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Case Report

Myelodysplastic Syndrome with 6q Deletion as the Sole Chromosome Abnormality in an Iranian Patient: A Case Report with Review of Literature

Shirin FERDOWSI [1], ***Reza SHIRKOOHI*** [2], ****Gholamreza TOOGEH*** [3]

1. *Dept. of Hematology, Iranian Blood Transfusion Organization, Tehran, Iran*
2. *Dept. of Molecular Genetics, Cancer Research Center, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*
3. *Dept. of Hematology-Oncology and BMT Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: h.hematology@yahoo.com

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Abstract

Background: The myelodysplastic syndrome (MDS) is a highly heterogenous disorder and karyotype analysis is helpful for diagnostic and prognostic estimation. Deletion in long arm chromosome 6 (6q del) as a sole abnormality is a rare event in MDS. This is the first case report of del (6q) as the only observed diagnostic change in Iran. We also reviewed the literature of this cytogenetic lesion.

Keywords: Myelodysplastic syndrome**,** Deletion 6q, Iran

Introduction

The myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell disorders characterized by cytopenia(s), dysplasia in one or more of the major myeloid cell lines, ineffective hematopoiesis, and increased risk for development of acute myeloid leukemia (AML) (1-3). Approximately 50% of patients have a detectable cytogenetic abnormality during routine GTG-banded karyotyping (4) and the most commonly involved chromosomal changes observed are monosomy 5 or del(5q), monosomy 7 or del(7q), trisomy 8, del (20q) and del(9q) (5-9). Several studies have established the prognostic value of cytogenetic analysis in MDS both for survival and progression to AML (10-12). For example, an isolated 5q deletion is characterized by longer survival and lower progression rates to AML (12). In MDS rare abnormalities can be observed frequently (7). To our knowledge, there has been no case report of del (6q) in MDS in Iran, and there are only four case reports worldwide (13-16).

Case Report

A 66-year-old woman was admitted at Imam Khomeini Hospital complexes affiliated to Tehran University of Medical Science, in August 2012 for further evaluation of moderate refractory anemia. The patient had received a treatment for iron, vitamins B12 and folic acid. This treatment had no influence on her hematologic condition. In addition, she had received supportive cure in the form of transfusions. At admission, the patient had ill appearance without fever and showed no

splenomegaly, lymphadenopathy, or organomegaly on physical examination. A complete blood evaluation revealed hematocrit of 24.7%, hemoglobin 7.7 g/dl, red cell count 2.26 × 10^6/µl, MCV 109 fL, reticulocytes 2.2% of red blood cells, leukocyte count 9.4× 10^3/µl (neutrophils 60%, lymphocytes 35%, monocytes 1%, eosinophils 1%) and platelet count 288× 10^3/µl. Blood film demonstrated red cell anisocytosis, with macrocytosis and moderate numbers of target cells. Schistocytes were not observed. Most biochemical tests for liver and renal function tests were within the normal limits. Bone marrow examination was performed and presented erythroid hyperplasia with macroblastic reaction. Granulocytes showed shift to the left and dysplastic changes without ring sideroblasts and blasts comprised 1% of nucleated cells and +4 iron store. Megakaryocytes were adequate in number. The pathologic findings of aplastic anemia or BM failure diseases such as hypocellular or acellular marrow were not observed. Nutritional deficiencies and metabolic diseases were excluded based on medical history and physical examination. There was no medical history of carcinogen exposure. Diagnostic cytogenetic analysis performed on the diagnostic bone marrow sample revealed the karyotype as 46, XX, Del (6) (q13q16) in all 20 metaphase cells which analyzed (Fig. 1).The patient was diagnosed as having refractory cytopenia with unilineage dysplasia (RCUD) based on the 2008 WHO classification system.(17). She received only supportive treatment. After her general condition recovered, she was discharged and followed up with CBC and liver function tests.

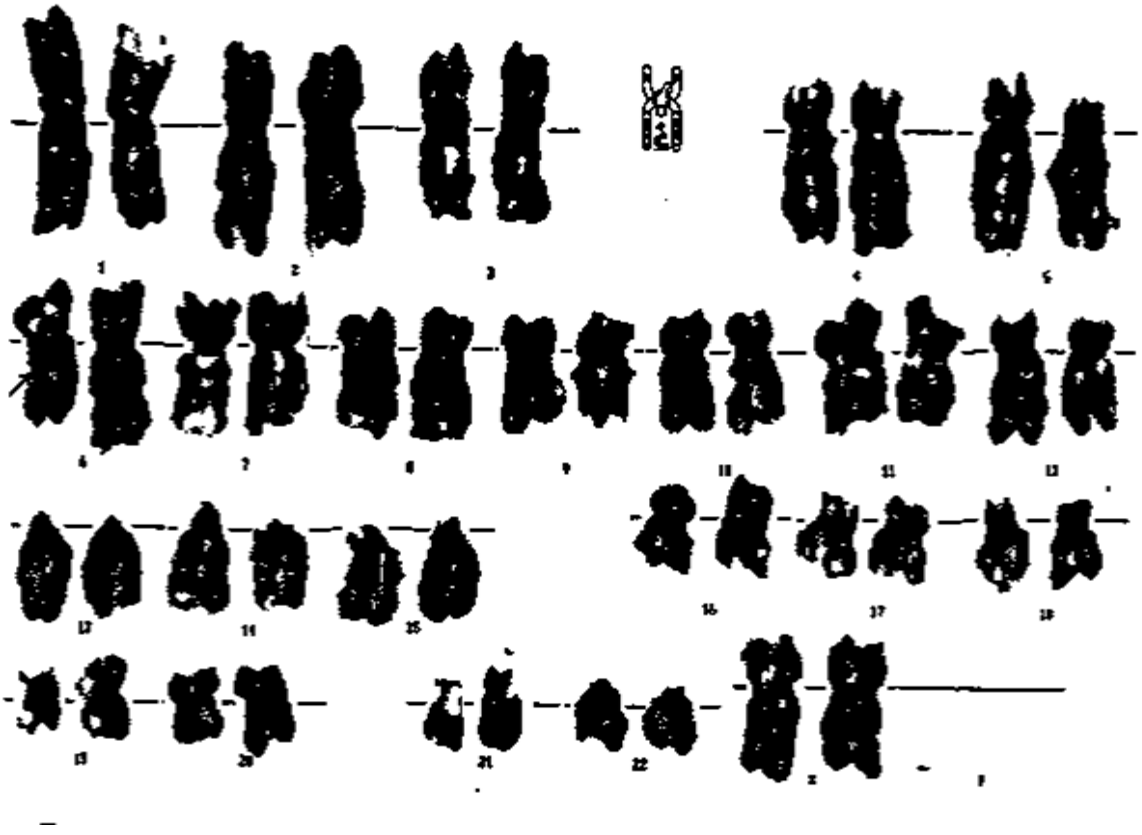

Fig. 1: Bone marrow karyotype of patient**.** 46, XX, Del (6) (q13q16)

Discussion

In our patient, a diagnosis of RCUD was made on the basis of peripheral blood and bone marrow findings. RCUD including 10%–20% of the cases of MDS (18) and deletion of the long arm of chromosome 6 as the only diagnostic finding is rare in MDS based on other studies (13-16). Cytogenetic abnormalities associated with RA include del (20q), +8 and abnormalities of chromosome 5 and/or chromosome 7 (11). Specific chromosomal abnormalities, such as -5/5q- and -7/7q-, play an important role in the development of new therapeutic options and clinical management of MDS. However, due to cytogenetic heterogeneity, the additive prognostic impact of distinct single additional abnormalities remains obscure as yet. To our knowledge there are only four case reports worldwide about del (6q) in MDS (13-16). In 2000, Fernandez et al. (13) described the chromosomal abnormality 46, XX,del (6)(q21) in a 18-year-old woman with RA and a 42-year-old man with "refractory anemia with excess blasts in transformation" (RAEB-T) that last one gradually progressed to AML. It should be noted that the category of RAEB-t has been abandoned in the new WHO classification of MDS. The majority of patients which previously belonged to this group are now including in AML classification (19). Therefore this chromosomal abnormality cannot attribute to AML progression. In 2006, Cen et al. (15) reported one case with 6q- in cytogenetic analysis of bone marrow cells of the 50 MDS patients. In 2009, Gozzetti et al. (14) reported 46,XX,del(6)(q15q27) in a 72-year-old woman with refractory anemia (MDS-RA). The patient did not demonstrate of progression after 10 months of follow up. In 2011, Chaubey et al. (16) described two rare chromosomal abnormalities (6q-, 3q-) with unknown prognostic significance. Approximately 90%–95% of patients with refractory anemia have low or intermediate International Prognostic Scoring System (IPSS) (11). In addition, when adjustments were made for age, patients with MDS and Transfusion dependency (TD) had more than a two-fold higher risk for mortality and six-fold higher risk of leukemic transformation compared with patients without TD during the initial three years after diagnosis (20). On the other hand, Mecucci et al. (21) recognized a significant correlation between myelodysplasia and previous exposure to toxic products such as alkylating agents. Our patient was not exposed to toxic products and she had Eastern Cooperative Oncology Group (ECOG) performance status of 1 (22) with no evidence of progression after 12 months of follow-up. The genetic changes in the malignant cells of MDS result mainly in the loss of genetic material, including probable tumor suppressor genes. It is noteworthy that deletions of the long arm of chromosome 6 and gain of chromosome 6 have already been described as poor prognosis in MDS and AML (23, 24). The finding indicates that 6q- deletions are accompanied by structural and functional alterations of the c-myb locus which may be involved in the pathogenesis of leukemias and lymphomas (25). Due to the profound cytogenetic heterogeneity, the impact of many rare abnormalities such as del (6q) in patients with MDS is still unknown and further such cases are needed to find the impact of this abnormality on progress and prognosis.

Conclusion

Identification of all possible rearrangements is valuable for obtaining a better understanding of the leukemogenic process and for determining genetic pathways. These may also play an important role in the development of new therapeutic options in MDS.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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