

Coexistence of deletion, ring, and monosomy of chromosome 7 in a patient with MDS-RAEB-2

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ABSTRACT

Monosomy 7 or partial deletion of chromosome 7 is a frequent cytogenetic finding in myelodysplastic syndrome (MDS). However, only a few cases of MDS with a ring chromosome 7 have been reported. We report a first case of MDS with 46,XX, der(7)del(7)(p22)del(q22)[7]/46,XX,r(7)(p22q22)[7]/46,XX[23] karyotype in a 30 year old female patient at diagnosis. The patient was diagnosed as MDS-refractory anemia excess blast type 2 (RAEB-2) (IPSS): 3, high risk). Acute myeloid leukemia (AML) induction type- chemotherapy was initiated. After second allogeneic hematopoietic stem cell transplantation, 46,XX [15] karyotype were detected in patient. She died due the acute graft versus host disease of the liver at the second month of the transplantation. Herein, we report a first case of MDS having the three abnormalities; ring 7, derivative 7; due to p and q arm deletion on the chromosome 7 and monosomy 7.

Key Words: Myelodysplastic syndromes, ring chromosome 7, monosomy 7

Introduction

The myelodysplastic syndromes (MDS) are a group of hematologic diseases affecting primarily elderly people and there is a high risk of developing into acute myeloid leukemia (AML). MDS is characterized by ineffective and dysplastic hematopoiesis in bone marrow. The clinical course of the disease is highly variable. Many of patients may survive with disease for several years, or cytopenias or leukemic development can cause death within a few months. The median age at diagnosis is 60 to 75 years in adult MDS (1,2). The incidence of cytogenetic abnormalities is about 35–60% in MDS patient. -5/del(5q), -7/del(7q), +8, del(20q) and -Y are the most frequent abnormalities are determined by conventional cytogenetics and FISH (3).

The Revised International Prognostic Scoring System (IPSS-R) defines with a complex karyotype (>3 abnormalities) and abnormalities of chromosome 7 as poor-risk group in MDS. Patients with de novo MDS can be categorized for the risk assessment based on IPSS-R is the gold standard. Monosomy 7 or partial deletion of long arm of chromosome 7 is found in 30-40% of

childhood MDS patients is associated with recurrent and nonrandom chromosomal abnormality. Monosomy 7 is the sole chromosomal abnormality in childhood MDS, however other chromosomal abnormalities can be found in addition to monosomy 7 in adult MDS (4). The pathophysiologic relationship between monosomy of 7/del (7q) chromosomal findings and MDS or AML is unclear.

The most frequent cytogenetic abnormalities observed in MDS are monosomy 7 or deletion of chromosome 7, on the other hand ring chromosome 7 is not common in MDS patients. In this report, we present unique case of adult MDS having the three chromosomal abnormalities; monosomy 7, ring chromosome 7 and derivative chromosome 7 resulting from deletions in both the short arm and long arm with breakpoints in bands 7p22 and 7q22.

Case Report

A 30-years old female patient with the history of blood transfusion was admitted to inpatient setting of Hematology Department with fatigue and pancytopenia (Hb : 10.9 g / dl, MCV: 90 fl,

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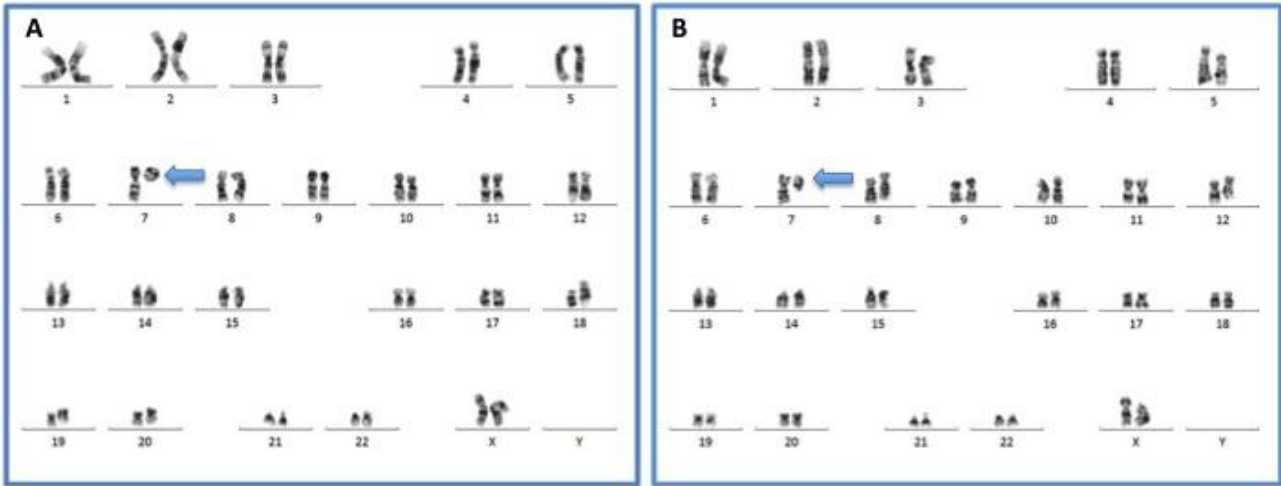


Fig. 1. Representative karyograms from the patient's showing ring chromosome 7(A) and derivative chromosome 7 (B)

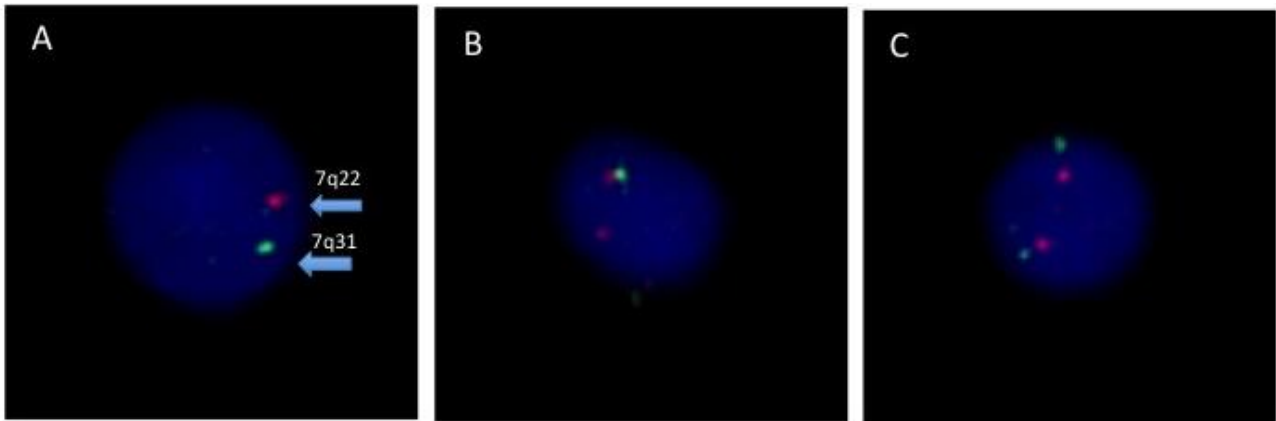


Fig. 2. FISH representations using locus specific probes for 7q31 (green) and 7q22 (red) illustrating a monosomy 7 signal (A), a ring chromosome 7 signal (B) and normal chromosome 7 signals (C) in interphase cells

neutrophil: 1600/mm³, Platelet: 46000/mm³). The bone marrow (BM) biopsy performed to patient after informed consent form was obtained. The BM revealed a decrease in granulocytic series with abnormal localization, was assessed as normocellular bone marrow with dysmegakaryopoiesis. Myeloblast percentage was detected as 14% by flow cytometric immunophenotyping. Her karyotype was determined with conventional cytogenetic analysis in the bone marrow sample and was designated as 46,XX, der(7) del(7) (p22) del (q22) [7]/46, XX, r(7) (p22q22) [7]/46, XX[23] (Figure 1A, 1B) according to the ISCN (International System for Human Cytogenetic Nomenclature) 2016 (5).

Ring 7 and monosomy 7 was also detected by FISH (del(7q) probe (LPH 025); Cytocell, Cambridge, UK) analysis (Figure 2A, 2B, 2C). The patient was diagnosed with MDS-RAEB-2 (IPSS:3, high risk) and immediately AML induction- type therapy (7+3) was started (100mg/m² cytarabine (Hospira, Victoria, Australia) and 12mg/m² Idarubicin (Idamen, Mustafa

Nevzat, Istanbul, Turkey). Minimal residual disease (MRD) was detected as 5 % at bone marrow on the 28th day of treatment with partial hematologic recovery. The karyotype of the patient was determined as 46,XX,del(7)(q22)[5]/46,XX,der(7)del(7)(p22)del(7)(q22)[2]/46,XX,r(7)(p22q22)[1]/46,XX[4] and confirmed by FISH. High dose cytarabine (3gr/m², bid, for 3 days) was given for re-induction. Also, levels of MRD were detected as 3% with partial hematologic recovery. One course of azacitidine (Vidaza, Baxter Oncology GmbH, Halle/Westfalen, Germany) was used as a bridge to the transplantation. Cytogenetic analysis revealed 45,XX, -7[6]/46,XX[9] and monosomy 7 was also detected in 31 % of interphase nuclei by FISH. Allogeneic HSCT with myeloablative conditioning was successfully performed four months later from diagnosis from a HLA full- matched sibling. Relaps occurred four months later from transplantation and after discontinuation of immunosuppressive treatment high

dose cytarabine was initiated. With best response of partial response to this treatment, second transplantation was performed from same donor. After second transplantation, 46,XX [15] karyotype were detected in patient. Unfortunately, she died due the acute graft versus host disease of the liver at the second month of the transplantation.

Discussion

We report the patient of non-therapy-related MDS (RAEB-2) having ring 7, monosomy 7 and derivative chromosome 7 resulting from deletions in both the short arm and long arm with breakpoints in bands 7p22 and 7q22.

Monosomy or partial deletion of the long arm of chromosome 7 has been commonly observed among patients with MDS. So far, however, very few MDS cases with ring 7 have been reported in the literature. Ring 7 has been described in one case of adult MDS with atypical eosinophilia (6). In this case, r(7)(p22q36) karyotype was determined in 85% of analyzed metaphases while r(7)(p22q10) karyotype are showed in remaining of the metaphases. On the other hand, the chromosomal abnormality of ring 7 has been reported in two cases with donor cell-derived MDS by Hamdi et al (7). First case has been reported by Hamdi et al. was diagnosed with follicular lymphoma, and after HSCT (Hematopoietic Stem Cell Transplantation), cytogenetic analysis found 46,XY,r(7)(p13q11.2),del(12)(p13) in 19 of 20 metaphases in donor cells. In this case, increased blasts have been detected in her BM biopsy, suggest that progression to secondary AML. Another case who was diagnosed with mantle cell lymphoma, after HSCT, it found 46,XX in all of 20 metaphases analyzed, but deletion of 7q was also detected in 18% of interphases by FISH technique. Eight months later, cytogenetic analysis revealed 46,XX,r(7)(p21q11.2)[3]/46,XX[17] and found del(7q) in 19% and monosomy 7 in 3% of interphases by FISH and this case was diagnosed with donor cell- derived MDS. Addition to these reports, this cytogenetic abnormality has been previously reported by some researchers in different cases diagnosed with vascular and skin lesions, malignant melanoma (8,9), multiple congenital anomalies, mental retardation (10) and neuropathological findings (11). To our knowledge, the first case who have both ring chromosome 7 and monosomy 7 and derivative chromosome 7. The breakpoints determined in our case are different from ring chromosome 7

previously described in other cases. About two-third of the previously reported cases was diagnosed with donor cell-derived MDS while ring 7 has been determined at diagnosis in our case. Taken together with the literature, to reveal the potential clinical outcome of ring chromosome 7 abnormality need to be studied in more cases with MDS.

Conflict of Interests: The authors declare that there is no conflict of interest regarding the publication of this paper.

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