When Clinico-Morphological and Molecular Studies Tell Different Stories: A Case of Myelodysplastic Syndrome

Abstract

Myelodysplastic syndromes (MDSs) are clonal hematopoietic stem cell disorders characterized by cytopenias, dysplasia in one or more of the major myeloid cell lines, ineffective hematopoiesis, with cellular marrow, and risk for leukemic transformation. We present a case of a 66-year-old male with a history of multiple packed red blood cell (PRBC) transfusions. Routine investigations, bone marrow aspiration, and biopsy were done. The clinical and morphological findings raised suspicion of MDS with isolated del (5q), so cytogenetics was done. When cytogenetics was done, there was a big mismatch in finding between clinical, morphological, and molecular findings which brought a major change in prognosis as well as treatment. It is, therefore, very essential to not rely only on the clinical and morphological findings to reach a diagnosis. Molecular findings play a pivotal role to come to a final conclusion.

Keywords: *5q deletion, cytogenetics, cytopenias, hematopoietic, Myelodysplastic syndrome, prognosis*

Niharika Jain, Parul Gautam[1], Atul Tiwari[2], Anjana Mittal, Naveen Gupta[3], Mohan Lal Yadav

Departments of Pathology and [3]Clinical Haematology, Mahatma Gandhi Medical College and Hospital, Jaipur, [1]Department of Pathology, JLN Medical College, Ajmer, [2]Department of Pathology, RNT Medical College and Hospital, Udaipur, Rajasthan, India

Introduction

Myelodysplastic syndromes (MDSs) are a group of clonal hematopoietic stem cell diseases characterized by cytopenia, dysplasia in one or more of the major myeloid lineages, ineffective hematopoiesis, recurrent genetic abnormalities, and increased risk of developing acute myeloid leukemia (AML).[1] There is an increased degree of apoptosis within the bone marrow progenitors, which contributes to the cytopenias. Cytopenia in at least one hematopoietic lineage is required for a diagnosis of MDS. The recommended thresholds for cytopenias established in the original International Prognostic Scoring System (IPSS) for risk stratification (hemoglobin concentration <10 g/dL, platelet count <100 × 10^9/L, and absolute neutrophil count <1.8 × 10^9/L), have traditionally been used to define cytopenias for MDS diagnosis and most MDS patients will have a cytopenia below at least one of these thresholds.[1]

Cytogenetic abnormalities mostly seen in MDS are almost 80% in secondary MDS cases (therapy-related) and around 50% in *de novo* cases of MDS.[2]

Case Report

We present a case of a 66-year-old male who came with a history of multiple packed red blood cell (RBC) transfusions. On physical examination, there was mild splenomegaly and no lymphadenopathy.

Complete blood count revealed total leukocyte count (TLC) of 8.3 × 10^3/μL, differential leukocyte count (DLC) within normal limits, hemoglobin of 3.7 g/dL, RBC count – 1.22 × 10^6/μL, hematocrit – 10.8%, mean corpuscular volume (MCV) – 88.8 fL, mean corpuscular hemoglobin (MCH) – 30.1 pg, mean corpuscular hemoglobin concentration (MCHC) – 34.0 g/dl, and marked thrombocytosis with a platelet count of 2144 × 10^3/μL. Peripheral smear showed normocytic normochromic RBCs with microcytic hypochromic cells, TLC and DLC within normal limits, and thrombocytosis. Bone marrow aspiration showed hypercellular marrow showing diminished erythroid and myeloid precursors and megakaryocytic hyperplasia. Bone marrow biopsy was hypercellular with marked megakaryocytic hyperplasia with the presence of many small and hypolobated forms [Figures 1 and 2].

How to cite this article: Jain N, Gautam P, Tiwari A, Mittal A, Gupta N, Yadav ML. When clinico-morphological and molecular studies tell different stories: A case of myelodysplastic syndrome. Int J App Basic Med Res 2022;12:288-90.

Submitted: 05-Dec-2021
Revised: 08-Aug-2022
Accepted: 28-Oct-2022
Published: 19-Dec-2022

Address for correspondence:
Dr. Parul Gautam, Superintendent of Police Residence, A-1, Jaipur Road, Opposite St. Sophie School, Ajmer - 305 001, Rajasthan, India.
E-mail: parulg15@gmail.com

Access this article online

Website: www.ijabmr.org

DOI: 10.4103/ijabmr.ijabmr_776_21

Quick Response Code:

Peripheral smear, bone marrow aspiration, and bone marrow biopsy features were suggestive of MDS and raised the suspicion of isolated del (5q), so fluorescent *in situ* hybridization and cytogenetic analysis was done. Meanwhile, the patient was started on lenalidomide which is beneficial for patients with isolated del (5q).

Cytogenetic study reported as absent del (5q) and instead del (7q) was present in 60% of the interphase cells studied [Figures 3 and 4].

The patient succumbed to the disease within 4 months of starting the treatment.

As a result, there was a big mismatch between clinical, morphological, and molecular findings.

Discussion

MDSs are a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis leading to peripheral blood cytopenias, hypercellular bone marrow in most of the cases, dysplasia in one or more of the major myeloid cell lines, and by the increased incidence of progression to AML.[2]

One of the common cytogenetic abnormalities seen in *de novo* cases is isolated deletion of the long arm of chromosome 5, i.e., del (5q). MDS with isolated del (5q) is an MDS characterized by anemia (with or without other cytopenias and/or thrombocytosis) and in which cytogenetic abnormality del (5q) occurs either in isolation or with one other cytogenetic abnormality, other than monosomy 7 or del (7q). Cases with del (5q) associated with loss of chromosome 7, del (7q), two or more additional abnormalities, or excess blasts have an inferior survival and are excluded from this diagnosis.[1]

In our case, even after an extensive search, no such case reports were found highlighting similar findings.

Loss of chromosome 7 material, either as complete loss of one chromosome (monosomy 7 or-7) or as deletion of its long arm [del (7q)], is among the most commonly observed chromosomal abnormalities in myeloid malignancies such as MDS.

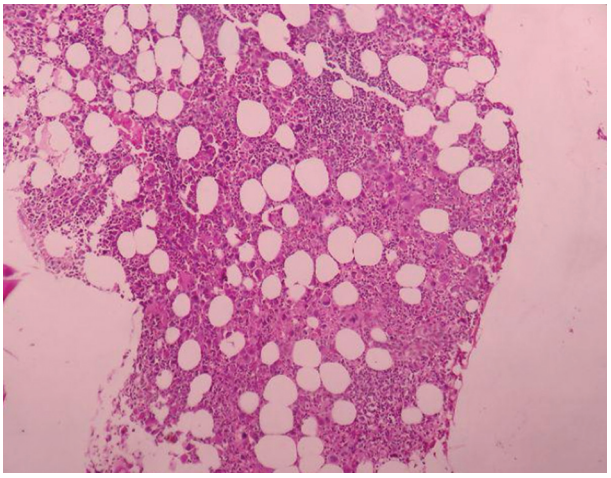

Figure 1: Marked megakaryocytic hyperplasia (×10)

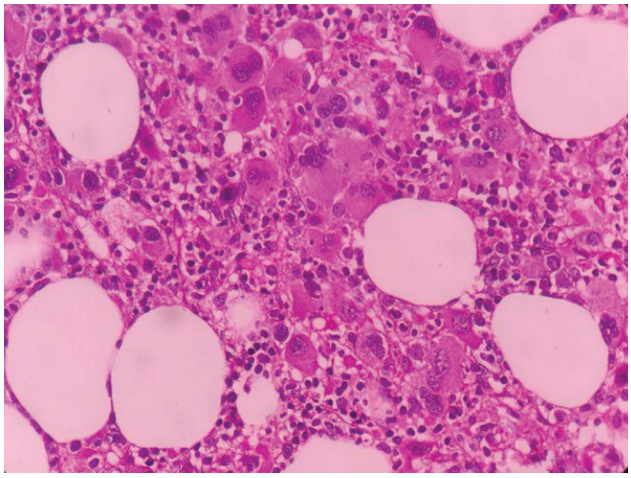

Figure 2: Megakaryocytic hyperplasia with many small and hypolobated forms with scattered lymphoid cells in the background (×40)

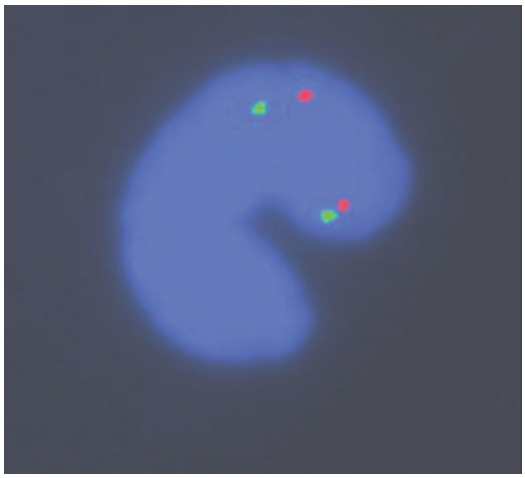

Figure 3: Negative deletion 5q. probes used - egr1 = orange, D5S23, D5S721 = green

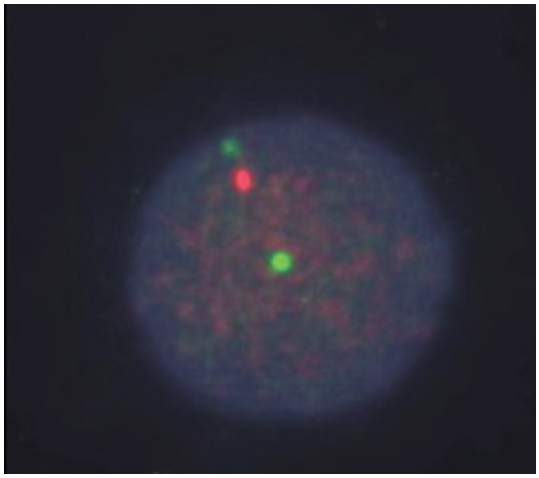

Figure 4: Positive 7q. probes used - D7S522 = orange, CCP7 = green

Deletions of 7q are variable and commonly occur in the region between 7q22 and 7q36.[3]

Patients with-7 and those with del (7q) have been considered together as one cytogenetic group with poor prognosis and reduced overall survival, thus they were treated on high-risk protocols and are candidates for hematopoietic stem cell transplantation during the first complete remission.[4] The IPSS of MDS grouped the two entities together in the poor-risk category.[5]

Conclusion

From this study, it can be concluded the cytogenetic analysis of chromosome 7 has a clear impact on the clinical outcome of myeloid malignancies and there is a greater degree of prognostic variations among the patients.

It is, therefore, very essential to not just rely on the clinical and morphological findings to reach a diagnosis. Morphological and clinical findings are helpful but the answer lies with the molecular findings which play a pivotal role to come to a final conclusion and also determine the prognosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hasserjian RP, Orazi A, Brunning RD, Germing U. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th Edition. Lyon: IARC Press; 2017.
2. Mona B, Ankita M, Sarjana D, Harsh D, Tejinder S. Myelodysplastic syndrome (MDS) with isolated 5q deletion (5q–Syndrome): Report of two cases with review of literature. World J Pathol 2018;7:1-6.
3. Le Beau MM, Espinosa R 3rd, Davis EM, Eisenbart JD, Larson RA, Green ED. Cytogenetic and molecular delineation of a region of chromosome 7 commonly deleted in malignant myeloid diseases. Blood 1996;88:1930-5.
4. Kalwinsky DK, Raimondi SC, Schell MJ, Mirro J Jr., Santana VM, Behm F, *et al.* Prognostic importance of cytogenetic subgroups in *de novo* pediatric acute nonlymphocytic leukemia. J Clin Oncol 1990;8:75-83.
5. Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel P, Sanz G, *et al.* International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997;89:2079-88.