Letter to the Editor
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t(12;17)(p13;q12)/*TAF15-ZNF384* Rearrangement in Acute Lymphoblastic Leukemia

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Dear Editor,

In ALL, cytogenetic subgroups according to recurrent genetic abnormalities are used to classify patients for risk stratification and to introduce them to the proper therapeutic strategies—such as the use of tyrosine kinase inhibitors in the case of t(9;22)(q34;q11.2)/*BCR-ABL1* fusion [1]. Therefore, the identification of genetic aberrations is clinically significant and crucial in understanding the leukemogenesis mechanisms.

t(12;17)(p13;q11.2)/*TAF15-ZNF384* rearrangement is a rare chromosomal abnormality [2]. It has been reported in lymphoid as well as myeloid leukemia and is thought to be involved in the early differentiation of common progenitors [3]. Although some cases of the disease have reported a poor outcome [4, 5], the clinical characteristics and prognostic impact of *TAF15-ZNF384* are not well characterized, since not all the previous studies investigated the precise molecular consequences of the translocation. We report a B-ALL case with t(12;17)(p13;q11.2) detected by cytogenetic analysis and confirmed by direct sequencing of the TAF15-ZNF384 transcripts, which substantiated genes involved in the rearrangement.

A 32-month-old girl was admitted following four days of fever and erythema of both legs. Initial complete blood counts demonstrated pancytopenia, with hemoglobin level of 5.5 g/dL, white blood cell counts of 2.63×10^9/L, and platelet counts of 123×10^9/L. Leukemic blasts up to 5% were observed in peripheral blood and 84.9% in bone marrow. The leukemic blasts varied in size, with scanty and occasionally granulated cytoplasms. Blasts were positive for CD34, CD19, CD13, CD33, cytoplasmic CD79a, and terminal deoxynucleotidyl transferase (TdT), and negative for CD2, CD7, CD10, CD14, myeloperoxidase, and cytoplasmic CD3, indicating pro-B cell stage ALL. The reverse transcription-polymerase chain reaction using the HemaVision kit (DNA technology, Aarhus, Denmark) and fluorescence *in situ* hybridization using Vysis *IGH/MYC/CEP8* tricolor dual fusion, *CDKN2A* (p16)/CEP9 dual spot, and *MLL* Break Apart probes (Abbott Molecular, Abbott Park, IL, USA) showed negative results. G(Giemsa)-T(Trypsin)-G-banding analysis using the bone marrow sample revealed a karyotype of 46,XX,t(12;17)(p13;q11.2)[8]/46,XX[11] (Fig. 1A). To confirm the *TAF15-ZNF384* fusion transcript, complementary DNA was synthesized from total RNA, amplified, and sequenced by using primers specific for *TAF15* and *ZNF384* [6]. The fusion transcript, amplified by using specific primers, was approximately 800 bp in length (Fig. 1B). Sequence alignment of the amplified

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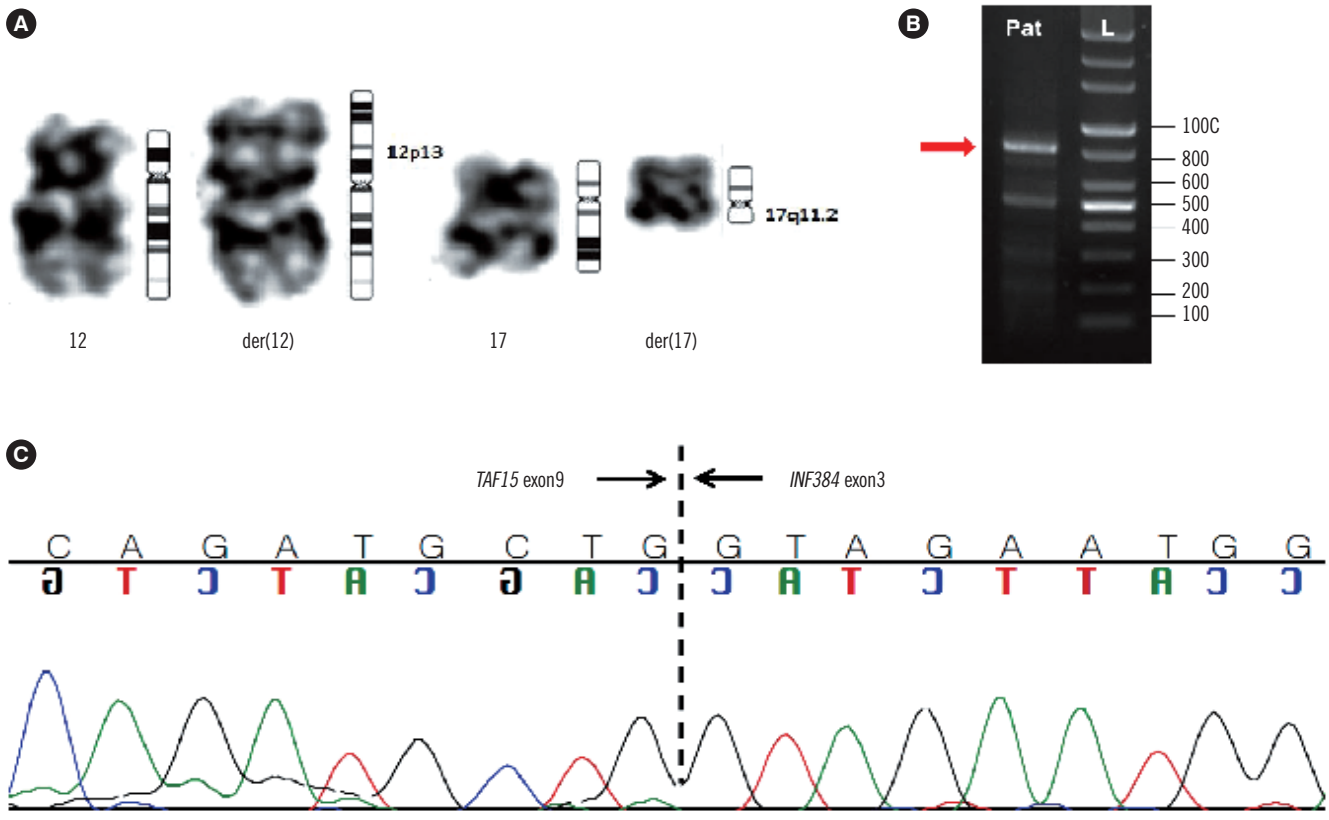

Fig. 1. (A) G(Giemsa)-T(Trypsin)-G-banding analysis using the bone marrow sample revealed a translocation involving the breakpoint on chromosome 12p13 and 17q11.2. (B) Agarose gel electrophoresis of the *TAF15-ZNF384* fusion transcript obtained from patient (approximately 800-bp-sized PCR product) (C) Direct sequencing of complementary DNA showed breakpoints between exon 9 of *TAF15* and exon 3 of *ZNF384*. Lane L, bp markers; Lane Pat, reported patient with *TAF15-ZNF384* fusion transcript.

Table 1. Summary of acute leukemia cases with the *TAF15-ZNF384* fusion transcript confirmed by molecular studies

Reference	Sex/Age (yr)	Extramedullary involvement	Initial WBC ($\times 10^9$/L)	Immunophenotype	Diagnosis	Treatment	Follow-up (month)
La Starza R, *et al*. [5]	M/24	No	22.9	HLA-DR+, CD34+, CD13+, CD19+, CD22+, TdT+	Pro-B ALL	aBMT 2 CR	89+
La Starza R, *et al*. [5]	F/44	No	2.9	HLA-DR+, CD34+, CD13+, CD33+, CD19+, CD22+, CD79a+, TdT+	Pro-B ALL	BMT 1 CR	60+
La Starza R, *et al*. [5]	F/16	No	30.4	HLA-DR+, CD34+, CD13+, CD19+, CD22+, CD45+	Pro-B ALL	BMT 2 CR	49+
La Starza R, *et al*. [5]	F/26	Spleen	4.8	HLA-DR+, CD34+, CD19+, sCD22+,TdT+	Pro-B ALL	BMT 1 CR	44+
La Starza R, *et al*. [5]	M/7	No	7.2	HLA-DR+, CD34+, CD33+, CD19+, CD22+, CD24+, cCD79A+, CD10+, TdT+	Pro-B ALL	1 CR	33+
La Starza R, *et al*. [5]	M/29	No	65.6	CD13+, CD33+, CD19+	AML (M1)	CHT relapse	8d
Nyquist KB, *et al*. [6]	M/19	No	92	HLA-DR+, CD34+, CD19+, CD22+, CD38+,CD45+, CD58+, CD123+, CD10+, TdT+	Pro-B ALL	1 CR	27+
Nyquist KB, *et al*. [6]	F/3	NA	36.5	HLA-DR+, CD33+, CD19+, CD22+, cCD79a+, CD10+, TdT+	Pro-B ALL	HR relapse	96d
Grammatico S, *et al*. [3]	F/25	No	3.1	CD34+, CD33+, CD19+, CD22+	Pro-B ALL	HR relapse	34d
This study	F/2	No	2.6	CD34+, CD13+, CD33+, CD19+, cCD79a+, TdT+	Pro-B ALL	1 CR	8+

Abbreviations: WBC, white blood cells; aBMT, autologous bone marrow transplantation; BMT, allogeneic bone marrow transplantation; CR, complete remission; CHT, standard chemotherapy; HR, high-risk chemotherapy; d, died; +, alive; NA, not available.

product revealed breakpoints between exon 9 of *TAF15* and exon 3 of *ZNF384* (Fig. 1C).

Diagnostic lumbar puncture and computed tomography ruled out the central nervous system (CNS) involvement. She achieved complete remission by day 35 following a single course of standard risk induction chemotherapy, including cytarabine, methotrexate, vincristine, hydrocortisone, and l-asparaginase. Thereafter, she received high-dose cyclophosphamide consolidation and intrathecal methotrexate CNS prophylaxis, followed by high-risk vincristine and methotrexate maintenance, and has been in remission for eight months after the initial diagnosis.

The t(12;17)(p13;q11), t(12;17)(p13;q12), or t(12;17)(p11-12;q11-12), for which the breakpoint assignment differs slightly, was first described in 1982 by Kaneko *et al*. [7]. Its molecular fusion gene, *TAF15-ZNF384*, was shown to be involved in tumorigenesis in 2002 [2]. To the best of our knowledge, there have been 10 cases of *TAF15-ZNF384* fusion confirmed using molecular studies (Table 1). In addition to the early B-cell morphology, coexpression of myeloid markers and a lack of expression of CD10 are common immunophenotypic features of this entity [8]. There are conflicting reports regarding the prognosis of cases with t(12;17) [3, 5, 6]. Owing to its low incidence, the treatment protocol differs between institutions, and the statistical significance of t(12;17) in terms of clinical outcome has not been analyzed to date [3]. Studies with a larger ALL patient group displaying such changes are required in order to determine the prognostic impact of *TAF15-ZNF384* fusion.

Primers and probes for *TAF15-ZNF384* are not usually included in commercial kits for screening leukemia translocations, so this abnormality may be missed in routine clinical settings. We suggest that special attention be paid when a translocation between 12p13 and 17q11 is suspected and that additional studies for *TAF15-ZNF384* may be useful in ALL diagnoses. Including this fusion transcript in the initial screening panel can assist in identifying underdiagnosed cases and distinguishing ambiguity of t(12;17), therefore establishing their incidence and clinical significance.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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