

MYELODYSPLASTIC SYNDROME FOLLOWING ESSENTIAL THROMBOCYTOPENIA IN HYPERTENSION -- A CASE REPORT

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ABSTRACT

Myelodysplastic Syndrome (MDS) is a disorder of haemopoietic stem cell. Since, it has not been commonly observed in Pakistan, thus, this case study is to understand the scientific and therapeutical comprehension of MDS. An 81 year old male hypertensive patient was presented in a private hospital of Islamabad, Pakistan, with anemia. On medical investigation the physician prescribed him, multi-vitamins OD for a month; injection G-CSF 300mcg once a week; Molgramostim 300µg on every alternate day for 3 weeks; Thalidomide 100mg OD with Alprazolam 0.5mg at night for 4 weeks and 5'-azacytidine for a month. Clinical and pharmaceutical inaccuracies were observed. Moreover; the high cost and long term therapy are major obstacles to cure this disease. Therefore, affordable method and short-term effective therapy and reduced cost of drugs will help to cure the disease in more efficient way and in less time with more promising results.

Keywords: Myelodysplastic Syndrome, MDS, refractory anemia, thalidomide, Pakistan.

INTRODUCTION

Myelodysplastic Syndrome (MDS) is a complex disorder of haemopoietic stem cell and is characterized by variable degree of trilineage dysplasia and cytopenias in the face of normal or hypercellular marrow reflecting ineffective haemopoiesis¹. It is primarily a disease of the elderly (most patients are older than age 70), but also can affect younger patients as well². MDS and aplastic anemia share several epidemiological, etiological, and clinical and hematological features at present. However, the bone marrow in aplastic anemia is grossly hypocellular, while in MDS it is classically hypercellular. In some cases of MDS, bone marrow can also be hypocellular (hypoplastic MDS)³.

With a few exceptions, the exact causes of MDS are unknown; some evidence suggests that certain people are born with a tendency to develop MDS². This tendency can be thought of as a switch that is triggered by an external factor. Chemotherapy, exposure to radiations, environmental or industrial chemicals such as aromatic hydrocarbons etc., can act as a trigger for MDS. Unfortunately, it is unclear which other chemicals may predispose individuals to MDS, although certain occupations have been labeled "at risk" for the development of MDS or Acute Myeloid Leukemia (AML)².

In the early stages of this disease, the blood cell counts are usually not so reduced that they produce symptoms. With the progression of disease, patients generally experience fatigue and report that they are tired much of the time and have no energy. Weight loss is also observed. Laboratory diagnosis reveals low red blood cell count, low white cell count and marked decrease in platelets.

The onset of a myelodysplastic syndrome before the age of 50 years is rare, but the various forms of this disease are among the commonest hematologic cancers in patients over the age of 70 years⁴. Age is recognized as an important adverse factor and in this regard co-morbidity is of particular importance and a frequent co-variable⁴. However, advanced age should not exclude a patient with MDS from appropriate treatment, and age alone should not be considered a surrogate marker for functional decline or co-morbidities⁵. Unfortunately, in Pakistan there is no statistics on national level. However, several cases have been reported⁶ and it has been observed that MDS is relatively uncommon and represents only 1-2% of the adults of age 60 years and above.

CASE REPORT

An 81 year old male was presented in the out-patient department of a private hospital, Islamabad, Pakistan, with chief complaints of progressive weakness, insomnia, shortness of breath and continuous loss in weight from past 15 days. Physical examination showed patchial spots over trunk, legs and feet were the positive findings.

Patient past medical record showed cardiac by-pass surgery twice in the last 20 years and has severe hypertension. Patient was taking furosemide, aspirin and amlodipine concomitantly for control of hypertension.

On the basis of his weakness and pale skin, patient was considered as anemic and was prescribed multi-vitamins therapy OD (once a day) for a month. After a month, patient complained about muscular fatigue and even more loss in weight. Complete blood count report showed WBC count 2900/mm³, RBC 3.15 million/mm³, hemoglobin 9.5g/dL and platelets 12000/mm³ with increased lymphocytes on differential count. Bone marrow aspiration and trephine biopsy showed trilineage hyperplasia with pancytopenia. Reticulocytes were found to be 3.5%. Diagnosis of refractory anemia was made.

Patient was immediately administered Granulocyte growth-stimulating factor (G-CSF) 300µg and was discharged. After a period of 7 days, patient blood was re-analyzed which showed decreased count of WBC, RBC and platelets with increased lymphocytes on differential count. The patient was admitted in the hospital for 3 weeks and in the mean time, he was given blood transfusion twice and was on Molgramostim 300µg on every alternate day. A little progress was observed in patient health with hemoglobin being increased from 10.2 to 12.4 g/dL, RBC increased to 3.98 million/mm³, WBC increased to 12000/mm³ and platelets increased to 32,000/mm³. Re-analysis after 14 days showed marked decrease in WBC, RBC, platelets and hemoglobin levels. Bone marrow aspiration and trephine biopsy showed increased cellularity, erythropoiesis grossly was megaloblastic and suppressed. Megakaryocytes were hyperplastic and moderately dysplastic. Diagnosis of peripheral blood and bone marrow findings were consistent with refractory anemia (Blasts <5%). Cytogenetics reported no chromosomal abnormality.

The physician prescribed the patient with Thalidomide 100mg OD with Alprazolam 0.5mg at night for 4 weeks and was discharged. After 30 days, patient blood count report was satisfactory and the therapy was continued for 2 months more. Following a total of 90 days, re-analysis of patient's blood was made which showed pancytopenia. Physician prescribed 5'-azacytidine to the patient but due to unavailability and high cost of drug, patient discontinued the therapy.

Incompliance with medicine, without any second opinion, patient shifted himself to homeopathic medicine from last two months and had recovered decreased count of RBCs and WBCs. Platelets had been increased from 15,000/mm³ to 48,000/mm³ in a course duration of 15 days and were increased with time and successive therapy. Hemoglobin level had been restored to normal level.

DISCUSSION

MDS is a relatively uncommon disorder of the bone marrow in Pakistan. Diagnosing MDS is difficult because of the similarities with other hematologic disorders including acute myeloid leukemia (AML), hypoplastic anemia and hereditary sideroblastic anemia. However, research efforts have been made to uncover the disease mechanisms that lead to MDS. Increased awareness and understanding of MDS has contributed to the refinement of criteria by which a diagnosis of MDS is made. Equally important, increased understanding of the disease mechanisms is driving the discovery of new drugs to treat specific MDS subtypes and risk factors.

MDS is perplexing, life threatening set of bone marrow disorder for which there are no easy cures. Most patients in the early stages of MDS experience anemia. Anemic patients typically have pale skin and experience fatigue along with shortness of breath. For this reason, such patients are often prescribed multi-vitamins at first. For most severe cases, granulocyte growth-stimulating factor (G-CSF) is administered.

An expanding number of experimental, or investigational, drugs are being evaluated for their potential use in treating MDS. These include low-dose or non-intensive, chemotherapy agents and many diverse types of drugs and compounds with sometimes different, sometimes overlapping modes of action. Some of these drugs, like thalidoamide, lenalidoamide and azacytidine are also prescribed, however, these drugs had shown positive effect at the start and after a certain time period with regular doses, the patients were unresponsive.

Another treatment for MDS is bone marrow transplantation, which may actually involve the transfusion of stem cells from the bone marrow or circulating blood. Although it offers a potential cure for MDS, this procedure is available to only a limited proportion of patients not only due to the age of MDS patients and lack of suitable donor, but also it is very costly and can't be afforded by an average person.

Moderate drug-drug interactions were observed in the prescription. During concomitant use of Alprazolam and Thalidomide, patients should be monitored for potentially excessive or prolonged CNS and respiratory depression, especially in elderly or debilitated patients. Alprazolam with Furosemide has moderate interaction and may result in lightheadedness, syncope, orthostasis, or tachycardia. Aspirin and Amlodipine concomitant use may result in increased blood pressure. Monitoring for altered blood pressure control and control over the taking of Alprazolam has been recommended.

CONCLUSION

The rational therapy of myelodysplastic syndrome with refractory anemia (MDS-RA) in hypertensive patients is a serious issue and needs unusual intention of health professionals. Also, it is required to check elderly patients for hypertension and close monitoring of blood pressure is recommended. Moreover, the high cost of anti-MDS drugs and non-affordability of the therapy are major obstacles to cure this disease. Most of the patients don't continue the therapy due to major side-effects and their high cost. Therefore, drugs with low dose and high potency, high progress against the disease, affordable, and with less side effects will help in treating MDS patients in a better way.

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