Myelodysplastic syndrome with monosomy 7

MYELODYSPASTIC SYNDROME WITH MONOSOMY 7- A RARE CASE OF MORPHOLOGICAL AND CYTOGENETIC REMISSION WITH LENALIDOMIDE

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ABSTRACT

Myelodysplastic syndromes(MDS) are a group of haemopoietic stem cell disorders characterised by cytopenias and dysplasia in one or more myeloid cell lines with a risk of developing acute leukemia. Remission can occur but is extremely rare. We present a case of MDS with Monosomy 7 in a 41 year old patient with morphological and cytogenetic remission with lenalidomide. Case Study and Case Report 2015; 5(1): 1 - 4.

INTRODUCTION

Myelodysplastic syndrome (MDS) is a clonal hematopoietic disorder that often results in progression to acute myeloid leukemia (AML), particularly when additional genetic abnormalities are present, such as monosomy7.1 Case reports of remission in patients with primary MDS occasionally appear in literature1.

CASE REPORT

48 year old male presented to us in January of 2011, with generalized weakness for 6 weeks. Examination revealed severe pallor. Complete blood counts (CBC) showed
Figure 1 Cytogenetic report showing Monosomy 7.
severe anaemia with hemoglobin (Hb) of 3.7g/dl, total leukocyte count (TLC) of 3,400/cmm, differential leukocyte count of (DLC) Neutrophils 51%, Lymphocytes 41%, Monocytes 5% and Eosinophils 3%. Platelet count was 101,000/cmm. Mean corpuscular volume (MCV) of 109 femtolitres. Cobalamin and red cell folate and iron levels were normal. Peripheral blood film showed macrocystosis with occasional tear drop cells. Liver and kidney function tests were normal. Bone marrow examination yielded a diagnosis of Myelodysplastic syndrome - Refractory cytopenia with unilineage dysplasia (RCUD) in the erythroid series. Cytogenetics demonstrated Monosomy of chromosome 7 in 70% of cells (Figure 1). A diagnosis of MDS was made, disease course and treatment options were discussed in detail with patient and his family, had no prospects for stem cell transplantation as this being the only treatment option for MDS with monosomy 7. After discussion it was decided to give a trial of Lenalidomide. The patient was started on Lenalidomide 10 mg OD with supportive care and was advised to follow up in clinical haematology outpatient department. Patient received 14 units of blood over a period of 8 months. Presently (as of May 2014) the patient is on follow up (from February 2011) and is transfusion independent and his complete blood counts (CBC) are normalizing with Hb of 12.2g/dl, TLC 5300/cmm and platelet count of 150,000/cmm. Bone marrow examination as of now reveals normal hematopoiesis devoid of any dysplastic changes. His latest cytogenetic report reveals complete disappearance of monosomy 7.

DISCUSSION

Monosomy 7 is the second most frequent distinct chromosomal abnormality in MDS, occurring in some 25% of abnormal cases. It can present as total or partial monosomy. In the latter case, variable deletions of parts of the long arm lead to loss of genetic material of different size. As yet, no significant differences concerning the prognostic relevance have been observed between total and partial monosomy 7. In the German–Austrian dataset, 36% of monosomy 7 were isolated ones, 14% displayed one additional abnormality, and 50% occurred as part of complex abnormalities. In an analysis of gene expression profiles in CD34 positive cells from MDS patients with monosomy 7, a malignant phenotype with highly proliferative potential was found with an over expression of HOX9A, PRAME, BMI-1, PLAB, and the DNA repair gene BRCA2. Parallel down regulation of the tumor suppressor gene p21, GATA2, and MAP was observed. Clinically, monosomy 7 is characterized by a lower median age of the affected patients as compared to 5q deletions, severe refractory cytopenias, and a proneness to life-threatening infections. In contrast to the situation in 5q deletions, in monosomy 7, additional abnormalities do not have such a profound impact on outcome as seen in 5q deletions, since monosomy 7 even as an isolated abnormality confers a significantly bad prognosis. Therapeutic options in the monosomy 7 subgroup are unsatisfying as yet. If age and clinical condition are adequate, patients should be treated with allogeneic stem cell transplantation whenever possible. Conventional intensive chemotherapy bears a high risk of early death and non response. Even if complete remission can be achieved, this frequently is of only short duration with a high risk of early relapse. In a recent report on 34 patients with MDS or AML treated with 5-azacytidine, the group of Mufti observed a preferentially good response of MDS patients with monosomy 7 to the demethylating agent 5-azacytidine. Another new therapeutic mechanism,
immunomodulation, might be effective in cases with complex karyotypic changes too. In this connection, a complete cytogenetic response to the immunomodulatory drug Lenalidomide has been reported in patients with high-risk MDS with complex chromosome abnormalities harboring 5q deletions. Therapeutic strategies targeting immunomodulation and epigenetic changes proved to be of outstanding effectiveness and tolerability in comparison to established therapies.

CONCLUSION

This case report of myelodysplastic syndrome with monosomy 7 on Lenalidomide is rather unusual as the patient achieved complete haematological and cytogenetic remission. Understanding the mechanism of remission in these rare cases may therefore improve our knowledge of leukemia transformation. Even more so, this case illustrates importance of the period of observation before proceeding to transplant even in prognostically high risk myelodysplastic syndrome cases.

CONSENT

Written informed consent was obtained from the patient for publication of this case report.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES