral blood may provide a way to monitor those individuals who have a potential risk of developing ATLL.

ACKNOWLEDGMENT

We are very grateful to Professor Janet D. Rowley (University of Chicago) for her advice and for reviewing this manuscript.

REFERENCES

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