Coexistence of acute myeloid leukemia with a complex chromosomal translocation and monoclonal gammopathy of undetermined significance: A case report and literature review

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Abstract. Acute myeloid leukemia (AML) with chromosomal translocation t(8;21)(q22;q22.1) is a rare subtype, accounting for 4-8% of all cases of AML. Despite its rarity, it has a favorable outcome. The translocation event culminates in the formation of the Runt-related transcription factor 1 (RUNX1)::RUNX1 partner transcriptional co-repressor 1 (RUNX1T1) fusion protein, which is implicated in hematopoietic differentiation and maturation. Furthermore, monoclonal gammopathy of undetermined significance (MGUS) is characterized by the presence of monoclonal immunoglobulins in the blood or urine, serum M protein level of <3 g/dl and <10% clonal plasma cells in the bone marrow, with no accompanying end-organ damage associated with myeloma. The simultaneous occurrence of AML and MGUS is exceedingly rare. The present report describes the case of a male patient with AML and a RUNX1::RUNX1T1 fusion gene, not arising from the usual chromosomal translocation but rather from a complex translocation event involving t(8;17;21) (q22;q24;q22). The patient achieved complete remission (CR) following an idarubicin (12 mg/m^2, days 1-3) + cytarabine (100 mg/m^2, d1-7) regimen chemotherapy. Subsequent bone marrow monitoring revealed CR of AML during consolidation chemotherapy; however, ~5% of plasma cells were detected in the bone marrow. Flow cytology confirmed the presence of monoclonal plasma cells, and a positive hematuria immune-fixed electrophoresis assessment led to a diagnosis of MGUS. Due to economic constraints, the patient and their family declined high-dose cytarabine-based combination chemotherapy and hematopoietic stem cell transplantation, opting instead for intermittent use of standard doses of anthracycline combined with cytarabine maintenance therapy. The disease relapsed after 10 months, the patient discontinued treatment and died shortly after.

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Introduction

Acute myeloid leukemia (AML) is a malignant clonal disease originating from hematopoietic stem progenitor cells (1). Chromosomal heterogeneous t(8; 21) (q22; q22.1) translocations occur in certain patients with AML, where the Runt-related transcription factor 1 (RUNX1) gene (also known as AML1) at 21q22 is fused to the RUNX1 partner transcriptional co-repressor 1 (RUNX1T1) gene (also known as ETO) at 8q22, resulting in a RUNX1::RUNX1T1 fusion gene on chromosome 8. This has a positive rate of 20-40% in AML with maturation (AML-M2) and is found to a lesser degree in acute myelomonocytic leukemia (AML-M4) and undifferentiated AML (AML-M1) (2). The 5th Edition of the World Health Organization Classification of Hematolymphoid Tumors defines RUNX1::RUNX1T1 fusion gene positivity as genetically abnormal AML; that is, a diagnosis of AML should be considered when the RUNX1::RUNX1T1 fusion gene is monitored, even if the blast cell count is <20% (1).

The presence of RUNX1::RUNX1T1-positive AML is a well-characterized karyotype associated with a favorable prognosis. Remission induction through combination chemotherapy has shown a complete response (CR) rate of 90%, with long-term disease-free survival rates ranging from 50-70% after 5 years (2). It is crucial to regularly monitor the quantitative levels of the RUNX1::RUNX1T1 fusion genes to assess treatment efficacy and detect disease recurrence (1).

Monoclonal gammopathy of undetermined significance (MGUS) refers to the presence of monoclonal immunoglobulins in serum and urine; however, the proportion of plasma cells in the bone marrow, clinical symptoms and biochemical indices is insufficient to diagnose multiple myeloma and other plasma cell diseases (3). MGUS is prevalent in ~3% of the population aged >50 years, and its incidence increases with age. The progression rate from MGUS to multiple myeloma

(MM) is ~1% of patients per year, suggesting that the majority of patients with MGUS remain undiagnosed and do not develop symptomatic malignancies (3).

AML with a complex chromosomal translocation t(8;17;21)(q22;q24;q22) is rarely reported, and at the same time, its coexistence with MGUS is extremely uncommon. The present study describes a case of AML with a RUNX1:RUNX1T1 fusion gene and the complex chromosomal translocation (8; 17; 21), which was found to be associated with MGUS during treatment. The therapeutic regimen and prognosis of this patient are described and the relevant literature on this rare type of AML is reviewed to improve awareness of this disease.

Case report

A 57-year-old male with no history of hematological diseases was admitted to the Second Hospital of Hebei Medical University (Shijiazhuang, China) for treatment in October 2022 due to a hemoglobin count decrease for >5 months and fatigue for 1 week. An assessment revealed the presence of anemia, devoid of any apparent bleeding diathesis, superficial lymphadenopathy or palpable enlargement of the liver and spleen. On admission, routine peripheral blood analysis demonstrated the following results: White blood cell count, $5.40x10^9$/l (3.5-9.5x10^9/l); hemoglobin level, 60 g/l (115-150 g/l); and platelet count, $29x10^9$/l (125-300x10^9/l). The bone marrow exhibited hypercellularity, with blast cells comprising 44.0% of the total cell population. Bone marrow fluid was collected for flow cytometry examination. The concentration of single-cell suspension was 1×10^7/ml. EDTA anticoagulant were added to single-cell suspension and antibodies were added: CD38 (FITC, Kuangbo Tongsheng Biotechnology Co., Ltd., 103802), CD117 (P, Kuangbo Tongsheng Biotechnology Co., Ltd., 111704), CD34 (PerCP/Cyanine5.5; Biolegend, 343522), CD33 (PE-CY7, Biolegend, 366618), CD13 (APC, Kuangbo Tongsheng Biotechnology Co., Ltd., A6009R12), CD123 (APC-A700, Biolegend, 306040), HLA-DR (APC/Cyanine7, Biolegend, 307618), CD11b (BV421, Biolegend, 301324), CD15 FITC, Biolegend, 301904), CD34 (PE, Kuangbo Tongsheng Biotechnology Co., Ltd., Z6410008), CD56 (PercpCy5.5, Kuangbo Tongsheng Biotechnology Co., Ltd., 105610), CD7 (APC, Kuangbo Tongsheng Biotechnology Co., Ltd., A6005R12), CD14 (APC/Fire 750, Biolegend, 301854), CD19 (BV421, Biolegend, 302234), CD45 (QB500, Kuangbo Tongsheng Biotechnology Co., Ltd., A6015V32) at 100 μl/tube, shaken, and kept in darkness at room temperature for 30 min. A total of 3% paraformaldehyde was added and incubated in the dark for 10 min at room temperature.1 ml of cell membrane breaking buffer was added, and the solution was incubated it at 4˚C in the dark for 30 min subsequent to shaking. The solution was centrifuged at 160 x g for 5 min at room temperature, and the supernatant was discarded. A total of 5 ml of PBS solution was added, shaken, and centrifuged at 160 x g for 5 min at room temperature. The above steps need to be repeated twice. The supernatant was discarded, and 300 μl of PBS was added to form a suspension. After adding FITC, phycoerythrin, peridinin chlorophy II protion (PreCP) and allophycocyanin (APC), flow cytometer (Beckman Coulter, Navios) to detect and analyze the cell suspension. Data analysis was performed using Kaluza 2.1.1 software (Beckman Coulter, Inc.). Flow cytometry analysis revealed abnormal myeloid blasts accounting for 44.23% of all myeloid blast cells (Fig. S1). We collect bone marrow fluid for next-generation sequencing. The extraction steps for DNA and RNA in next-generation sequencing were as aforementioned. The DNA and RNA were extracted using commercial kits (Tiangen Biotech, Co., Ltd.). The purities and concentrations of DNA and RNA were confirmed using a Nanodrop 2000 (Thermo Scientific, Inc.) and a Qubit 3.0 Fluorometer (Thermo Fisher Scientific, Inc.). The integrity of the DNA and RNA was evaluated with the Qsep400 nucleic acid fragment analyzer (Hangzhou Houze Bio-Technology Co., Ltd.). The DNA was transformed into libraries with the help of KAPA EvoPlus kits (Kapa Biosystems; Roche Diagnostics;9420053001). The libraries were analyzed on the Illumina sequencing platform NextSeq550 using 150bp paired-end sequencing. Sequencing was performed with the NextSeq 500/550 High Output Kit v2.5 (300 cycles; 20024908; Illumina Inc.). The final library concentration was quantified using the Qubit 3.0 Fluorometer. The loading concentration of the final library was ~14 pM. The mutation data was screened through dbSNP (bioinfo.org.cn/relative/dbSNP% 20Home%20 Page.htm), gnomAD (ngdc.cncb.ac.cn/databasecommons/database/id/6934), COSMIC (cancer.sanger.ac.uk/cosmic/download), and Polyphen2 SIFT (http://provean.jcvi.org/protein_batch_submit. php? species=human), as well as the internal database of Tianjin Jiankang Huamei Laboratory. Then the data was analyzed using BWA (github.com/bwa-mem2/bwa-mem2), Sambamba (github. com/biod/sambamba/releases), Bamdst (https://github.com/shiquan/bamdst), VarDict (GitHub-AstraZeneca-NGS/VarDict: VarDict), CNV kit (cnvkit. readthedocs.io/en/stable/), Pinde (gmt.genome.wustl.edu/packages/pindel/), ANNOVAR (annovar. openbioinformatics. org/en/latest/). Next-generation sequencing showed the presence of Fms-related receptor tyrosine kinase 3 (Exon20.c2516>G.p.D839G) and isocitrate dehydrogenase [NADP(+)] 2 (Exon4.c.419> A.p.R140Q) mutations.200 μl of chloroform was added to the bone marrow fluid and mixed it before placing it on ice for 5 min. The mixture was centrifuged at 12,000 x g at 4˚C for 15 min and were used a pipette to aspirate 400-500 μl of the top supernatant. The Specimens were transferred the supernatant to another new EP tube and were added 400-500 μl of isopropanol (in a volume ratio of 1:1 to the supernatant). The mixture were placed on ice until the RNA was completely precipitated. The Specimens were used by a low-temperature high-speed centrifuge to centrifuge at 12,000 x g for 10 min at 4˚C, then discarded the supernatant and thoroughly mixed it with 1 ml of 75% ethanol. The mixed liquid and discard the supernatant. The supernatant was transferred into a DECP-treated EP tube. The resuspended liquid was incubated at 65˚C for 5 min and mixed. RNA was obtained by centrifugation again at 2-8˚C at 12,000 x g for 5 min.cDNA was synthesized from 2 μg of total RNA using a 1st Strand cDNA Synthesis Kit (Hifair III cDNA,Yeasen Biotechnology (Shanghai) Co., Ltd., 11150ES10). The following primer sequences were used: RUNX1::RUNX1T1, (forward) 5'-AML1-FCACCTACC ACAGAGCCATCAAA-3' and (reverse) 5'-ETO-RATCCA CAGGTGAGTCTGGCATT-3'; housekeeping genes: ABL, (forward) 5'-ENF1003TGG AGATAACACTCTAAGCATAAC TAAAGGT-3' and (reverse) 5'-ENR1063GA TGTAGTTGC TTGGGACCCA-3' (SINO-US Diagnostics; Tianjin Jiankang Huamei Medical Diagnostic Technology Co., Ltd.) (4,5). The

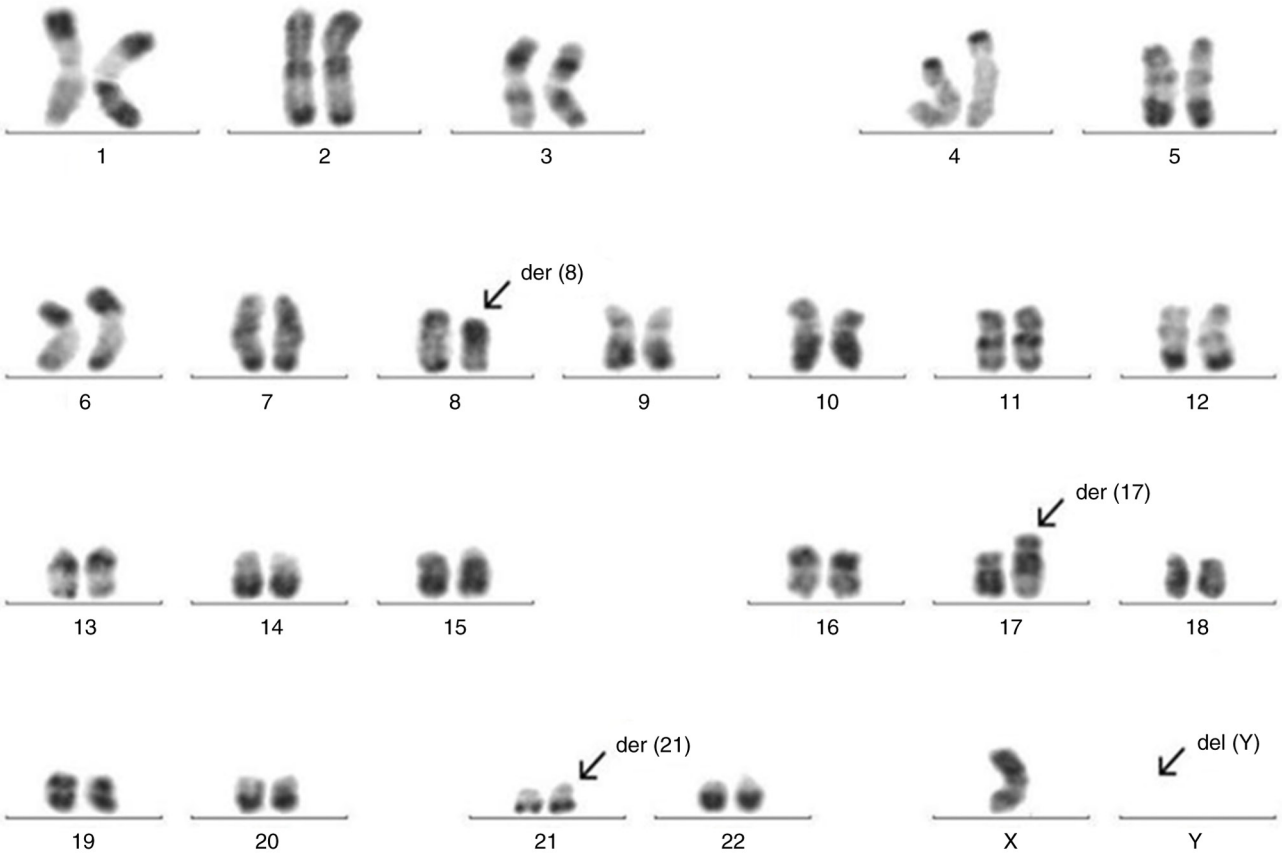

Figure 1. G-banded karyotype of bone marrow cells demonstrating a complex karyotype: 46, XY, t(8:17:21)(q22:q24:22.1)[9]/45, idem, -Y[10]/46,XY[1].

main sample for testing was fresh anticoagulant bone marrow fluid, with a standard bone marrow collection volume of 3-5 ml. The anticoagulant used was EDTA or 3.2% sodium citrate. The optimal concentration of RNA was 300 ng/μl and the optimal purity was 1.8-2.0 for A260:A280 and 2.0-2.2 for A260:A230. Amplification conditions were as follows (40 cycles: 2 min at 50˚C, 10 min at 95˚C, 15 sec at 95˚C and 60 sec at 95˚C. The sample was then stored at 4˚C. The results of reverse transcription-PCR confirmed the presence of a RUNX1::RUNX1T1 fusion gene. The 20 metaphase chromosomes were subjected to R-banding analysis, which revealed a complex karyotype with the following abnormalities: 46,XY, t(8;17;21)(q22;q24;22.1)[9]/45, idem,-Y[10]/46,XY[1] (Fig. 1).

Given that the chromosomal karyotype findings deviated from the typical presentation associated with the RUNX1::RUNX1T1 fusion gene, additional fluorescence *in situ* hybridization (FISH) tests were performed to corroborate the presence of the fusion gene and validate the chromosomal anomalies. The samples were fixed three times in methanol and acetic acid (3:1) following a prefixation step using a 10% solution. The fixed cells were washed with a 2X sodium citrate saline buffer solution at 37˚C for 30 min, then dehydrated in 75, 85, and 100% ethanol for 1 min each, sequentially. The FISH probes for RUNX1 (Abnov, no. FA0446) and RUNX1T1 (Abnov, no. H00000862-M01) were utilized with a hybridization instrument (HANGZHOU RUICHENG INSTRUMENT CO., LTD., SH2000) for hybridization, denaturing at 78˚C for 8 min, and hybridizing at 42˚C for 16 h. The next day, the samples were washed with 0.3% NP40 detergent at 68˚C for 2 min, and then were washed with deionized water at 37˚C for 1 mi. DAPI nuclear staining was performed at room temperature for 20 min. FISH probe kits were purchased from Wuhan Kanglu Biotechnology Co., Ltd. Results were observed using a fluorescence microscope (Olympus; catalog number BX63), and Metasystem ISIS V5.8.11 (Metasystem Co., Ltd.) FISH analysis software was used for photography and analysis. AML1 (21q22) gene labeled green and ETO (8q22) gene labeled in red. The AML1-ETO fusion gene displayed a yellow or red-green superimposed signal, with a normal signal characteristic of 2R2G and a positive signal characteristic of 1R1G2F (G is a green signal, R is a red signal, and F is a fusion signal). The FISH analysis revealed distinct fluorescence patterns: The derivative chromosome 17 involving the t(8;17) translocation exhibited red fluorescence, the derivative chromosome 21 involving the t(17;21) translocation displayed green fluorescence and the derivative chromosome 8 involving the t(8;21) translocation showed a merged red-green fluorescence, indicative of a complex chromosome translocation event t(8;17;21) (Fig. 2). The diagnosis was finally determined as AML with t(8;17;21) (q22;q24;q22.1) chromosome karyotype.

After a course of idarubicin (12 mg/m^2, d1-3) + cytarabine (100 mg/m^2, d1-7) regimen induction treatment, the patient achieved a CR. However, due to financial constraints, the family of the patient opted out of pursuing intensive treatment involving high-dose cytarabine and declined hematopoietic stem cell transplantation. The patient instead requested a standard dose of chemotherapy. After 2 cycles of consolidation chemotherapy with a daunorubicin (12 mg/m^2, d1-3) + cytarabine (100 mg/m^2, d1-7) regimen, primitive and immature cells accounted for less than

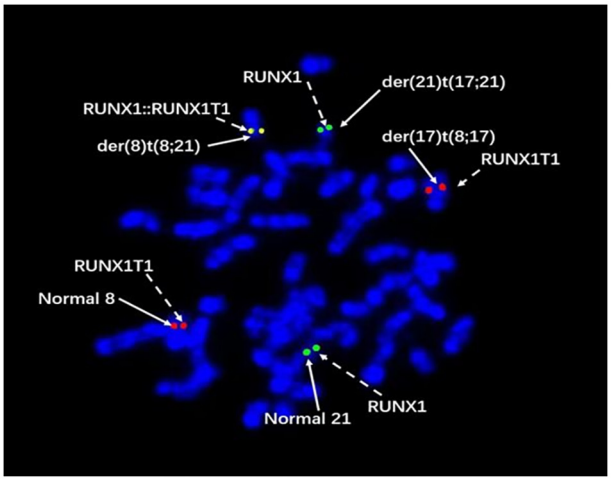

Figure 2. Fluorescence *in situ* hybridization analyses. Magnification, x1,000 Arrows indicate der(17) t(8;17) as red fluorescence, der(21) t(17;21) as green fluorescence and der(8)t(8;21) as yellow fluorescence (red-green co-presence), suggesting a complex translocation involving chromosomes 8,17 and 21. RUNX1, Runt-related transcription factor 1; RUNX1T1, RUNX1 partner transcriptional co-repressor 1.

5% of bone marrow nucleated cells, indicating CR according to The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours diagnostic criteria (1). But monitoring of the RUNX1::RUNX1T1 fusion gene of the patient showed positivity at low levels. After 4 months, bone marrow fluid was collected for bone marrow cytology examination. The bone marrow smears were dried naturally before addition of 2-3 drops of Wright Giemsa staining solution at room temperature for 1-2 min. An equal amount of 0.01 mol/l sodium dihydrogen phosphate was added at room temperature for 3-5 min. The smear was washed with double distilled water, dried and examined under a light microscope (Olympus Corporation). Bone marrow cytology during the fourth hospitalization of the patient demonstrated 0.5% blasts and 4.5% mature plasma cells. Flow cytology revealed 0.11% abnormal myeloid blasts and 2.07% monoclonal plasma cells (expressing CD38, CD138, CD117 and CD56; Fig. 3). Peripheral venous blood and urine from patients were collected for quantitative detection of immunoglobulin. A total of 100 μl of diluent was added to a 20 μl patient serum sample. Specimens were examined using electrophoresis apparatus (Instrument and model: Sebia Hydrasys 2/Helena SPIFE). Urine samples do not require dilution.10 μl of diluted serum or original urine samples were added into the wells of the electrophoresis apparatus sampler, respectively. After the last sample is added, the samples were diffused in the comb for 5 min. The buffer strips were removed from the electrophoresis apparatus. The perforated plastic end of the sponge was inserted into the pin on the electrode transporter, with the northern part of the plastic end facing towards the transporter. The gels were taken out and the excess liquid on their surface was gently absorbed with a thin filter paper. A total of 120 μl of distilled water was added to the bottom third box on the temperature control board of the electrophoresis module. The adhesive side of the film was placed upwards, and the edge of the film was pressed tightly against the bottom edge of the frame. The film should be free of bubbles, with distilled water evenly distributed across it, and aligned with the frame. Mode selection electrophoresis program: [HYDRAGEL 1 IF] select '1 IF SM/DM'; [HYDRAGEL IF 2/4] Select '2/4 IF SM/DM'; [HYDRAGEL 9 IF] Select '9 IF SM'. After placing the dynamic mask mounting bracket on a flat surface, the immune fixation was opened and set on the electrophoresis instrument. An anti serum cup was placed on the dynamic mask mounting bracket. Then, the reagent sample reference color card was placed on the cup holder in front of the liquid cup well.12 μl of antibody was added to each lane. The sample comb was removed and discarded. After installing the two brackets, the buffer strip was removed and discarded. Two transporters were removed. After wiping the electrode wire, the gel sheet was placed on the electrophoresis module. The cup holder of the anti-serum cup was in contact with the film. The reagent diffused in the lane below. The program of the electrophoresis instrument was initiated incubation. A thick filter paper was placed on the film to dry the gel. The dried gel holder was inserted into the dye vat for dyeing.

The specific anti immunoglobulin antiserum is deposited on the gel to fix the immunoglobulin. The immunoglobulin bands on the gel were stained. The detected data was analyzed by Phoresis 9.3.0 (SEBIA). The results of the subsequent quantitative immunoglobulin assessment of the blood and urine revealed the following: A serum-fixed quantitative immunoglobulin, monoclonal IgG/λ component, M protein content of 3.2 g/l (reference, 0 g/l) in the γ region (Fig. 4A) and urine-fixed quantitative immunoglobulin, monoclonal light chain λ component, M protein content of 0.26 g/24 h (The normal value is 0 g/24h) in the β region (Fig. 4B). The patient was diagnosed with AML concomitant with MGUS. Throughout this period, the patient was monitored for the persistent presence of positive RUNX1::RUNX1T1 fusion genes. Despite recommendations for intensive therapy involving moderate-to-high doses of cytarabine or potential consideration of allogeneic hematopoietic stem cell transplantation, the patient and their family opted against such measures. Subsequently, the patient was initiated on a regimen of maintenance therapy with standard doses of chemotherapy for a total of four courses (daunorubicin 60 mg/m^2, d1-3 + cytarabine 100 mg/m^2, d1-5; pirarubicin 25 mg/m^2, d1-3 + cytarabine 100 mg/m^2, d1-5; pirarubicin 25 mg/m^2, d1-3 + cytarabine 100 mg/m^2; homoharringtonine 4 mg/m^2, d1-3 + cytarabine 100 mg/m^2, d1-5). In August 2023, the patient was readmitted to Second Hospital of Hebei Medical University with a hematological relapse. The family opted to discontinue treatment and the patient died shortly thereafter.

Discussion

AML characterized by the presence of the RUNX1::RUNX1T1 fusion gene is classified under the genetic aberration category of AML. This fusion gene is frequently associated with the t(8;21)(q22;q22.1) translocation. Patients who test negative for C-kit mutations in conjunction with this genetic alteration are categorized into the low-risk group. Compared with standard dosing regimen chemotherapy, treatment strategies such as anthracycline drugs combined with cytarabine, high-dose cytarabine and other regimens have demonstrated superior therapeutic efficacy (1,6). Previous research has suggested that patients with AML harboring a RUNX1::RUNX1T1 fusion gene may exhibit complex chromosomal translocations involving abnormalities affecting ≥3 chromosomes. Presence

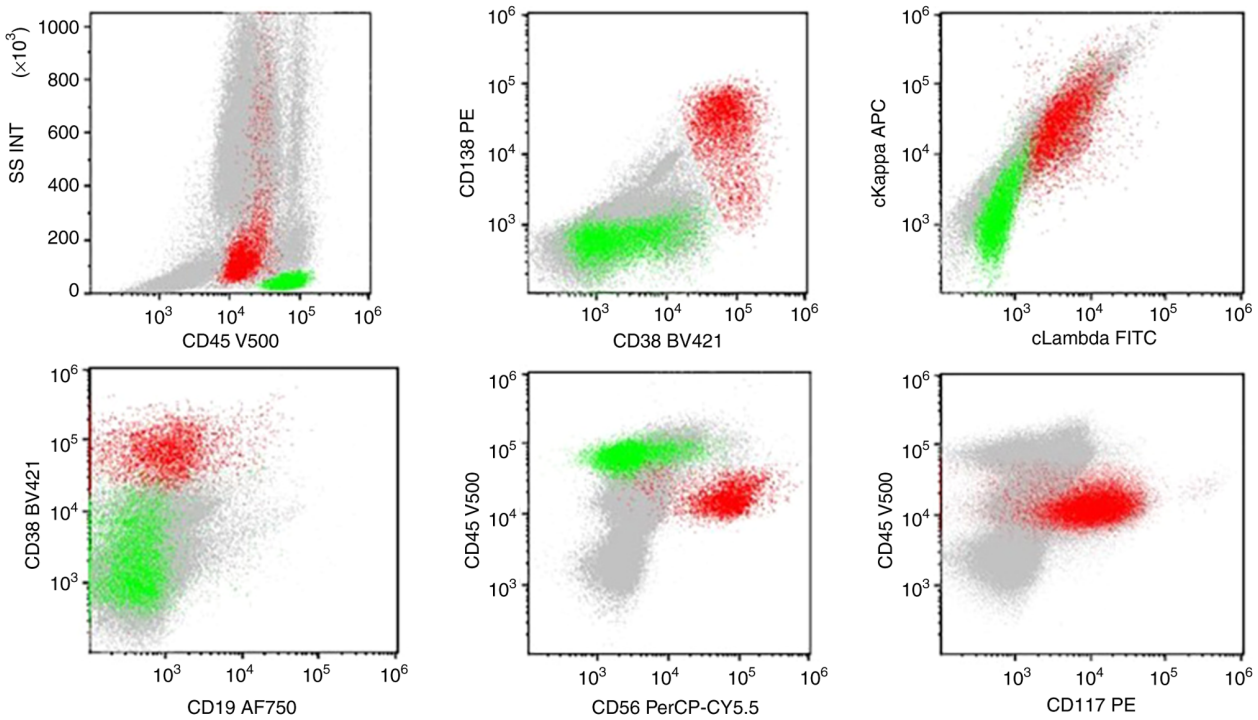

Figure 3. Flow cytometry analysis of bone marrow aspirate. Bone marrow flow cytometry shows positive CD38, positive CD138, positive CD117, negative CD19 and positive CD56. Red represents plasma cells; green represents lymphocyte populations; and gray represents other nucleated cell populations.

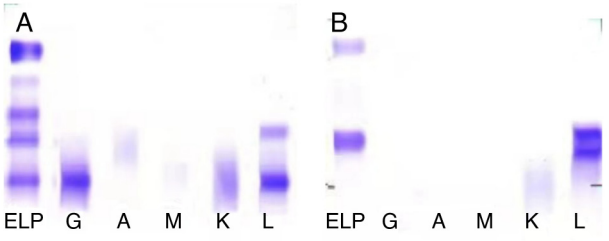

Figure 4. Immune fixed electrophoresis results. (A) Serum-fixed quantitative immunoglobulin analysis showed a monoclonal IgG/λ component M protein content of 3.2 g/l in the γ region. (B) Urine-fixed quantitative immunoglobulin analysis showed a monoclonal light chain λ component M protein content of 0.26 g/24 h in the β region.

of a positive RUNX1::RUNX1T1 fusion gene can lead to chromosomal abnormalities not only on chromosomes 8 and 21, but also on chromosomes 1-7, 11, 14, 15, 17, and 20 (7-17).

Kim *et al* (8) reported a patient with AML with a RUNX1::RUNX1T1 fusion gene with a complex translocation involving chromosomes 1, 8, and 21. The patient was treated using chemotherapy with norepinephrine and cytarabine, and a CR was achieved. Additionally, they reviewed 24 patients with AML with the t(8;21) variant in which 7 patients failed to achieve a CR and the remaining 17 patients achieved CR, with only 3 patients experiencing a relapse. Of the 12 cases included in the review of relevant literature in the present study (Table I), 8 patients (67%) achieved a CR following treatment. Only in 2/12 cases (17%) was the presence of complex chromosomal abnormalities in the context of the RUNX1::RUNX1T1 fusion gene suggested and was indicative of a poor prognosis. In summary, trisomy abnormalities can be considered as complex karyotypes to a certain extent. Furthermore, in terms of treatment, previous research indicates that high-intensity chemotherapy based on high-dose cytarabine and sequential allogeneic hematopoietic stem cell transplantation may fundamentally improve the prognosis of such patients.

In the present report, the case of a patient with AML with a RUNX1::RUNX1T1 fusion gene is described. Further investigation revealed a complex chromosomal translocation t(8;17;21)(q22;q24;q22.1) and a CR was attained after a single cycle of induction-remission chemotherapy. Nevertheless, during subsequent consolidation-intensification therapy, the ongoing presence of the RUNX1::RUNX1T1 fusion gene was detected, indicating an unfavorable prognosis. The patient then experienced a disease relapse 10 months later.

Due to the limited number of cases and the lack of clinical information, the current evidence is insufficient to distinguish the prognostic differences between variant complex karyotype t(8;21) and classical t(8;21) chromosome translocations. Traditionally, the prognosis for patients with AML with RUNX1::RUNX1T1 positivity is favorable. However, complex chromosomal karyotypes are a predictor of a poor prognosis (1). In cases where intricate chromosomal changes are present, we still recommended that these patients should undergo allogeneic hematopoietic stem cell transplantation as soon as possible after achieving a CR with chemotherapy.

There is a paucity of literature documenting cases of AML co-occurring with either MGUS or MM. Wu *et al* (18) performed a retrospective analysis on 14 elderly patients presenting with both MGUS and AML. Luca and Almanaseer (19) described a case involving an elderly patient with AML and MM, in which the condition of the patient rapidly deteriorated post-diagnosis, leading to their death from acute myocardial infarction and congestive heart failure within a month. Wang *et al* (20) reported the case of a 77-year-old male patient with AML

Table I. Review of the literature on cases of acute myeloid leukemia with a RUNX1::RUNX1T1 complex chromosomal translocation.

First author/s, year	Sex	Age, years	Karyotype of AML	AML therapy	Response to AML therapy	Outcome	(Refs.)
Kawakami *et al*, 2008	M	37	45,X,-Y,der(8)t(8;21)(q22;q22), der(9)(8;9)(q22;q34), and der(21)t (9;21)(q34;q22)	IA was not achieved CR; HD-CA induced CR	CR	Relapsed after 3 months	(7)
Kim *et al*, 2011	F	63	46,XX,t(1; 21; 8)(q21;q22;q22)	IA was achieved CR	CR	Clinically stable for 6 months	(8)
Udayakumar *et al*, 2008	F	33	46,XX,t(8;13;21)(q22;q14;q22)	DA	CR	Alive after allogeneic hematopoietic stem cell transplantation	(9)
Ihida *et al*, 2002	M	38	45,X,Y,del(3)(p25),t(8;21;14) (q22; q22;q24),der(19)t(3;19)(?p25;p13)	IA was not achieved CR; HD-CA induced CR	CR	NA	(11)
Gmidène *et al*, 2011	M	30	46,XY,t(1;21;8)(p34 ~ p35;q22;q22)	NA	NA	NA	(12)
Al Bahar *et al*, 2009	F	25	46,XX,t(6;8;21)(p22;q22;q22)	Treated with conventional chemotherapy regimen	CR	NA	(13)
Tay Za *et al*, 2019	F	23	46, XX,t(8;22;21)(q22;q12;q22)	Treated with conventional chemotherapy regimen	CR	NA	(14)
Mishra *et al*, 2021	F	19	46,XX,t(8;21;17)(q22;q22;p13)	DA	CR	CR >2 years of diagnosis	(15)
Akhila Raj *et al*, 2022	F	22	46, XX,der(8) del(8q), der(13), t(8;21;13), der(21)t(13;21).ishder(8) del(8q)(RUNX1T1+), der(13)t (8;21;13)(RUNX1T1+, RUNX1+), der(21)(RUNX1+)	Cytarabine for AML	CR	CR for 59 months	(16)
	F	68	45, XX,+idicder(8)(q11.1) t(8;21) (q22;q11.1),-17, 21.ishidicder (8) (q11.1) t(8;21)(RUNX1T1X2, RUNX1+)	Palliative chemotherapy 7 days	NA	Died 2 months after discharge	
	F	25	45,X,-X, der(8) t(8;21)(q22;q22), der(12) del(12q), der(21) t(8;12;21) (q22;q?;q22)[7]/45,X,-X,t(8;21) (q22;q22)[3]/46,XX[10].ish der(8) t(8;21)(q22;q22),(RUNX1T1+, RUNX1+),der(21) t(8;12;21) (q22;q?;q22)(RUNX1+)[40/100]	No treatment	NA	NA	
Han *et al*, 2024	F	57	46,XX,t(2;2;21;8)(p21;q37; q22;q22)[18]/46,XX[2]	DA	NA	NA	(17)
Present case	M	57	46,XY, t(8;17;21)(q22;q24;22.1) [9]/45, idem,-Y[10]/46,XY[10]	DA	CR	Relapsed after 10 months	-

AML, acute myeloid leukemia; NA, not available; CR, complete response; DA, daunorubicin + cytosine arabinoside; IA, idarubicin + cytosine arabinoside; HD-CA, high-dose cytarabine; RUNX1, Runt-related transcription factor 1; RUNX1T1, RUNX1 partner transcriptional co-repressor 1.

complicated by MM, who underwent treatment with a regimen comprising low-dose cytarabine, a combination of aroubicin and granulocyte-stimulating factor (CAG regimen), as well as bortezomib. Notably, these interventions resulted in the patient achieving and maintaining a CR for >6 months until the end of the follow-up period. Additionally, the case of a 51-year-old male patient with AML and MM was reported by Kim *et al* (21). Despite initial treatment failure with bortezomib and unsuccessful attempts to achieve a CR with two cycles of induction-remission chemotherapy, the patient achieved CR following allogeneic hematopoietic stem cell transplantation.

AML and MGUS/MM originate in different cell lines. The precise mechanisms underlying the co-occurrence of AML with MGUS/MM are incompletely understood, suggesting a potential shared etiological agent. Platanias (22) reported that activation of the MAP kinase pathway was critically implicated in the pathogenesis of AML, MDS and MM. Wu *et al* (18) postulated a potential association with underlying immune triggers, positing that these stimuli may contribute to the development of AML and aberrant plasma cell function. Lloyd *et al* (23) constructed a conceptual model of tumors through Darwinian dynamics. They state that prior to the onset of disease, the human body exists in a relatively stable state. In a tumor, cancer cells may evolve to an evolutionary stable state. Therefore, it was hypothesized that homeostasis of the microenvironment is an important external factor for the existence of AML.

In the present case report, MGUS presented during the consolidation and intensification chemotherapy for AML, which has not previously been documented in the literature, to the best of our knowledge. Based on the hypothesis of Lloyd *et al*, we hypothesize that the stable microenvironment of AML was disrupted, driving the malignant transformation and proliferation of leukemia cells, resulting in clonal the evolution of the leukemia cells in that specific environment. This promoted the development of monoclonal plasma cells and the coexistence of MGUS in the treated patient. The management approach for such individuals poses a dilemma of whether they be meticulously monitored for plasma cell activity and monoclonal immunoglobulin levels without immediate MGUS-specific intervention, or whether proactive inclusion of anti-plasma cell agents, such as proteasome inhibitors and immunomodulators should be considered at an early juncture. This remains an unresolved query in clinical practice.

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Availability of data and materials

The high-throughput sequencing data generated in the present study may be found in the NCBI SRA database under accession number SRP542525 or at the following URL: https://www.ncbi.nlm.nih.gov/sra/?term=SRP542525. All other data generated in the present study may be requested from the corresponding author.

Authors' contributions

XQ interpreted the results and drafted the manuscript. SQ designed the study and analyzed patient data. JZ and TT confirm the authenticity of all the raw data. LG, JZ and TT performed the experiments. XG advised on treatment of the patient. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for publication of the case report, including the clinical details and images was provided by a relative of the patient.

Competing interests

The authors declare that they have no competing interests.

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