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RARE PRESENTATION OF MYELODYSPLASTIC SYNDROME IN A YOUNG MALE

Pathology

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ABSTRACT

Myelodysplastic syndrome (MDS) constitutes a group of clonal hematopoietic stem cell disorders. It was renamed as Myelodysplastic neoplasm (MPN) according to the 5th edition WHO classification of the Hematolymphoid Tumors. MDS is considered a disorder of the older age group. Herein we present a case of MDS in a 34-year-old male patient. The case was diagnosed based on examination of peripheral blood smear and bone marrow and later by flow cytometric evaluation and Fluorescent in situ hybridization (FISH). Flow cytometry revealed 5 – 8% blasts of myeloid phenotype and FISH revealed the presence of double deletion at the 7q22 and 7q36 locus along with the presence of monosomy 7. All these findings were suggestive of a poor prognosis. This case reveals the importance of genetic studies in determining the prognosis of the patient.

KEYWORDS

Myelodysplastic neoplasm, flow cytometry, FISH

INTRODUCTION

Myelodysplastic syndrome (MDS) constitutes a group of clonal hematopoietic stem cell disorders characterized by cytopenia, dysplasia in one or more major myeloid lineages, ineffective hematopoiesis, presence of recurrent genetic abnormalities and an increased risk of developing acute myeloid leukemia (AML). The most common pathogenic mechanism behind the development of MDS is considered to be the neoplastic transformation of myeloid stem cells which may subsequently mature in an ineffective and disordered fashion. These neoplastic stem cells can gain additional cytogenetic abnormalities which may cause progression to acute myeloid leukemia. According to the latest WHO guidelines, the recommended thresholds for diagnosing a case of MDS are hemoglobin concentration of less than 13g/dl in males or less than 12g/dl in females, platelet count of less than 1.5 lakh cells/mm^3 and an absolute neutrophil count less than 1800 cells/mm^3.(1) Traditionally, primary or de novo MDS has been associated with the elderly, typically manifesting in the seventh decade of life. MDS occurrence in children and young adults is rare, and a familial association has been suggested.(2)

CASE PRESENTATION

A previously healthy 34-year-old male patient presented with complaints of persistent cough, fatigue, loss of weight, and loss of appetite for 1 month. Physical examination was unremarkable except for pallor. A complete blood count revealed moderate anemia (RBC: 2.85x 10^6 cells/mm^3, Hb: 7.9 g/dl) with mild to moderate leukopenia (WBC: 2830 cells/mm^3) and severe thrombocytopenia (platelet count-11000 cells/mm^3). A peripheral blood smear examination showed pancytopenia with a leucoerythroblastic blood picture and the presence of 1 – 2% atypical cells. Renal function test, liver function test and serum electrolytes were all normal.

Bone marrow aspirate and biopsy of the patient revealed hypercellular marrow with dysplasia in all three lineages and the presence of 16% blasts, morphologically.

Flow cytometric analysis was performed on the bone marrow aspirate which showed 5 – 8 % blasts that were of myeloid phenotype. Fluorescent in situ hybridization study revealed 75% of the cells positive for deletion 7q22 and 7q36 regions and 10% of cells showed monosomy for chromosome 7.

A diagnosis of myelodysplastic neoplasm with increased blasts was made. The risk assessment of the patient was done according to the revised International Prognostic Scoring System which revealed a high-risk disease. The patient is currently awaiting bone marrow transplant at a tertiary oncology center.

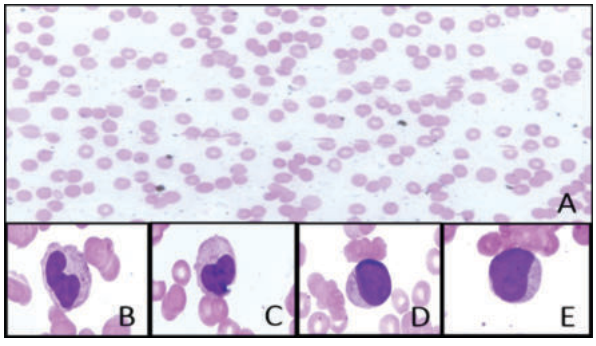

Figure 01: Peripheral blood smear findings. A: Pancytopenia; B: Band forms; C: Metamyelocyte; D: Myelocyte; E: Atypical cell

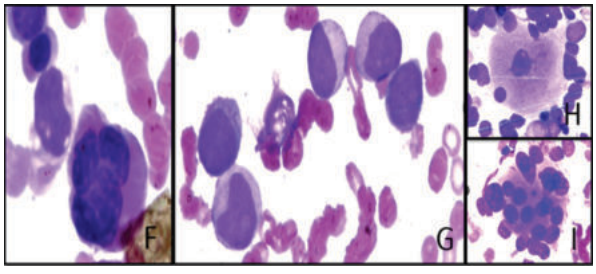

Figure 02: Bone Marrow smears; F: Multinucleation in erythroid series; G: Blast forms; H: Micromegakaryocyte; I: Multinucleated megakaryocyte

DISCUSSION

Myelodysplastic syndrome is a heterogeneous group of hematologic neoplasms with an increased risk of transformation to acute myeloid leukemia. MDS is a clonal disorder and can occur de novo or secondary to various insults to the bone marrow. It may present with symptoms related to cytopenias and has a variable disease course. Primary or de novo MDS is a disease of the elderly (7th decade). Various environmental and iatrogenic etiologies have been implicated in the development of secondary MDS which include exposure to chemotherapy, radiation, or environmental toxins. These can result in an oncogenic process leading to one or more somatic mutations.

According to the 5th edition WHO classification (2022), myelodysplastic syndrome has been renamed as myelodysplastic neoplasms which includes 2 categories – MDS with defining genetic abnormalities (isolated deletion 5q, SF3B1 mutation, and TP53 inactivation) and MDS, morphologically defined. Most common

cytogenetic abnormalities identified in MDS with the help of FISH include loss of 17p, abnormalities of chromosome 5 and/or 7, isolated deletion 20q, inversion 3, trisomy 8, etc.(3) They can appear singly or in combination. When there is presence of more than three abnormalities concurrently, we consider it as a complex karyotype. Patients showing complex karyotypes are associated with a poorer prognosis according to the revised International Prognostic Scoring System. Genetic abnormality documentation is necessary while making a diagnosis of MDS as they are integral in the subclassification as well as risk stratification of MDS.

The diagnosis of MDS for this patient in our center was made based on the presence of pancytopenia, bone marrow hypercellularity, trilineage dysplasia, and the presence of increased blasts. This was supported by the detection of cytogenetic abnormality by FISH and the confirmation of blast forms by flow cytometry.

Chromosome 7 abnormalities are commonly implicated in the development of MDS. In this, deletion at 7q22 is most commonly implicated in the pathogenesis of myelodysplastic syndrome. Our patient had double deletion at 7q22 and 7q36 along with 10% cells showing positivity for monosomy 7. Double deletion in chromosome 7 along with monosomy 7 forms part of complex chromosomal abnormality and is associated with a poor prognosis.(4) (5)

Our patient is a 34-year-old male with no known history of toxic exposures or significant family history suggestive of genetic association. The occurrence of MDS in young adults is extremely rare. Pediatric MDS is associated with a distinct pathophysiology and has an increased predisposition to developing hereditary syndromes. However, it is still debated whether to consider MDS in young adults as a unique molecular entity or as a continuum of adult disease. (6) (7)

CONCLUSION

Primary myelodysplastic syndrome is rare in young adults. The presence of concurrent deletions at 7q22 and 7q36 is extremely rare and reports of the same were not found after extensive literature search. These deletions along with monosomy of chromosome 7 are associated with a poor prognosis. This case report highlights the importance of genetic abnormality detection and documentation as well as its role in determining patient prognosis.

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