Primary Myelodysplastic Syndrome in Jordan: A Single-Centre Experience

Abdalla Awidi^a Ahmad Magableh^a Ziad Taimeh^a Hashim Ayyad^a
Nazzal Bsoul^a Musleh Tarawneh^b

Departments of ^aHematology and Oncology and ^bPathology, Jordan University Hospital, Amman, Jordan

Key Words

Myelodysplasia • Pancytopenia • Sideroblasts • Refractory anemia

Abstract

Objective: Study of the disease patterns and clinical evaluation of myelodysplastic syndrome (MDS). **Subjects and Methods:** A retrospective analysis was carried out on 85 patients, with MDS who were followed up over a period of 23 years at Jordan University Hospital, Amman, Jordan. Cases were analyzed according to the French, American and British Classification. **Results:** Of the 85 patients, 42 (49.4%) were females and 43 (50%) males; mean age was 59 ± 19 years (range 18–88). Most subtypes found in patients were refractory anemia (RA) in 27 (31.8%) and RA with excess blasts (RAEB) in 28 (32.9%). Adverse prognostic indicators were RAEB subtype and requirement for blood transfusion. **Conclusion:** Our findings showed that MDSs appeared at a younger age and tended to be of the aggressive subtype. Chronic myelomonocytic leukemia subtype seemed to appear dominantly in men.

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Introduction

Myelodysplastic syndrome (MDS) comprises a spectrum of heterogeneous clonal hematopoietic disorders characterized by dysplastic and ineffective blood cell production, resulting in chronic cytopenia, abnormal cellular maturation and a variable risk of transformation into acute leukemia [1–3]. These disorders may arise de novo or years after exposure to potentially mutagenic treatments such as irradiation and chemotherapy [4]. The incidence of de novo MDS is variable. The objective of this study was to document the disease pattern and evolution in Jordan.

Subjects and Methods

The medical records of all patients with a laboratory diagnosis of MDS at Jordan University Hospital, Jordan, between January 1, 1985 and the end of 2007 (23 years) were reviewed. The following data were gathered: gender, age, presenting symptoms, blood transfusions, French-American-British (FAB) Classification, blood count, serum ferritin and lactate dehydrogenase (LDH), blasts in bone marrow, cytogenetics, progress to acute leukemia and survival.

For the purpose of calculating the length of follow-up and survival, the period until the last documented visit was taken and approximated to the nearest month. If the patient was lost to follow-up or was transferred somewhere else, the last visit was con-

Table 1. Gender, age and frequency according to the FAB classification

Gender	Age, years	FAB subtypes					
		RA	RAS	RAEB	RAEB-T	CMML	unclassified
Male (n = 43)	57 ± 18.4	10	6	12	5	8	2
Female (n = 42)	58.8 ± 19.5	17	4	16	3	2	0
Total (n = 85)	58 ± 19	27	10	28	8	10	2

Table 2. Blood findings, serum ferritin, LDH (±SD) at presentation, and blood transfusions during the period of follow-up

	Cumulative		Subtype			Total ^a
	CMML	RA	RAEB	RAEB-T	RAS	
Age, years	60.7 ± 12.2 (10)	59.9 ± 19.2 (27)	58.6 ± 19.5 (28)	52.0 ± 20.9 (8)	52.1 ± 24.5 (10)	57.8 ± 19.3 (83)
Hb, g/dl	8.4 ± 2.1 (10)	8.7 ± 1.8 (27)	9.2 ± 2.2 (28)	8.3 ± 2.3 (8)	8.7 ± 1.2 (10)	8.8 ± 1.9 (83)
Platelets × 10 ³ /μl	164.3 ± 141.1 (10)	249.8 ± 184.5 (27)	153.1 ± 82.2 (28)	60.3 ± 53.3 (8)	204.2 ± 103.7 (10)	183.1 ± 141.3 (83)
WBC, × 10 ³ /μl	5.8 ± 3.6 (10)	6.1 ± 4.2 (27)	6.4 ± 4.2 (28)	4.9 ± 3.4 (8)	5.3 ± 2.0 (10)	5.9 ± 3.8 (83)
LDH, IU/l	488.4 ± 324.7 (10)	413.2 ± 328.8 (27)	538.7 ± 446.2 (28)	318.2 ± 249.2 (8)	481.6 ± 302.1 (10)	463.7 ± 362.8 (83)
Ferritin, ng/ml ^b	1,035 ± 324 (7)	396.2 ± 381.7 (25)	452.1 ± 489.1 (23)	346.8 ± 310.9 (6)	715.7 ± 308.9 (6)	506.3 ± 445.4 (67)
Blood transfusion (only for patients who received blood units), units/month	4.6 ± 3.2 (9)	2.1 ± 1.7 (17)	3.9 ± 2 (23)	2.9 ± 1.9 (8)	2 ± 1.0 (8)	3.2 ± 2.3 (65)

Figures in parentheses are number of patients.

^a Two patients with unclassified subtype were not included in this table.

^b Sixteen patients were not included in ferritin means because data were unavailable.

sidered for the length of follow-up. Death was documented if it occurred at the university hospital or if it was documented by relatives. If death was not documented as such, it was entered as unknown. Patients diagnosed with MDS at another hospital were excluded because of difficulty in calculating the follow-up period and/or survival.

Results

A total of 85 patient records were reviewed; there were 42 (49.4%) females and 43 (50.6%) males; ages ranged from 15 to 88 years; mean age of males was 63 ± 16.2 years, and mean age of females was 53 ± 20.7 years. As shown in tables 1 and 2, the most frequently seen subtypes were refractory anemia with excess blasts (RAEB) and refractory anemia (RA). Females had more often RA and RAEB while males had more often chronic myelomonocytic leukemia (CMML), RA with ringed sideroblasts (RAS) and RA with excess blasts in transformation (RAEB-T).

The mean survival of patients with RA and RAEB was 59.7 ± 9 and 30.7 ± 4 months, respectively. The mean

survival of patients who did not receive any blood transfusions was 55.9 ± 8 months and that of patients who received blood transfusions was 31.8 ± 4.1 months.

Cytogenetic investigations were documented in 26 patients since they have become available only recently. Of these, 16 patients had normal cytogenetics, 5 with deletion of the long arm of chromosome 5 (5q-), 3 with complex chromosomal abnormalities and the 2 remaining had cytogenetic abnormalities. Twenty patients (11 males and 9 females) transformed into acute myeloid leukemia during the follow-up period.

At presentation, there was no difference in the hemoglobin level between males and females: 9.4 ± 5.9 g/dl in males and 9 ± 2 g/dl in females. Platelet count at presentation was higher in males (280.7 ± 131 × 10⁹/l) than in females (82.3 ± 52.2 × 10⁹/l). Males required a mean of 3.6 units of blood transfusion per month while females required a mean of 2 units per month. Patients were followed up for 2,144 patient-months with a mean of 25.2 months and a range of 1–127 months. During the follow-up period, there were 40 documented deaths: 22 males and 18 females. Among the males, death occurred in the

Fig. 1. Overall Kaplan-Meier survival of 66 patients whose survival is known.

Fig. 2. Kaplan-Meier survival curves of 21 RA and 26 RAEB patients.

following subtypes: 12 died of RAEB, 3 of CMML, 3 of RAEB-T, and 2 each of RA and RAS. Among the females, 9 died of RAEB, 4 of RA, 2 each of CMML, RAEB-T, and 1 of RAS. Mean patient survival was 36.96 ± 4 months as shown in the Kaplan-Meier survival curve of figure 1. There were enough patients for calculation of survival rates only for the RA and RAEB subtypes as shown in figure 2. The mean survival rates of patients with RA and RAEB were $59.74 \pm (\text{SE}) 9$ and $30.76 \pm (\text{SE}) 4$ months, respectively; the difference is statistically significant ($p < 0.029$). The mean survival rates for patients with and without blood transfusion were $31.85 \pm (\text{SE}) 4.17$ and $55.89 \pm (\text{SE}) 8.42$ months, respectively; the difference is also statistically significant ($p < 0.023$) as shown in figure 3. No statistical difference was observed in the survival of patients who had higher than normal LDH levels compared to those with normal LDH levels ($p = 0.583$) as shown in figure 4.

Discussion

MDS is considered an important condition in developed nations, with a reported crude annual incidence of 4.1 per 100,000 in Germany and the incidence is increasing as the population ages [5]. Fortunately, the development of new therapies such as lenalidomide, oral iron chelators, hypomethylating agents as well as erythropoie-

tin are helping to improve the outcome of this disease and the patients' quality of life [6].

In developing nations, MDS has not been studied and little is known about its epidemiology, behavior and prevalence. This retrospective study reviewed the experience of a large university center in Jordan. In view of the small number of cases reviewed, the clinical spectrum of this syndrome in this developing nation, where the population is dominantly very young, is uncertain and will need to be studied prospectively. The age of onset of MDS is between 60 and 70 years without any gender preference nor a younger age of onset [1, 2, 7–13]. Consequently, MDS is considered a disease of aging [14, 15]. Yet in our study, the age of onset is younger than reported in the literature [14, 15].

Our findings concerning the incidence of RAEB (33%) and RA (32%) are similar to previously reported values [16]. The incidence of CMML and RAS (11.7% each) is also comparable to that reported in the literature [17]. The observation that CMML was predominantly observed in men in this study, with a 4:1 male to female ratio, is different from that reported in the literature, where the male to female ratio is 2:1 [17]. The reason for this is unclear and warrants further study in the future.

Survival according to FAB subtype in this study is consistent with that reported in the literature [12]: survival was the longest in patients with RA while survival was the shortest in patients with RAEB. Because of the

Fig. 3. Kaplan-Meier survival curve of 51 patients who received blood transfusions and 15 patients who did not receive any blood transfusion.

Fig. 4. Kaplan-Meier survival curves of 29 patients with normal and 35 patients with higher than normal LDH. There is no statistical difference between the two groups.

small number in other subtypes, statistical evaluation of survival was not considered meaningful. Since cytogenetic studies were carried out only in a few patients, the International Prognostic Score (IPSS) could not be applied.

The survival of transfused patients was shorter compared with patients who were not transfused; this observation is consistent with Malcovati's [18] findings. The contribution of LDH level to survival was not evident in this study due to the small number of patients and is different from that reported in the literature [19].

The significance of high serum ferritin at presentation in MDS in this study is not well understood, and its prog-

nostic significance remains to be clarified. However, in the setting of repeated transfusions, iron overload may play an important role in shortening survival unless proper iron chelation is implemented with iron chelators as part of the care for MDS [20].

Conclusion

MDS in Jordan appeared to affect younger age groups, and tended to be of the aggressive subtype. Blood transfusion and possibly iron overload seem to be associated with shorter survival.

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