T-Cell Acute Lymphoblastic Leukemia as a Secondary Leukemia after a 3-Year Remission of Acute Myelocytic Leukemia

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Abstract
Therapy-related myelodysplastic syndrome and therapy-related acute myelocytic leukemia (AML) are now recognized as hematologic malignancies that occur a few years after chemotherapy for primary malignancy with alkylating agents or topoisomerase II inhibitors. The secondary leukemia is usually AML and sometimes is preceded by a myelodysplastic syndrome. Acute lymphoblastic leukemia (ALL) as a secondary leukemia is quite rare, and secondary T-cell ALL after AML is even rarer. We report a case of a 56-year-old woman who developed T-cell ALL after a 3-year remission of AML (M2). We thought that this case would be extremely valuable for studying the etiology and biological characteristics of T-cell ALL as a secondary leukemia after AML. Int J Hematol. 2003;77:518-521.

Key words: Secondary T-ALL; Chromosome 6q23; TCR β gene; TCR γ gene

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1. Introduction

Therapy-related myelodysplastic syndrome and therapy-related acute myelocytic leukemia (AML) are now recognized as among the most serious long-term complications of the use of cytotoxic drugs [1-3]. Alkylating agents can cause secondary malignancies, especially leukemia, and several recent studies have reported therapy-related AML in patients treated with cytotoxic drugs not belonging to the alkylating family of agents [1,4,5]. These drugs include those targeting DNA topoisomerase II, such as etoposide, doxorubicin, and mitoxantrone [3,4,6]. These drugs are important for treating many tumors, such as acute lymphoblastic leukemia (ALL), non-Hodgkin’s lymphoma, and testicular cancer. Several studies have reported leukemogenic risk with chromosomal translocation, especially involving the 11q23 breakpoint (MLL gene), among patients with these tumors following their treatment with topoisomerase II inhibitors [2,4,6].

ALL as a secondary leukemia is quite rare, and secondary T-cell ALL (T-ALL) after AML is even rarer. A chromosome translocation, t(6;14)(q23;q11), has been observed, although no 11q23 abnormality has been found [4,6]. We describe a patient with an initial diagnosis of AML and who was found after a 3-year remission to have T-ALL at relapse. We thought this case to be extremely valuable for studying the etiology and the biological characteristics of T-ALL as a secondary leukemia after AML.

2. Case Report

In March 1993, a 56-year-old woman was admitted because of cough and a slight fever. The laboratory findings revealed leukocytosis (8.5 × 10^9/L) with 69% leukemic blasts in the blood. The nucleated cell count was 500 × 10^9/L with 76.2% blasts in the bone marrow. The results of myeloperoxidase staining of the blasts were positive. Thus, the diagnosis of AML-M2 was made according to French-American-British classification (Figure 1A). Intensive chemotherapy (a BHAC-DMP regimen including behenoyl cytosine arabinoside [BHAC], daunomycin, 6-mercaptopurine, and prednisolone) brought about complete remission. The patient then received 3 courses of consolidation chemotherapies consisting of BHAC-DMP and B–triple V (BHAC, etoposide [VP-16], vincristine, and vinblastine) and 3 courses of
maintenance therapy including mitoxantrone and Ara-C. Her complete remission persisted for 3 years. The total doses of alkylating agents and topoisomerase II inhibitors were: etoposide, 720 mg/m²; daunomycin, 410 mg/m²; and mitoxantrone, 44 mg/m² (Figure 2).

In October 1996, a blood examination revealed a white blood cell count of $23.6 \times 10^9$/L (51% blasts, 6% metamyelocytes, 24% stab leukocytes, 28% segmented leukocytes), a hemoglobin concentration of 84 g/L, and a platelet count of $230 \times 10^9$/L. Aspiration of the bone marrow revealed hypercellularity with remarkably increased levels of leukemic blasts (79.8%). A diagnosis of relapse of acute leukemia was made (Figure 1B), and the patient was readmitted to our hospital. Immunophenotypic analysis showed that the blasts were positive for CD2 (99.1%), CD5 (98.0%), CD7 (98.6%), and CD8 (98.0%). The results of myeloperoxidase staining at this time were negative. The results of serial cytogenetic analysis of bone marrow cells are summarized in Table 1. A diagnosis of T-ALL was made (Figure 1B). Reinduction therapy was started immediately with a regimen containing mitoxantrone and Ara-C. The levels of leukemic blasts decreased, and this treatment was effective.

**Figure 1.** Leukemic blasts in the patient’s bone marrow. A, Blasts at first diagnosis (acute myelocytic leukemia M2). B, Blasts at relapse (T-cell acute lymphoblastic leukemia).

**Figure 2.** The patient’s clinical course and therapy. Intensive chemotherapy consisting of a BHAC-DMP regimen (behenoyl cytosine arabinoside [BHAC], daunomycin, 6-mercaptopurine, and prednisolone) brought about complete remission. She then received 3 courses of consolidation chemotherapies consisting of BHAC-DMP and B–triple V (BHAC, etoposide [VP-16], vincristine, and vinblastine) and 3 courses of maintenance therapy including mitoxantrone (MIT) and cytosine arabinoside (Ara-C). After a 3-year remission, she experienced a relapse of acute leukemia. Hb indicates hemoglobin; LD, low-dose; MEC, regimen of MIT, etoposide, and Ara-C; WBC, white blood cells; Ery, erythrocytes; Gra, granulocytes; Mono, monocytes; Lymph, lymphocytes; PLT, platelets.