Observational Study

An analysis of 30 cases of myelodysplastic syndrome

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30 Cases of MDS presented from April 98 to May 2006 are included in this study. 15 cases were male and 15 cases were female. Mean age at presentation was 55 years (range 8-73 years). Majority of patients presented with weakness (63.33%). 13.33 % of the patients had autoimmune manifestations (AIMs) in the form of joint pain. Patients were symptomatic for prolong period before diagnosis could be reached (average 358.8). Majority of patients had MDS-RA or MDS-RAEB-2 at presentation. 3 patients had complex chromosomal abnormalities (25 %). 8 patients (26.7 %) were relatively young at presentation, less than 50 years of age. 3 (10%) were children. Majority of the patients opted for symptomatic treatment only. 60 % of the patients were lost to follow-up.

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Key words **: Myelodysplastic syndrome, thalidomide, cyclosporine, ciprofloxacin, steroids, autoimmune.**

MDS is a clonal disorder of pluripotential stem cells of the bone marrow. Majority of patients are affected in middle age. The onset of the disease before 50 years is uncommon except in cases preceded by irradiation or chemotherapy. Patient can be asymptomatic at the diagnosis or can have severe pallor, weakness, loss of sense of well being and exertional dyspnea. Small proportions of patients have repeated infective episodes or bleeding due to neutropenia and thrombocytopenia respectively. Some patients have features of autoimmune inflammation (like arthralgia) as the initial presentation. Hepatomegaly occurs in about 5-10% of patients.

WHO classification[1] is now replacing FAB classification[2]. (Table 1). International prognostic scoring system (IPSS) is used to predict median survival, chances of evolution in AML and hence it is useful to decide type of the therapy[3]. The only curative treatment of MDS is bone marrow transplantation. Various other treatments are used for palliation: anabolic steroids, corticosteroids, amifostine, ciprofloxacin, pentoxifylline, cytosine arabinoside, thalidomide, erythropoitin etc.

Material and Method

30 patients seen from April 98 to May 2006 at the haematology clinic are included in this study.

Complete blood counts were done on automated cell counter. Bone Marrow was done in 23 cases. Iliac crest was the preferred site for bone marrow. Injection Glycopyrolate was given subcutaneously as a premedication to prevent anaphylaxis. The procedure was done as an out patient procedure where local anaesthesia was given. Short general anesthesia (Ketamine + midazolam) was used in uncooperative patient or children. Aspiration was done followed by trephine from the same site but from different points. Sample for cytogenetic study was also collected. Dry films were stained using a Romanwasky stain and perl's stain.

Trephine biopsy specimens were decalcified and embedded in paraffin wax. Thin sections were cut and stained with haematoxylin and eosin.

Chromosomal study was done in 11 cases. Bone marrow cells were collected in collection medium and grown in RPMI 1640 (Himedia, India) supplementeddd with 20% fetal calf serum (centron, India) for 24 hours as per standard protocol. The chromosome banding was done by trypsin-giemsa staining. At least 20 well spread metaphase plates were analyzed from each sample and 3 to 4 well spread plates were photographed and karyotyped.

Response evaluation criteria [4]:

The hematologic response was evaluated using the International Working Group criteria

- The erythroid response was classified as follows:

Major response :

(1) > 2-g/dl increase in their hemoglobin level (pretreatment level < 11 gm %)

(2) Independence from RBC transfusions for the RBC transfusion-dependent patient.

Minor response :

(1) 1 to 2-g/dl increase in their hemoglobin level (pretreatment level < 11 gm %)

(2) 50% decrease in the transfusion requirement for the RBC transfusion-dependent patient.

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CATEGORY	P/S	BONE MARROW
Refractory Anaemia (RA)	Blasts < 1% Monocyte < 1000/cmm	Erythroid dysplasia only Blasts < 5% Ringed sideroblasts < 15%
Refractory anaemia with ringed sideroblasts (RARS)	Blasts < 1% Monocyte < 1000/cmm	Erythroid dysplasia only Blasts < 5% Ringed sideroblasts ≥ 15%
Refractory anaemia with multi-lineage dysplasia (RCMD)	Cytopenias (bi or pan) No or rare blasts No Auer rods <1 X 10^9/ litre monocytes	Dysplasia in >10% cells in ➢ 2 myeloid cell lines < 15 % ringed sideroblasts <5% blasts No Auer rods
RCMD with ringed sideroblasts	Cytopenias (bi or pan) No or rare blasts No Auer rods <1 X 10^9/ litre monocytes	Dysplasia in >10% cells in ➢ 2 myeloid cell lines ≥ 15 % ringed sideroblasts <5% blasts No Auer rods
Refractory anaemia with excess blasts (RAEB) RAEB- I	Cytopenias < 5 % blasts No Auer rods <1 X 10^9/ litre monocytes	Unilineage or multilineage No Auer rods Blasts - 5-9 %
RAEB-II	Cytopenias 5-19 % blasts Auer rods ± <1 X 10^9/ litre monocytes	Unilineage or multilineage dysplasia Auer rods ± Blasts – 10 -19%
MDS - Unclassified	Cytopenias No or rare blasts No Auer rods	Unilineage dysplasia in granulocytes or megakaryocytes < 5 % blasts No Auer rods
MDS associated with isolated del (5q)	Anaemia < 5 % blasts Platelets normal or increased	Normal to increased megakaryocytes with hypolobated nuclei < 5 % blasts No Auer rods Isolated del (5q)

Table 1 — WHO Classification

- The platelet response was identified as follows;

Major response :

(1) An absolute increase of 30,000/ul or more (Pretreatment platelet count < 100000/ul)

(2) For the platelet transfusion-dependent patients, stabilization of the platelet counts and independence from platelet transfusion.

Minor response :

(1) 50% or more increase in the platelet count with a net increase > 10,000/ul, but < 30,000/ul. (Pretreatment platelet count < 100000/ul)

- The neutrophil response was classified as follows;

Major response:

(1) At least a 100% increase or an absolute increase of > 500/ul (an absolute neutrophil count <1,500/ul before therapy)

Minor response:

(2) An ANC increase of at least 100%, but an absolute increase < 500/ul (an absolute neutrophil count <1,500/ul before therapy)

To be considered as a major or minor improvement, the hematologic improvements must have lasted for at least 2 months in the absence of ongoing cytotoxic therapy.

Results

30 cases of MDS, from April 98 to May 2006 are included in this study. 15 were male and 15 were female with mean age 55 years (range: 8 to 73 years).

63.33% of the patients had pallor, 10 % had bleeding from various sites, 6.66 % had splenomegaly and 10 % had hepatomegaly. Follow up examination revealed weight loss in 30%, ashen grey skin in 3.33%, weakness in 16.66%, hepatomegaly in 3.33% and lymphadenopathy in 3.33%.

Patients were symptomatic for 358.8 days (range: 1-7300 days) before diagnosis was made.

Out of 30 cases, complete blood count and peripheral smears showed pancytopenia in 37%, bicytopenia in 40.75%, anaemia in 70%, and leucopoenia in 46.66% and thrombocytopenia in 53.33%.

Cellularity of bone marrow was as follows: hypercellular-65.21%, cellular- 8.66%, dry tap-21.79%, and hypocellular- 4.34%. Megakaryocytes were adequate in 34.78%, reduced in 30.43 %, increased in-21.7% and absent in 13.03%. 60.86% had myeloid dysplasia, which includes hypogranular cytoplasm, hypergranular cyto-

plasm, pelger-huet anomaly and large size of the cells. 4.34% had megakaryocytic dysplasia. Trephine biopsy measured 0.5-1.5 cm in length.

Majority of patients had MDS-RA or MDS-RAEB-2 at presentation (Table 2)

Chromosomal study was done in 12 cases: 3 patients had complex chromosomal abnormalities (25 %), 8 had normal chromosomal study (66.66%) and in one case metaphases could not be obtained. Following abnormalities were seen in 3 patients:

Patient 1: 46, XY, -5, –7, -13, + marker I, II, III

Patient 2: 46 XY, inv (3), (q 12, q 26)

Patient 3: 43-45, X, -5, -7, -22, + marker 1 & 2

Out of 30 cases, according to IPSS scoring, 3 cases were of low risk, 11 cases were of intermediate risk-I, 8 cases were of intermediate risk -II and 3 cases were of high risk.

Discussion

Weakness (46.66 %) and breathlessness on exertion (16.66 %) were the major complains on presentation. Bleeding (10%) and joint pain (3.33 %) at presentation was uncommon. 10 % of patients developed joint pain on follow-up. Thus 13.33 % of the patients had autoimmune manifestations (AIMs) in the form of joint pain. This incidence is similar to the reported incidence of 18.7 % by S. Giannouli *et al*[5].

Majority of the patients were > 50 years. However 3 patients were children and 5 patients were less than 50 years of age. This finding is unlike the observation of western literature[6]. High incidence of MDS in relatively young patients is previously reported from India[7].

Our series had more female patients (Male: female ratio=1:1) unlike published literature[6,7]. This could be due small number of patients in our series.

Majority of the patients had long history of symptoms (average 358.8 days) and 13 (43.3 %) cases had previous history of blood transfusions before the diagnosis. This is due to lack of diagnostic facility or lack of awareness amongst the clinicians.

Out of 30 cases, 7 patients were not classified in to sub groups as bone marrow was performed elsewhere and slides/blocks were not available for review. Majority of the patients had MDS-RA, MDS- RAEB-1 and MDS-RAEB II.

Cytogenetic study could be done only in 12 patients due to economical constrains. Two had poor cytogenetic abnormalities (Patient 1: 46, XY, -5, –7, -13, + marker I, II, III, Patient 2: 43-45, X, -5, -7, -22, + marker 1 & 2) while one had intermediate abnormality (46 XY, inv (3), (q 12, q 26)).

According to the International Working Group criteria, two patients responded to the treatment. One patient had minor response in platelets with anabolic steroids (56days) and prednisolone after 2 months of treatment. Another patient had major response in hemoglobin and minor response in platelet count after treatment of prednisolone (95days), anabolic steroids-stenazolol (90days) and ciprofloxacin (32days).

Two patients had improvement in hemoglobin with haematinics as they had associated iron deficiency. One patient had Haemoglobin rise of 1 gm% and in another it was 7 gm%. None received any other treatment except haematinics.

One patient had improvement in hemoglobin of 2 gm% after treatment with folic acid, vitamin B12 and prednisolone due to associated immune hemolytic anaemia.

One patient had improvement in counts with treatment of infection. White cells improved to 2.73 x 109/L (Abso-

RA	RCMD	RAEB-1	RAEB-2	Designated to AML
9 cases (39.1%)	2 cases (8.7 %)	4 cases (17.4%)	7 cases (30.4%)	1 case (4.34 %)

Table 2 — Category Of Mds As Per Who Classification

CELLULARITY	DYSPLASIA IN MYLOID SERIES	DYSPLASIA IN ERYTHROID SERIES	MEGAKARYOCYTES
Hypercellular 30.4%	Hypogranular Cytoplasm- 26%	Megaloblastic changes – 13%	Adequate – 34.78%
Cellular – 8.69%	Hypergranular Cytoplasm – 8.69%		Reduced – 30.34%
Dry tap – 21.79%	Pelger-huet Anomaly- 26%		Hypercellular – 21.7%
Hypocellular – 4.39%	Large Myeloid Series- 8.69%		Absent – 13.03%

Table 3 — Findings of Bone-marrow Aspiration

lute neutrophil count 1283) from 0.67 x 109/L (Absolute neutrophil count -201) indicating infection induced neutropenia.

Two patients didn't respond to cyclosporin, anabolic steroids (stenazolol), ciprofloxacin, etoposide, erythropoietin, cyclophosphamide and thalidomide.

Majority of the patients opted for the palliative therapy as evident from the Table 4. Reason for opting for the palliation was economical in most of the cases while in old patients; there was reluctance for hospital admission and intravenous chemotherapy.

60% patients were lost to follow-up and hence were not evaluable. 4 (13.33%) patients expired due to septic shock, DIC and intra cranial bleeding.

Median follow-up was 128.9 days (0 – 970 days). Median survival was 119.2 days for RA (0-515 days), 302.7 days for RAEB –1(0-970), 233.7 days for RAEB-2 (0-515 days) and 165 days for RCMD (0-330 days).

DRUGS	NO. OF PATIENTS (% OF CASES)	AVERAGE DURATION (DAYS)	AVERAGE NO. OF UNITS PER PERSON
Folic acid	20 (66.66)	131	
Iron therapy	8 (26.66)	428.8	
Prednisolone	9 (30)	68.77	
Stanozolol	10 (33.33)	88.6	
Ciprofloxacin	10 (33.33)	20.7	
Etoside	6 (20)	8.83	
Hydroxyurea	2 (6.66)	110	
Pentoxyphylin	2 (6.66)	30	
Thalidomide	2 (6.66)	56	
Cytarabine	1 (3.33)	24 Days	
Erythropoietin	2 (6.66)	38	
Cyclosporin	2 (6.66)	225	
PCV	14 (46.66%)		8.42
PRC	7 (23.33%)		4
WHOLE BLOOD	14 (46.66%)		7.46

Table 4 — Treatment

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