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Tetrasomy 8 and isochromosome 7q in CD5-positive hepatosplenic T-cell lymphoma with leukemic presentation

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A 45-year-old woman was admitted to our hospital to undergo unrelated stem cell transplantation for primary resistant hepatosplenic $\gamma\delta$ T-cell lymphoma (HSTCL). Liver histopathological findings and the patient's clinical course have been reported previously [1]. After two courses of salvage chemotherapy with a hyper-CVAD regimen, abnormal lymphoid cells appeared in the peripheral blood: hemoglobin 83 g/L, platelets 38×10^9 /L, and white blood cells (WBC) 7.5×10^9 /L with 2% myelocytes, 9% metamyelocytes, 7% band forms, 70% segmented neutrophils, 7% monocytes, 3% lymphocytes, and 2% abnormal lymphoid cells (Fig. 1a). The bone marrow was normocellular, with 54.6% abnormal lymphoid cells, 31.2% myeloid cells, 8.4% erythroblasts, 3.6% monocytes, and 1.4% lymphocytes (Fig. 1b). These lymphoid cells were immunophenotypically positive for CD2, CD3, CD5, CD7, CD16, and CD56, and negative for CD4, CD8, HLA-DR, and other B-lymphoid and myeloid markers (Fig. 1c). Chromosome analysis of bone marrow cells showed 47,X,-X,i(7)(q10),+8,+8[17]/48,XX,+mar1x2[3] (Fig. 1d). We were unable to identify the origin of the marker chromosomes. Fluorescence *in situ* hybridization (FISH) with D7S486/CEP 7 probes detected two D7S486 signals and one CEP 7 signal on i(7)(q10) in all 18 metaphase spreads (Fig. 1e). FISH with a CEP 8 probe confirmed four CEP 8 signals on chromosome 8 in 17 of 20 metaphase spreads (Fig. 1f). No cell showed three CEP 8 signals. Monoclonal rearrangements of *TRB*, *TRD* and *TRG* were shown by polymerase chain reaction. After one month, the WBC count was 4.1×10^9 /L with 48% abnormal lymphoid cells. Based on these specific immunophenotypic and cytogenetic findings, a diagnosis of leukemic presentation and bone marrow infiltration of CD5-positive HSTCL was made.

HSTCL is a rare and aggressive subtype of T-cell lymphoma characterized by marked hepatosplenomegaly in the absence of lymphadenopathy, with frequent bone marrow involvement. Cytogenetically, the coexistence of isochromosome 7q and trisomy 8 is a

consistent, non-random abnormality associated with HSTCL. Furthermore, isochromosome 7q has been reported as a sole abnormality, indicating that isochromosome 7q and trisomy 8 may be a primary and secondary abnormality, respectively. Loss of a sex chromosome is also found as an additional anomaly. Isochromosome 7q that results in the loss of 7p including *TRG* at 7p14, and the gain of 7q including *TRB* at 7q34, may play a crucial role in the pathogenesis of HSTCL. Considering the rare cases of HSTCL with ring chromosome 7 leading to 7q amplification, the gain of 7q appears more important in the development of the disease than the loss of 7p. Trisomy 8 is also supposed to contribute to tumorigenesis by a gene dosage effect. An interaction may exist between genes located on both chromosomes.

In the present case, instead of trisomy 8, tetrasomy 8 as well as isochromosome 7q were detected. To our knowledge, only one case of HSTCL with tetrasomy 8 and isochromosome 7q has been reported, the karyotype and immunophenotype being 47,X,-X,i(7)(q10),+8,+8,der(21)t(7;21)q11.2;p11.2)[8]/48,sl,+i(7)(q10)[1]/46,XX[11] and CD3+CD7+CD8+CD16+CD56+, respectively [2]. The recurrent appearance of tetrasomy 8 in association with isochromosome 7q support the concept that the acquisition of chromosome 8 may be implicated as a secondary change in the disease progression of HSTCL.

Interestingly, lymphoma cells were positive for CD5, as well as CD2, CD3, CD7, CD16, and CD56. The most frequent immunophenotype of HSTCL is CD2+, CD3+, CD4-, CD5-, CD7±, CD8-, CD16±, CD38+, and CD56+. Notably, CD5 is usually negative, but the clinical significance of CD5 expression remains to be elucidated. As described above, CD8 was positive in another case of HSTCL with tetrasomy 8. An unusual case of HSTCL expressing CD19 with ring chromosome 7 and trisomy 8 has also been reported [3]. Thus, it is important to investigate whether aberrant surface marker expression is associated with atypical cytogenetic abnormalities in HSTCL.

Conflict of interest

The authors declare that they have no conflict of interest.

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Figure legends

Fig. 1

a, b Peripheral blood (a) and bone marrow (b) smears showing lymphoma cells with fine nuclear chromatin, nucleoli and basophilic cytoplasm (May–Grünwald–Giemsa staining, $\times 1000$).

c Flow cytometric findings of bone marrow cells by CD45/side scatter (SSC) gating. The corresponding cell percentage demarcated by the gate is 41.3%. The results of two-color analyses with CD19 and CD2, CD8 and CD3, CD25 and CD4, CD5 and CD23, CD11c and CD20, CD56 and CD16, and CD7 and CD30 for gated cells are shown. Corresponding cell percentages in each fraction are indicated. The gated cells are positive ($>20\%$) for CD5 as well as CD2, CD3, CD7, CD11c, CD16, and CD56.

d G-banded karyotype of bone marrow cells: 47,X,-X,i(7)(q10),+8,+8. Arrows indicate the rearranged chromosome.

e Fluorescence *in situ* hybridization (FISH) with a Vysis D7S486/CEP 7 FISH Probe Kit (Abbott Molecular, Abbott Park, IL, USA) on metaphase spreads and interphase nuclei of bone marrow cells. Two D7S486 signals (7q31, red) and one CEP 7 signal (7p11.1-q11.2, green) were detected on i(7)(q10) (arrow). One signal each of D7S486 and CEP 7 were observed on a normal chromosome 7 (arrowhead). Three D7S486 and two CEP 7 signals were found in an interphase nucleus (inset).

f FISH with a Vysis CEP 8 Probe (Abbott Molecular) on metaphase spreads and interphase nuclei of bone marrow cells. Four CEP 8 signals (8p11.1-q11.2, yellow) were detected on chromosome 8. Four CEP 8 signals were also found in an interphase nucleus (inset).

Fig. 1

