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Acute Undifferentiated Leukemia With a Balanced t(5;10)(q35;p12) Resulting in Fusion of *HNRNPH1* With *MLLT10*

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Abstract. *Background/Aim: Acute undifferentiated leukemia (AUL) is leukemia which does not express lineage-specific antigens. Such cases are rare, accounting for 2.7% of all acute leukemia. The reported genetic information of AULs is limited to less than 100 cases with abnormal karyotypes and a few cases carrying chimeric genes or point mutation of a gene. We herein present the genetic findings and clinical features of a case of AUL. Case Report: Bone marrow cells obtained at diagnosis from a 31-year-old patient with AUL were genetically investigated. G-Banding karyotyping revealed an abnormal karyotype: 45,X,-Y,t(5;10)(q35;p12),del(12)(p13)[12]/46,XY[5]. Array comparative genomic hybridization examination confirmed the del(12)(p13) seen by G-banding but also detected additional losses from 1q, 17q, Xp, and Xq corresponding to the deletion of approximately 150 genes from these five chromosome arms. RNA sequencing detected six HNRNPH1::MLLT10 and four MLLT10::HNRNPH1 chimeric transcripts, later confirmed by reverse-transcription polymerase chain reaction together with Sanger sequencing. Fluorescence in situ hybridization analysis showed the presence of HNRNPH1::MLLT10 and MLLT10::HNRNPH1 chimeric genes. Conclusion: To the best of our knowledge, this is the first AUL in which a balanced t(5;10)(q35;p12) leading to fusion of HNRNPH1 with MLLT10 has been detected. The relative leukemogenic importance of the chimeras and gene losses cannot be reliably assessed, but both mechanisms were probably important in the development of AUL.*

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Acute undifferentiated leukemias (AULs) do not express lineage-specific antigens inasmuch as they lack the T-cell lineage marker cytoplasmic CD3, the myeloid marker myeloperoxidase, and B-cell markers (1). AULs account for only 2.7% of acute leukemias, corresponding to an incidence of 1.6 cases per 1,000,000 person-years (2, 3). Age is a very strong predictor for overall survival, with adult patients with AUL faring much worse than do children (3). Genetic information on AULs is limited: The Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (last updated on January 19, 2023) contains 82 AULs with an abnormal karyotype (4). By comparison, the same database contains 21,738 entries on acute myeloid leukemia (AML) and 12,339 entries on acute lymphoblastic leukemia (ALL) with abnormal karyotypes. The following fusion genes have been reported in AUL: *BCR::ABL1* (5, 6), *ETV6::ABL1* (7), *EWSR1::ZNF384* (8), *KMT2A::FOXO3* (9), *KMT2A::GIMAP8* (10), *KMT2A::GPHN* (11), *KMT2A::MLLT10* (12), and *SET::NUP214* (13, 14). In a recent study, mutations of *PHF6*, *SRSF2*, *RUNX1*, and *ASXL1* were found in 33%, 40%, 46%, and 33% of examined AUL cases, respectively (15). We herein present the acquired chromosomal aberrations, the presence of a fusion gene, and the heterozygous losses of many gene loci in the bone marrow cells, together with the clinical features, of a patient with acute undifferentiated leukemia.

Case Report and Methods

Ethics statement. The study was approved by the Regional Ethics Committee (Regional komité for medisinsk forskningsetikk Sør-Øst, Norge, http://helseforskning.etikkom.no). All patient information has been anonymized.

Patient. A 31-year-old man was transferred to our university hospital due to significant leukocytosis and suspicion of ALL. He had had intermittent headaches for a few months and in the week before admission, his general condition was poor with pronounced night sweats and difficulty swallowing. On clinical examination, he was tired and lethargic. He had slightly enlarged lymph nodes bilaterally above the collarbone, in the axillae and groin. No hepatosplenomegaly or tumor testis was found but there was a hint of gingival hyperplasia. The patient was afebrile. Blood tests showed severe anemia (Hb 5.4 g/dl), pronounced leukocytosis (656×10^9/l), and thrombocytopenia (58×10^9/l). There were no signs of disseminated intravascular coagulation, spontaneous tumor lysis or renal failure, but lactate dehydrogenase was elevated. Blood and bone marrow smears were dominated by blasts with little cytoplasm and no grains or Auer rods, suggesting acute lymphoblastic leukemia.

Because of pronounced leukocytosis with a risk of tumor lysis syndrome and central nervous system complications, pre-phase treatment was initiated with 20 mg/m^2 prednisolone as well as tumor lysis prophylaxis while awaiting the results of diagnostic tests. Erythrocyte transfusion was not given to avoid increased blood viscosity. By flow cytometry, 97% of nucleated cells in the bone marrow were CD45$^-$, CD34$^+$, heterogeneously HLA-DR$^+$, CD1a$^-$, CD2$^-$, CD3$^-$, cytCD3$^-$, CD4$^-$, bimodally CD5$^+$, CD7$^+$, CD8$^-$, CD10$^-$, CD56$^-$, weakly CD99$^+$, weakly ndTdT$^+$, CD13$^+$, CD33$^+$, CD117$^+$, weakly CD11b$^+$, cytCD79a$^-$, cytMPO$^-$, CD19$^-$, dimly CD48$^+$, CD16$^-$, CD35$^-$, CD64$^-$, IREM2$^-$, CD14$^-$, CD25$^-$, CD41a$^-$, CD42b$^-$, CD36$^-$, weakly CD105$^+$, weakly CD71$^+$, CD15$^-$, NG2$^-$, CD2$^-$, CD96$^-$, weakly CD123$^+$, CD38$^+$, CD11a$^+$, bimodally CD133$^+$, CD4$^-$, CD3$^-$, and weakly CD22$^+$. These flow cytometric findings best fit a diagnosis of acute undifferentiated leukemia. Polymerase chain reaction (PCR) analyses showed none of the common fusion transcripts seen in acute leukemia. After an initial drop in the leukocyte count to 476×10^9/l, there was a rise 1 day after prednisolone had been given and ALL induction treatment was started in accordance with the NOPHO ALL 2008 high-risk protocol with dexamethasone, doxorubicin, and vincristine (16). After a relatively uncomplicated initial course, however, the patient became unconscious 4 days after admission with bilaterally dilated pupils. A computed tomographic scan showed multiple minor cerebral hemorrhages with bilateral hydrocephalus. Death occurred 5 days after admission to hospital.

G-Banding and karyotyping. Bone marrow cells obtained at diagnosis were cytogenetically investigated (17, 18). Chromosomal preparations were G-banded using Leishman's stain (Sigma-Aldrich, St. Louis, MO, USA) and karyotyped according to the 2020 Guidelines of the International System for Human Cytogenomic Nomenclature (19).

DNA and RNA isolation. Genomic DNA and total RNA samples were extracted from the patient's bone marrow at diagnosis as previously described (20-22).

Array comparative genomic hybridization (aCGH) analysis. aCGH was performed using CytoSure array products (Oxford Gene Technology, Begbroke, UK) following the company's protocols (21, 22). The reference DNA was Promega's human genomic male DNA (Promega, Madison, WI, USA). The slides (CytoSure Cancer +SNP array) were scanned in an Agilent SureScan Dx microarray scanner using Agilent Feature Extraction Software (version 12.1.1.1) (Santa Clara, CA, USA). Data were analyzed using CytoSure Interpret analysis software (version 4.11.36) (Oxford Gene Technology). Annotations are based on human genome build 19.

RNA sequencing. High-throughput paired-end RNA-sequencing was performed at the Genomics Core Facility, Norwegian Radium Hospital, Oslo University Hospital (http://genomics.no/oslo/). The software FusionCatcher was used to find fusion transcripts (23).

Reverse transcription polymerase chain reaction (RT-PCR) and Sanger sequencing analyses. To confirm the presence of fusion transcripts (see below), a BigDye Direct Cycle Sequencing Kit was used for both PCR and cycle (Sanger) sequencing following the company's recommendations (ThermoFisher Scientific, Waltham, MA, USA) (20-22). The primers used are listed in Table I. The forward primers had the M13 forward primer sequence TGTAAAACGACGGCCAGT at their 5'-end whereas the reverse primers had the M13 reverse primer sequence CAGGAAACAGCTATGACC at their 5'-end. The primer combinations were HNRNPH1-1171F1/MLLT10-2135R1 and MLLT10-1968F1/HNRNPH1-1353R1. Sequence analyses were performed on an Applied Biosystems SeqStudio Genetic Analyzer system (ThermoFisher Scientific). The basic local alignment search tool (BLAST) software (https://blast.ncbi.nlm.nih.gov/Blast.cgi) was used for computer analysis of sequence data (24). The reference sequences were: NM_005520.3 for heterogeneous nuclear ribonucleoprotein H1 (*HNRNPH1*) gene and NM_004641.4 for the MLLT10 histone lysine methyltransferase DOT1L cofactor (*MLLT10*) gene. The BLAST-like alignment tool (BLAT) and the human genome browser at the University of California, Santa Cruz were used to map the sequences on the Human GRCh37/hg19 assembly (25, 26).

Table I. *Designation, sequence (5'->3'), and position in reference sequences of the forward (F1) and reverse (R1) primers used for polymerase chain reaction amplification and Sanger sequencing analyses. For Sanger sequencing, the forward primers had the M13 primer sequence TGTAAAACGACGGCCAGT at their 5'-end. The reverse primers had the M13 primer sequence CAGGAAACAGCTATGACC at their 5'-end.*

Designation	Sequence (5'->3')	Reference sequence: position
HNRNPH1-1171F1	CGGTGGTGCTTACGAACACAGATA	NM_005520.3: 1171-1194
HNRNPH1-1207F1	CTTGAATTCTACAGCAGGAGCAAGC	NM_005520.3: 1207-1231
HNRNPH1-1336R1	TGCTGCTCTGGCCACCGTAG	NM_005520.3: 1355-1336
HNRNPH1-1323R1	ACCGTAGCCGCCTCCGTAAC	NM_005520.3: 1342-1323
HNRNPH1-1353R1	AAAACTTGGTCGTATCCACTCATGC	NM_005520.3: 1377-1353
MLLT10-1968F1	TGCTGAATGCAATACACAACGACA	NM_004641.4: 1968-1991
MLLT10-1976F1	GCAATACACAACGACAGAGGTGACA	NM_004641.4: 1976-2000
MLLT10-2135R1	TACTTGTTGCAAATGCCCAGAAGA	NM_004641.4: 2158-2135
MLLT10-2110R1	CTGCTGAGGTAAGTGAGAGCTGGAG	NM_004641.4: 2134-2110

Table II. *Bacterial artificial chromosome (BAC) probes used for interphase fluorescence in-situ hybridization experiments to detect the fusion of HNRNPH1 with MLLT10. The positions of the HNRNPH1 and MLLT10 genes are also given.*

BAC clones	Accession number	Chromosome position	Targeted gene	Position on GRCh38/hg38 assembly	Labeling
RP11-798K23	AC136628.2	5q35.3	*HNRNPH1*	chr5:179417999-179550126	Red
RP11-1379J22	AC136604.2	5q35.3	*HNRNPH1*	chr5:179550127-179682356	Red
	NM_005520.3	5q35.3	*HNRNPH1*	chr5:179614179-179624669	
RP11-718N2	AC113426.2	5q35.3	*HNRNPH1*	chr5:179682357-179790268	Red
RP11-275N1	AL158209.23	10p12.31	*MLLT10*	chr10:21340172-21470498	Green
RP11-418C1	AL358780.22	10p12.31	*MLLT10*	chr10:21470499-21580809	Green
	NM_004641.4	10p12.31	*MLLT10*	chr10:21524675-21743630	Green
RP11-177H22	AL161799.19	10p12.31	*MLLT10*	chr10:21580810-21654103 chr10:21654499-21697085	Green
RP11-86F19	AL357372.12	10p12.31	*MLLT10*	chr10:21697086-21738638	Green
RP11-399C16	AL359697.23	10p12.31	*MLLT10*	chr10:21738639-21908506	Green
RP11-365J16	AL445431.16	10p12.31	*MLLT10*	chr10:21908507-22045159	Green

Fluorescence in-situ hybridization (FISH) analysis. On the basis of findings obtained by RNA sequencing, RT-PCR, and Sanger sequencing (see below), FISH was performed on interphase nuclei of bone marrow cells from the patient using an in house-prepared double fusion *HNRNPH1::MLLT10* probe. The probe was made from commercially available bacterial artificial chromosomes purchased from the BACPAC Resource Center (BACPAC Genomics, Emeryville, CA, USA) (Table II). Bacterial artificial chromosome DNAs and probe labeling were as previously described (27-29).

Results

Diagnostic cytogenetic examination of short-term cultured cells from the patient's bone marrow revealed clonal chromosomal aberrations resulting in the following karyotype: 45,X,-Y,t(5;10)(q35;p12),del(12)(p13)[12]/46,XY[5] (Figure 1A). aCGH confirmed the del(12)(p13) seen by G-banding but also detected additional, smaller losses from chromosome arms 1q, 17q, Xp, and Xq. Thus, around 150 gene loci appeared to have been heterozygously deleted from the bone marrow cells of our case (Table III).

Analysis of the RNA sequencing data in the fastq files using FusionCatcher software detected six *HNRNPH1: :MLLT10* and four *MLLT10::HNRNPH1* chimeric transcripts (Table IV). RT-PCR with primer combinations HNRNPH1-1171F1/MLLT10-2135R1 and MLLT10-1968F1/HNRNPH1-1353R1 amplified approximately 250 bp-long cDNA fragments (Figure 1B). Sanger sequencing of the PCR products amplified with the primer combination HNRNPH1-1171F1/MLLT10-2135R1 confirmed the presence of the chimeric transcripts in which exon 11 of *HNRNPH1* was fused to exon 15 of *MLLT10* (*HNRNPH1::MLLT10*) (Figure 1C). Sanger sequencing of the fragment amplified with the primer combination MLLT10-1968F1/HNRNPH1-1336R1 showed that it contained two *MLLT10::HNRNPH1* fusion transcripts (Figure 1D and E), one in which *MLLT10* exon 14 was fused with *HNRNPH1* exon 12 (Figure 1D) and another in which a sequence of *MLLT10*

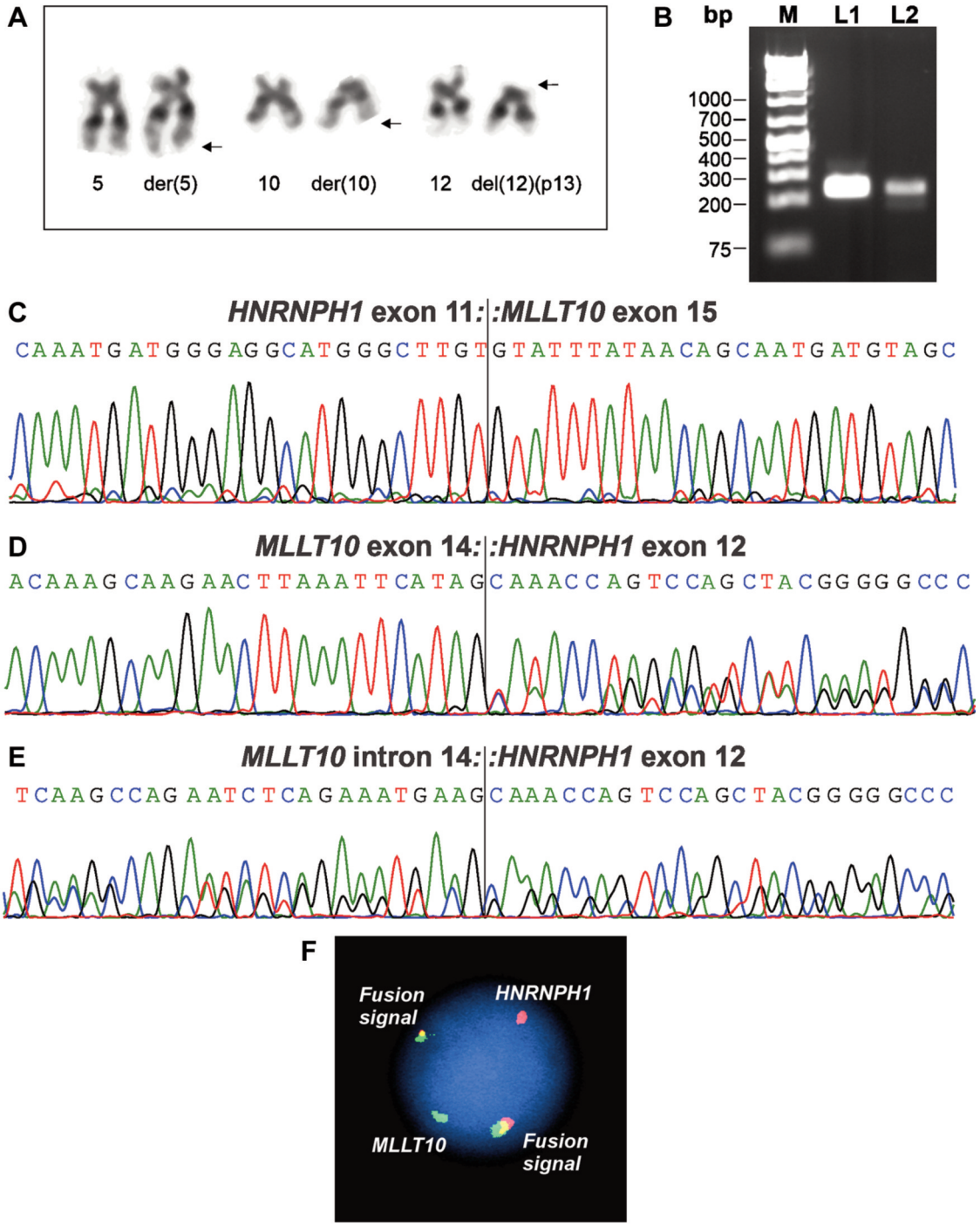

Figure 1. *Genetic investigation of the patient with acute undifferentiated leukemia. A: G-Banding analysis of the bone marrow cells. A partial G-banded karyogram showing the der(5)t(5;10)(q35;p12), der(10)t(5;10)(q35;p12), and del(12)(p13) together with the corresponding normal chromosome homologs. Arrows indicate breakpoints. B: Reverse transcription polymerase chain reaction (RT-PCR). Gel electrophoresis of the RT-PCR-amplified products using HNRNPH1-1171F1/MLLT10-2135R1 (lane L1) and MLLT10-1968F1/HNRNPH1-1353R1 (lane L2) primer combinations. M: GeneRuler 1 kb Plus DNA ladder (ThermoFisher Scientific). C: Partial sequence chromatograms of cDNA-amplified fragment (L1) showing the junction position of exon 11 of HNRNPH1 with exon 15 of MLLT10. D: Partial sequence chromatograms of cDNA-amplified fragment (L2) showing the junction of exon 14 of MLLT10 with exon 12 of HNRNPH1. E: Partial sequence chromatograms of cDNA-amplified fragment (L2) showing the junction of sequence from intron 14 of MLLT10 with exon 12 of HNRNPH1. F: Fluorescence in-situ hybridization. An interphase nucleus showing a red signal corresponding to HNRNPH1, a green signal corresponding to MLLT10, and two yellow signals corresponding to the HNRNPH1::MLLT10 and MLLT10::HNRNPH1 chimeric genes.*

Table III. *Imbalances detected by array comparative genomic hybridization analysis of the bone marrow cells.*

Cytogenetic location	Position on GRCh37/hg19 assembly	Size (Mbp)	Gain/loss	Comment
1q31.3q32.1	Chr1:198448460-199629054	1.18	Loss	Deletion of 6 genes
12p13.2p12.3	Chr12:10700050-16863997	6.16	Loss	Deletion of 79 genes, among them *ETV6*
17q11.2	Chr17:28432171-30485890	2.05	Loss	Deletion of 46 genes, among them *NF1* and *SUZ12*
Xp22.33	ChrX:61491-2733380	2.67	Loss	Deletion of pseudoautosomal region 1 (PAR1), which contains 15 genes, among them *CRLF2*, *P2RY8*, and *CD99*
Xq21.31q21.32	ChrX:88478700-91841735	3.36	Loss	Deletion of 3 genes

Table IV. *The HNRNPH1::MLLT10 and MLLT10::HNRNPH1 fusion transcripts detected in the patient with acute undifferentiated leukemia after analysis of RNA sequencing data with FusionCatcher. Fusion point positions are based on the Human GRCh37/hg19 assembly. Exons are based on the reference sequences NM_005520.3 for HNRNPH1 and NM_004641.4 for MLLT10.*

Fusion transcript	Spanning unique reads	Fusion sequence
HNRNPH1::MLLT10 (exon 11-exon15)*	36	AGCAAGCGGTGGTGCTTATGGTAGCCAAATGATGGGAGGCATGGGCTTGT::GTATTTATAACAGCAATGATGTAGCAGTATCGTTTCCAAATGTAGTATCT
HNRNPH1::MLLT10 (intron 10-exon 15)*	25	AGCAAGCGGTGGTGCTTACGGTAGCCAAATGCTAGGAGGCATGGGTTTGT::GTATTTATAACAGCAATGATGTAGCAGTATCGTTTCCAAATGTAGTATCT
HNRNPH1::MLLT10 (exon 10-exon 15)*	15	CTCTTCTTGAATTCTACAGCAGGAGCAAGCGGTGGTGCTTACG::GTATTTATAACAGCAATGATGTAGCAGTATCGTTTCCAAATGT
HNRNPH1::MLLT10 (exon 11-exon 15)*	6	TGTAGAACTCTTCTTGAATTCTACAGCAGGAGCAAGCGGTGGTGCTTATG::GTATTTATAACAGCAATGATGTAGCAGTATCGTTTCCAAATGTAGTATCT
HNRNPH1::MLLT10 (intron 11-exon 15)*	4	TGGTGCTTATGGTAGCCAAATGATGGGAGGCATGGGCTTGTGTAAATATC::GTATTTATAACAGCAATGATGTAGCAGTATCGTTTCCAAATGTAGTATCT
HNRNPH1::MLLT10 (exon 11-intron 14)	2	AGCAAGCGGTGGTGCTTATGGTAGCCAAATGATGGGAGGCATGGGCTTGT::ACAGAGTCTTGCTTTATTGCCAAGGCTGGAGTGCAGTGATACAATCACGG
MLLT10::HNRNPH1 (intron 14-exon 12)	27	CCTAGAGTTCATCAAATGGGCTTACTCAAGCCAGAATCTCAGAAATGAAG::CAAACCAGTCCAGCTACGGGGGCCCAGCCAGCCAGCAGCTGAGTGGGGGT
MLLT10::HNRNPH1 (exon 13-exon 12)*	21	CCAACAACTACGTTCTCAGAGTTGCTGAATGCAATACACAACG::CAAACCAGTCCAGCTACGGGGGCCCAGCCAGCCAGCAGCTGAG
*MLLT10::HNRNPH1** (exon 14-exon 12)	11	GGTGACAGTTCTACACTAACAAAGCAAGAACTTAAATTCATAG::CAAACCAGTCCAGCTACGGGGGCCCAGCCAGCCAGCAGCTGAG
MLLT10::HNRNPH1 (exon 17-exon 4)	2	TAGTTGGCAGAGGAAGCTCACCCCGAGGAAGTCTCTCGCCACG::TATTCAAGTCAAACAACGTTGAAATGGATTGGGTGTTGAAGCA

*In-frame fusion transcript.

intron 14 was fused with *HNRNPH1* exon 12 (Figure 1E). No other fusion transcripts were examined.

FISH analysis of bone marrow cells using probes for *HNRNPH1* and *MLLT10* showed two yellow signals together with one red and one green signal in 82 out of 100 nuclei examined (Figure 1F). The yellow signals corresponded to *HNRNPH1::MLLT10* and *MLLT10::HNRNPH1* chimeric genes, whereas the red and green signals corresponded to intact *HNRNPH1* and *MLLT10* loci, respectively.

Discussion

Variants of the translocation t(5;10)(q35;p12), as well as fusion between *HNRNPH1* and *MLLT10,* are rare but recurrent acquired genetic abnormalities in leukemias. The unbalanced der(10)t(5;10)(q35.3;p12.3) chromosomal aberration and a t(2;5;10)(q13;q35;p12) three-way translocation were previously reported in two T-ALLs (30, 31). To the best of our knowledge, the balanced translocation t(5;10)(q35;p12) is described for the first time here. The *HNRNPH1::MLLT10* chimera was reported in only three leukemia cases prior to the present one (31-33). In addition, Othman *et al*. (30) used FISH analysis to show that *HNRNPH1* and *MLLT10* were recombined in a case of leukemia with der(10)t(5;10)(q35.3;p12.3).

Because both *HNRNPH1* and *MLLT10* are transcribed from telomere to centromere, a simple balanced translocation between 5q35 and 10p12 should be sufficient to give rise to the chimeric genes *HNRNPH1::MLLT10* and *MLLT10:*

:HNRNPH1 on the der(10)t(5;10)(q35;p12) and der(5)t(5;10)(q35;p12) chromosomes, respectively. *HNRNPH1* is ubiquitously expressed and codes for one of the heterogeneous nuclear ribonucleoproteins (34). HNRNPH1 is very similar to HNRPF and has three RNA recognition motifs (RRMs) that bind to RNA (34). In the HNRNPH1 protein with reference sequence number NP_005511.1 (coded by NM_005520.3), the RRMs are found in regions 10-88 (RRM1), 103-192 (RRM2), and 289-364 (RRM3).

Apart from the *HNRNPH1::MLLT10* chimera, other *HNRNPH1* fusion genes have also been described in various leukemias (4). *HNRNPH1::ERG* chimeras were reported in AML (35-37), *MEF2D::HNRNPH1* in B-lineage ALL (38), and *HNRNPH1::DDX5* in CLL (39).

MLLT10 is a promiscuous fusion partner in leukemia (4, 40). In the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer, 26 *MLLT10* chimeric genes are registered in various types of leukemia (4). The most frequent are *KMT2A::MLLT10* found in 8% of all *KMT2A*-rearranged leukemias and *PICAML::MLLT10* found in 6-10% of T-ALLs. The MLLT10 protein is a transcription factor known to interact with many proteins but especially with DOT1-like histone lysine methyltransferase (40). MLLT10 has two PHD finger domains at its *N*-terminal end that are collectively referred to as leukemia-associated-protein (LAP) finger(s) (40). In the MLLT10 protein with reference number NP_004632.1 (coded by NM_004641.4), LAP is located from amino acid position 24 to 206. LAP was shown to mediate protein–protein interactions and homo-oligomerization of recombinant MLLT10 *in vitro* (40). Recently, disruption of LAP in MLLT10 fusion proteins was found to lead to malignant transformation (41). Towards its *C*-terminal end (amino acids 731-794 in NP_004632.1), the MLLT10 protein has a coiled-coil domain which contains a conserved octapeptide (EQLLERQW) motif separated by a short non-conserved sequence from a leucine zipper domain (42). The MLLT10 coiled-coil domain interacts with several proteins such as DOT1 like histone lysine methyltransferase, IKAROS family zinc finger 1, and YEATS domain containing 4 (42-45). The presence of MLLT10 fusion proteins was found to be both necessary and sufficient to induce leukemogenesis (42-45).

In our patient, the chimeric isoforms of the HNRNPH1::MLLT10 proteins are predicted to contain the RNA recognition motifs of HNRNPH1 and the coiled-coil domain of MLLT10. The reciprocal chimeric isoforms of MLLT10::HNRNPH1 contain the LAP of MLLT10 and the *C*-terminal part of HNRNPH1; the function of these is currently unknown.

In addition to t(5;10) leading to the chimeric genes *HNRNPH1::MLLT10* and *MLLT10::HNRNPH1*, the bone marrow cells had losses from 12p, 1q, 17q, Xp, and Xq resulting in heterozygous deletion of 150 genes, some of which are of known importance in hematopoiesis and leukemogenesis. For example, the deletion on 1q includes the *PTPRC* gene that codes for protein tyrosine phosphatase receptor type C (also known as CD45), a leucocyte common antigen important in the proliferation and differentiation of hematopoietic stem cells (46, 47). Deficiency of *PTPRC* or alteration of its expression is associated with various diseases, including leukemia and lymphoma (46, 47). The deletion on 12p includes *ETV6*, a gene that encodes a transcriptional repressor implicated in both hematopoiesis and leukemogenesis (48, 49). The 17q deletion contains the tumor-suppressor gene *NF1* (50) as well as *SUZ12* that codes for a protein of the polycomb repressive complex 2 which is deregulated in several hematological malignancies (51, 52). Finally, the deletion in Xp harbors the entire pseudoautosomal region 1 (PAR1) which contains 15 genes, some of which (*CD99* and *P2RY8*) are known to be involved in leukemogenesis (53-55). We assume that these losses also played a role in leukemogenesis in the present case but cannot speculate about the relative pathogenetic contributions of the acquired balanced and imbalanced genomic changes.

Conclusion

We identified acquired chromosomal aberrations, the presence of a fusion gene, and heterozygous losses of many gene loci in the bone marrow cells of a patient diagnosed with AUL. To the best of our knowledge, this is first case of AUL in which the balanced chromosomal translocation t(5;10)(q35;p12), leading to fusion of *HNRNPH1* with *MLLT10*, has been detected. We believe that both the *HNRNPH1::MLLT10* and *MLLT10::HNRNPH1* chimeras and the genomic losses contributed to leukemogenesis in this patient.

Conflicts of Interest

The Authors declare that they have no potential conflicts of interest.

Authors' Contributions

IP designed and supervised the research, performed molecular genetic and bioinformatics analyses, and wrote the article. KA performed molecular genetic analyses and interpreted the data. MRT evaluated aCGH, FISH, and cytogenetic data. HSW made clinical evaluations and treated the patient. FM evaluated the data. SH assisted with study design and writing of the article. All Authors read and approved the final article.

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