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Prognostic Factors of Acute Myelocytic Leukemia : An Analysis of 132 Patients in a Single Institution

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Patients with acute myelocytic leukemia (AML) have varied outlooks for survival after the diagnosis. To identify pretreatment prognostic indicators in AML, we analyzed 132 cases of AML seen at our hospital between June, 1989 and December, 1994. The median age of the patients was 40 years (range, 15-81). There were 63 male and 69 female patients. One hundred eight patients (82%) received induction chemotherapy which was based on cytarabine plus anthracyclines. Sixty six patients achieved complete remission (CR) and the CR rate among the patients given induction chemotherapy was 61%. The median duration of CR was 11.2 months. After median follow up of 6.6 months (range 0.5-51.4), 26 patients (39%) remain in continuous CR. The median duration of overall survival of the patients was 6.7 months. After median follow up of 10.6 months (range, 0.1-52.7), 41 patients (31%) are alive. Variables affecting duration of CR included the age of the patients, performance status of the patients, percentage of blast in the peripheral blood, hemoglobin level, percentage of blast in the bone marrow, FAB subtype, and CD7 marker positivity. Variables affecting survival duration included age of the patients, performance status of the patients, absolute blast count (ABC) in the peripheral blood, bone marrow cellularity, the percentage of blast in the bone marrow, and CD5 marker positivity. Multivariate analysis showed that the age of the patients and percentage of blast in the bone marrow were significant independent indicators for overall survival of the patients. Further studies utilizing cytogenetics and molecular characteristics of leukemic cell are warranted to better define the prognostic factors of patients with AML.

Key Words : *Acute Myelocytic Leukemia, Prognostic factors*

INTRODUCTION

Acute myelocytic leukemia (AML) results from the malignant transformation of a hematopoietic progenitor, followed by clonal expansion and accumulation of the transformed cells. It affects approximately 1.5/100,000 persons in Korea annually (Ahn

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et al., 19 91). If untreated, 90% of patients with AML die within a year of diagnosis. With modern combination chemotherapy including cytarabine and anthracyclines, approximately 65 % of previously untreated adults with AML enter complete remission and about 25 % of such patients achieve long term remission (Berman et al., 1991 ; Cassileth et al., 199 2). The age of the patients, white blood cell (WBC) count at the time of diagnosis, and French-American-British (FAB) histologic subtype classification were known to affect prognosis of the patients with AML (Berman et al., 1991 ; Lee et al., 19 94 ; Mayer et al., 1994). The purpose of this study was to analyze the prognostic indicators in Korean patients with AML seen in a single institution over a period of 6 years.

MATERIALS AND METHODS

Materials consisted of a total of 132 adult patients who were admitted to the Department of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea from June, 1989 to December, 1994 and subsequently diagnosed to have AML, were included in the study.

Various clinical data of the patients at the time of diagnosis, such as age, sex, initial symptom, duration of symptom, complete blood count, and blood chemistry were collected.

Absolute blast count (ABC) of peripheral blood was obtained by multiplying WBC count in the peripheral blood by the percentage of blast/100. Bone marrow smears and core biopsy sections were examined by a pathologist (H.S.C) and the cases were further classified according to the standard FAB criteria (Bennet et al., 1985 ; Bennet et al., 1976). Leukemic cell immunophenotype studies were done using a panel of monoclonal antibodies including antibody against terminal deoxynucleotidyl transferase (TDT), HLA-DR, CD2, CD5, CD7, CD10, CD13, CD14, CD19, CD33 and CD61. The cases were considered positive if 20% or more of cells were reactive to particular monoclonal antibody except to TDT where a 10% cut off value was used.

Induction chemotherapy was based on cytarabine 100-200 mg/m^2 intravenous infusion daily for 7 days and anthracyclines (either daunorubicin 40 mg/m^2 intravenously daily for 3 days or idarubicin 12 mg/m^2 intravenously daily for 3 days). One hundred and eight patients (82%) received induction chemotherapy. When the bone marrow examination performed on 15th day of chemotherapy showed persistence of leukemic blasts in the marrow, an additional cycle of chemotherapy was given with similar regimen with either full 7 days of cytarabine and 3 days of anthracyclines or abbreviated cycle with 5 days of cytarabine and 2 days of anthracyclines. Seventeen patients (13%) did not receive induction chemotherapy for various reasons such as poor performance status, overwhelming sepsis, and/or old age. Seven patients (5%) received symptomatic care with low dose cytarabine infusion (10-20 mg/m^2 daily). After induction chemotherapy, patients were considered to be in complete remission (CR) when the peripheral blood counts were normal (the neutrophil count greater than 1,000/ $\mu\ell$ and the platelet count greater than 100,000 / $\mu\ell$ and the results of bone marrow examination were normal (blasts less than 5% and cellularity over 25%). The data regarding the treatment given to patients and subsequent clinical courses of the patients such as presence of CR, duration of CRs, and duration of overall survival were recorded. This study used survival data up to March, 1995.

Statistical methods : Differences in the proportions of CRs among patient subgroups were analyzed using Fisher's exact test. The duration of CR was defined to be the time from achieving a CR to relapse (bone marrow or extramedullary) or date of last follow-up. Survival was defined as the time from the date of diagnosis of AML to death or date of last follow-up. Probability of surviving and remaining in CR was estimated by the Kaplan-Meier method. Differences in remission duration or survival between patient subgroups were tested using logrank statistics. Follow up duration of those in CR or alive were considered for the calculation of median follow up time for CR duration or survival.

The prognostic significance of various clinicopathologic variables of the patients were assessed with respect to CR rate (in overall patients as well as in patients who were given induction chemotherapy), CR duration, and survival. The analysis of CR rate was performed using the logistic regression model, whereas the analysis of CR duration and survival was performed using the Cox proportional hazards regression model.

RESULTS

The median age of patients was 40 years (range, 15-81). There were 63 male and 69 female patients. Seven patients (5%) had previous history of hematologic illness (myelodysplastic syndrome, 4 patients; aplastic anemia, 1 ; multiple myeloma, 1 ; and malignant histiocytosis, 1).

Complete remission : Sixty six patients achieved CR and the CR rate among patients who were given induction chemotherapy was 61% (Table 1A). The CR rate among the total 132 patients was 50%. Forty three (65%) of the 66 patients required 1 cycle of induction chemotherapy to achieve CR and 23 patients (35%) required 2 cycles of induction chemotherapy. The median time from the diagnosis of AML to the achievement of CR was 35 days (range, 22-167).

When the patients who were given induction chemotherapy were considered, the age of the patients, history of previous hematologic disease, and blood hemoglobin level were important factors predicting achievement of CR (P=0.074, 0.070, and 0.059 respectively) although none reached statistical significance (Table 1A, 1B, and 1C). Younger patients, patients without history of previous hematologic disease, and patients with higher blood hemoglobin level had higher CR rate. When overall patients were considered, the age of the patients was a significant factor in predicting achievement of CR (P=0.005, Table 1A). Fifty five of 92 patients (60%) who were 55 years or younger achieved CR in contrast to 11 of 40 patients (28%) who were over 55 years of age. CR rates were similar for those younger than 35 years and between 36 to 55 years of age (60% in both groups).

The results of leukemia marker study showed patients with leukemic cells positive for CD5 and/or CD7 showed lower CR rate (P=0.052 and 0.044 respectively, Table 2).

Duration of complete remission : The median duration of CR was 11.2 months. After median follow up of 6.6 months (range 0.5-51.4 months), 26 patients(39%) remain in continuous CR(Table 1A, Fig. 1).

Factors affecting CR duration included the age of the patients (P=0.031, Table 1A and 1B), performance status of the patients (P=0.013), percentage of blast in the peripheral blood (P=0.012), hemoglobin level (P=0.036), percentage of blast in the bone marrow (P=0.039), and FAB subtype (P=0.016). Number of courses of chemotherapy required to achieve CR and time from the diagnosis of AML to the achievement of CR did not correlate with CR duration (P= 0.797 and 0.403 respectively, Table 1C).

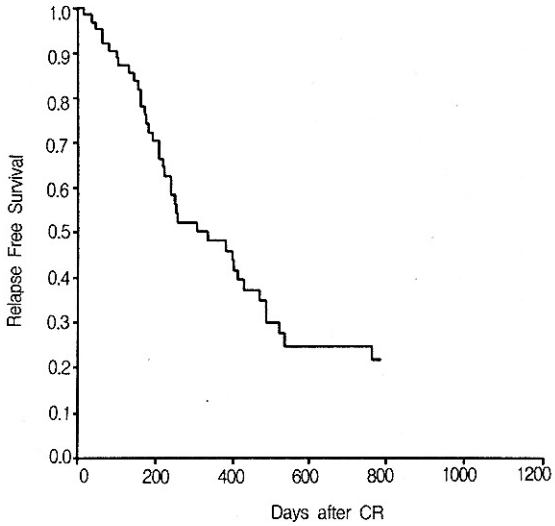

Fig. 1. Kapian-Meier estimate of relapse free survival of 66 patients with AML who achieved CR after induction chemotherapy.

Patients with leukemic cells which were positive for CD7 had significantly shorter duration of CR when compared to patients with leukemic cells negative for CD7 (8.5 vs 15.8 months, P=0.044, Table 2).

Overall survival of the patients : The median duration of overall survival of the patients was 6.7 months. After median follow up of 10.6 months (range, 0.1-52.7 months), 41 patients(31%) are alive (Table 1A, Fig. 2). Factors affecting the survival of the patients included the age of the patients (P< 0.001, Table 1A), performance status of the patients (P=0.004), ABC of the peripheral blood (P= 0.035), bone marrow cellularity (P= 0.017, Table 1B), and percentage of blast in the bone marrow (P= 0.016). Number of courses of chemotherapy required to achieve CR and the time from the diagnosis of AML to the achievement of CR did not correlate with survival of the patients (P=0.991 and 0.677 respectively, Table 1C).

Patients with leukemic cells which were positive for CD5 and/or CD10 had significantly shorter survival when compared to patients with leukemic cells negative for CD5 and/or CD10 (0.7 vs 7.3

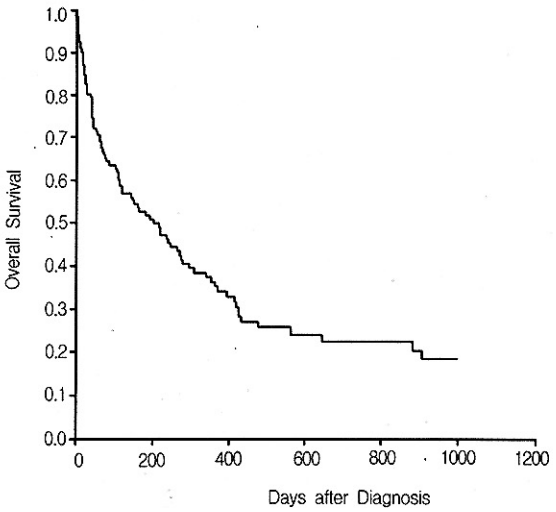

Fig. 2. Kaplan-Meier estimate of overall survial of 132 patient with AML.

months, P<0.001; 0.8 vs 5.4 months, P=0.023, respectively, Table 2).

Multivariate analysis: For the regression analyses, the following variables were considered in the variable selection process; the age, sex, Karnofsky performance status, fever, history of previous hematologic disease, WBC count, percentage of blast in the peripheral blood, ABC, bone marrow cellularity, percentage of blast in the bone marrow, FAB subtype, total bilirubin level, and leukemia markers including HLA-DR, CD2, CD5, CD7, CD10, CD19, and CD33.

The age of the patients remained to be the most important predictor for the achievement of CR both in terms of overall patient population as well as when only those patients who were given induction chemotherapy were considered (Table 3). Patients who were older than 55 years had a relative risk of 3.33 in failure to achieve CR when compared to those 35 years or younger. Sex was also significant predictor of CR with female/male relative risk of 0.42. For the duration of CR, better Karnofsky performance status and M3 FAB subtype were the significant independent predictors of longer CR duration. For the overall survival of the patients, the youth of patients and lower percentage of blast in the bone marrow were the significant independent predictors of longer survival.

DISCUSSION

With the advent of modern combination chemotherapy, the outlook for survival of patients with AML improved markedly with the majority of patients experiencing prolongation of survival and a fraction of patients achieving long term survival (Champlin et al., 1990; Cassileth et al., 1992). Despite the improvement, 70-80% of patients eventually die from the disease. The purpose of this study was to investigate which pretreatment clinicopathologic variables were important in predicting the outcome of Korean patients with AML.

A total of 132 adult patients with median age of 40 years (range, 15-81) and male/female ratio of 63/69 were seen over the period of 6 years. Of 132 patients, 108 patients received induction chemotherapy based on cytarabine plus anthracyclines and 66 (61%) achieved CR. CR rate in our study is comparable to those reported from other studies especially considering stricter patient eligibility criteria used in the prospective studies (Champlin et al., 1990; Berman et al., 1991; Cassileth et al., 1992). CR rate among overall patients (treated and untreated) was 50%.

Univariate analysis showed that the age of patients was significant factors predicting achievement of CR (Table 1A). When treated with induction chemotherapy, CR rates were similar between the patient groups of 35 years or younger and over 35 and up to 55 years (67% and 68% respectively). CR rate for patients over 55 years of age was significantly lower (42%, P=0.074). The adverse effect of old age for the achievement of CR is more obvious when the overall patients (including those who received palliative care with low dose cytarabine or supportive care only) were considered (60% vs 28%, P=0.005), since larger proportion of older patients were not given induction chemotherapy. Lower CR rate for patients older than 55 years of age remained significant after multivariate analysis suggesting that the old age itself is an adverse prognostic factor for the achievement of CR. Lower CR rate in elderly patients accounts for the significantly shorter survival time of these patients after the diagnosis of AML, which is apparent in both univariate and multivariate analyses in our study (Table 1A and Table 3). The effect of old age was also significant in terms of CR

Table 1A. Clinical and pathologic characteristics of patients in relation to complete remission, complete remission duration, and survival (I)

Variable	Total patients N (%)	CR rate, total patients		Patients given ind chemo N (%)	CR rate among patients given ind chemo		CR duration			Survival		
		N (%)	P		N (%)	P	Median (mo)	N of patients in CR (% of CR)	P	Median (mo)	N of patients surviving (% of total)	P
Total	132	66 (50)		108	66 (61)		11.2	26 (39)		6.7	41 (31)	
Age (yr)			0.005			0.074			0.031			< 0.001
35 or younger	50 (38)	30 (60)		45 (42)	30 (67)		7.8	10 (33)		9.1	16 (32)	
36-55	42 (32)	25 (60)		37 (34)	25 (68)		14.4	12 (48)		14.5	21 (50)	
> 55	40 (30)	11 (28)		26 (24)	11 (42)		5.4	4 (36)		2.5	4 (10)	
Sex			0.157			0.163			0.141			0.751
Male	63 (48)	27 (43)		51 (47)	27 (53)		14.4	11 (41)		5.1	16 (25)	
Female	69 (52)	39 (57)		57 (53)	39 (68)		8.4	15 (38)		7.3	25 (36)	
Initial Sx			0.504			0.803			0.481			0.122
Infection	44 (40)	20 (45)		34 (37)	20 (59)		13.5	10 (50)		3.8	11 (25)	
Anemia	38 (35)	20 (53)		33 (36)	20 (61)		8.5	6 (30)		8.3	12 (32)	
Bleeding	25 (23)	12 (48)		22 (24)	12 (55)		13.8	7 (58)		7.4	10 (40)	
None	2 (2)	2 (100)		2 (2)	2 (100)		-	2 (100)		-	-	
Sx duration (mo)			0.421			0.715			0.304			0.748
0.5 or less	56 (42)	26 (46)		45 (42)	26 (58)		13.5	11 (42)		7.3	19 (34)	
0.6-1	33 (25)	20 (61)		29 (27)	20 (69)		7.5	8 (40)		9.8	10 (30)	
> 1	43 (33)	20 (47)		33 (31)	20 (61)		8.5	7 (35)		5.6	12 (28)	
PS			0.109			0.449			0.013			0.004
90	15 (12)	10 (67)		15 (15)	10 (67)		26.2	8 (80)		8.3	9 (60)	
80	28 (22)	14 (50)		26 (25)	14 (54)		13.8	7 (50)		9.3	10 (36)	
70	38 (30)	21 (55)		34 (33)	21 (62)		13.4	9 (43)		11.8	13 (34)	
60	23 (18)	11 (48)		15 (15)	11 (73)		7.3	1 (9)		2.5	4 (17)	
50 or less	22 (17)	6 (27)		13 (13)	6 (46)		4.1	1 (17)		2.7	2 (9)	
Fever			0.859			0.845			0.058			0.109
Yes	69 (52)	34 (49)		57 (53)	34 (60)		8.0	12 (35)		6.1	17 (25)	
No	63 (48)	32 (51)		51 (47)	32 (63)		14.4	14 (44)		8.3	24 (38)	
Weight loss			0.840			0.828			0.198			0.616
Yes	34 (26)	18 (53)		30 (28)	18 (60)		17.9	10 (56)		5.6	11 (32)	
No	98 (74)	48 (49)		78 (72)	48 (62)		8.4	16 (33)		7.3	30 (31)	
PHD			0.102			0.070			0.191			0.052
Yes	7 (5)	1 (14)		5 (5)	1 (20)		5.9	0 (0)		1.5	0 (0)	
No	124 (95)	65 (52)		103 (95)	65 (63)		11.2	26 (40)		7.3	41 (33)	

*abbreviations: N=number, ind chemo=induction chemotherapy, yr=years, mo=months, Sx=symptom, PS=performance status(Karnofsky), PHD=previous hematologic disease

Table 1B. Clinical and pathologic charactersistics of patients in relation to complete remission, complete remission duration, and survival (II)

Variable	Total patients N (%)	CR rate, total patients		Patients given ind chemo N (%)	CR rate among patients given ind chemo		CR duration			Survival		
		N (%)	P		N (%)	P	Median (mo)	N of patients in CR (% of CR)	P	Median (mo)	N of patients surviving (% of total)	P
WBC ($x10^3/\mu l$)			0.162			0.383			0.225			0.151
<1.0	10 (8)	7 (70)		9 (8)	7 (78)		17.5	5 (71)		18.8	5 (50)	
1.0-99.9	109 (83)	55 (50)		90 (83)	55 (61)		8.5	18 (33)		7.3	32 (29)	
100 or over	13 (10)	4 (31)		9 (8)	4 (44)		-	3 (75)		1.4	4 (30)	
% Blast			0.289			0.603			0.012			0.294
<10	22 (17)	13 (59)		19 (18)	13 (68)		13.8	6 (46)		6.1	11 (50)	
11-49	55 (42)	28 (51)		48 (45)	28 (58)		8.6	12 (43)		7.3	16 (29)	
50-79	26 (20)	14 (54)		21 (20)	14 (67)		7.1	3 (21)		5.1	4 (15)	
80 or over	28 (21)	10 (36)		19 (18)	10 (53)		17.9	4 (40)		5.4	9 (32)	
ABC ($x10^3/\mu l$)			0.102			0.374			0.378			0.035
<1.0	40 (31)	23 (58)		35 (33)	23 (66)		14.4	12 (52)		6.4	16 (40)	
1-9.9	38 (29)	21 (55)		32 (30)	21 (66)		8.6	7 (33)		8.9	13 (34)	
10-99.9	43 (33)	19 (44)		34 (32)	19 (56)		8.0	5 (26)		7.3	9 (21)	
100 or over	10 (8)	2 (20)		6 (6)	2 (33)		-	1 (50)		1.3	2 (20)	
Hemoglobin(gm/dl)			0.574			0.059			0.036			0.149
8 or less	66 (50)	34 (52)		53 (49)	34 (64)		8.6	11 (32)		6.4	19 (29)	
8.1-12.0	57 (43)	26 (46)		49 (45)	26 (53)		13.4	11 (42)		5.0	18 (34)	
>12.0	9 (7)	6 (67)		6 (6)	6 (100)		31.8	4 (67)		33.7	4 (29)	
Platelet ($x10^3/\mu l$)			0.897			0.643			0.607			0.753
20 or less	28 (21)	13 (46)		23 (21)	13 (57)		10.6	4 (31)		3.7	8 (29)	
21-50	56 (42)	30 (54)		46 (43)	30 (65)		13.8	13 (43)		7.9	19 (34)	
>50	48 (36)	23 (48)		39 (36)	23 (59)		8.5	9 (39)		6.1	14 (29)	
BM cellularity (%)			0.244			0.193			0.114			0.017
<90	40 (31)	17 (43)		32 (30)	17 (53)		7.5	6 (35)		3.8	7 (18)	
90 or over	89 (69)	49 (55)		74 (70)	49 (66)		13.4	20 (41)		8.3	33 (37)	
% of BM blast			0.332			0.521			0.039			
<50	41 (32)	23 (56)		33 (31)	23 (70)		15.8	11 (48)		11.4	17 (41)	0.016
50-79	51 (40)	28 (55)		46 (43)	28 (61)		8.5	8 (29)		9.1	15 (29)	
80 or over	37 (29)	15 (41)		27 (25)	15 (56)		8.0	7 (47)		3.8	8 (22)	
FAB subtype			0.638			0.301			0.016			0.448
M0-M2	69 (53)	36 (52)		53 (50)	36 (68)		8.0	10 (28)		7.3	20 (29)	
M3	19 (15)	10 (53)		15 (14)	10 (67)		-	8 (80)		14.2	9 (47)	
M4-M5	33 (25)	17 (52)		30 (28)	17 (57)		8.6	6 (35)		6.4	11 (33)	
M6-M7	9 (7)	3 (33)		8 (8)	3 (38)		13.4	2 (67)		5.6	1 (11)	

*abbreviations: N=number, ind chemo=induction chemotherapy, mo=months, ABC=absolute blast count in the peripheral blood, %Blast=percentage of blast in the peripheral blood, BM=bone marrow

Table 1C. Clinical and pathologic charactersistics of patients in relation to complete remission, complete remission duration, and survival (III)

Variable	Total patients N (%)	CR rate, total patients		Patients given ind chemo N (%)	CR rate among patients given ind chemo		CR duration			Survival		
		N (%)	P		N (%)	P	Median (mo)	N of patients in CR (% of CR)	P	Median (mo)	N of patients surviving (% of total)	P
Albumin (gm/dl)			0.145			0.201			0.153			0.051
3.2 or less	35 (27)	13 (37)		27 (25)	13 (48)		11.2	6 (46)		2.7	6 (17)	
3.3-4.0	58 (45)	32 (55)		47 (44)	32 (68)		8.6	9 (28)		7.9	20 (35)	
)4.0	37 (28)	21 (57)		33 (31)	21 (64)		16.4	11 (52)		9.8	14 (38)	
Total bilirubin (mg/dl)			0.082			0.132			0,971			0.095
1.2 or less	103 (79)	56 (54)		85 (80)	56 (66)		8.6	21 (38)		7.4	33 (32)	
)1.2	27 (21)	10 (37)		21 (20)	10 (48)		13.4	5 (50)		2.7	7 (26)	
AST (IU/dl)			0.660			0.625			0.282			0.975
40 or less	105 (80)	51 (49)		85 (79)	51 (60)		12.8	19 (37)		6.1	31 (30)	
)40	26 (20)	15 (58)		22 (21)	15 (68)		7.3	7 (47)		8.1	9 (35)	
Creatinine (mg/dl)			0.737			0.479			0.565			0.679
1.4 or less	123 (93)	62 (50)		100 (93)	62 (62)		11.2	25 (40)		7.3	39 (32)	
)1.4	9 (7)	4 (44)		8 (7)	4 (68)		7.0	1 (25)		5.0	2 (22)	
LDH (IU/dl)			0.218			0.268			0.257			0.250
2000 or less	68 (76)	40 (59)		59 (76)	40 (68)		12.8	15 (38)		9.8	24 (35)	
)2000	22 (24)	10 (45)		19 (24)	10 (53)		13.5	3 (30)		5.1	5 (23)	
N of cycles of ind chemo until CR									0.797			0.991
1				43 (65)			13.4	17 (40)		16.0	23 (53)	
2				23 (35)			8.5	9 (39)		14.5	11 (47)	
Days from Dx to CR									0.403			0.677
35 or less				33 (50)			10.3	10 (30)		14.3	16 (48)	
)35				33 (50)			11.2	16 (48)		18.8	18 (55)	

*abbreviations: N=number, ind chemo=induction chemotherapy, mo=months, AST=aspartate aminotransferase, LDH=lactate dehydrogenase, Dx=diagnosis

Table 2. Results of leukemia marker studies in relation to complete remission, complete remission duration, and patient survival

Variable	Total patients N (%)	CR rate, total patients		Patients given ind chemo N (%)	CR rate among patients given ind chemo		CR duration			Survival		
		N (%)	P		N (%)	P	Median (mo)	N of patients in CR (% of CR)	P	Median (mo)	N of patients surviving (% of total)	P
TDT			0.751			1.000			0.845			0.560
Yes	12 (11)	5 (42)		8 (9)	5 (63)		8.5	3 (60)		4.9	4 (33)	
No	94 (89)	49 (52)		80 (91)	49 (61)		13.4	19 (39)		6.7	31 (33)	
HLA-DR			0.834			0.464			0.051			0.385
Yes	83 (72)	41 (49)		70 (74)	41 (59)		10.3	14 (34)		6.7	25 (30)	
No	32 (28)	17 (53)		24 (26)	17 (71)		16.4	10 (59)		4.4	12 (38)	
CD2			0.486			0.308			-			0.053
Yes	2 (5)	0 (0)		1 (4)	0 (0)		-	-		1.1	0 (0)	
No	37 (95)	18 (49)		26 (96)	18 (69)		16.4	4 (22)		3.8	9 (24)	
CD5			0.052			0.217			-			(0.001
Yes	5 (8)	0 (0)		2 (4)	0 (0)		-	-		0.7	0 (0)	
No	56 (92)	28 (50)		43 (96)	28 (65)		12.8	8 (29)		7.3	14 (25)	
CD7			0.044			1.000			0.044			0.917
Yes	17 (34)	8 (47)		15 (33)	8 (53)		8.5	4 (50)		9.8	9 (13)	
No	33 (66)	18 (55)		31 (67)	18 (58)		15.8	12 (67)		5.6	13 (39)	
CD 10			0.216			0.267			-			0.023
Yes	2 (5)	0 (0)		1 (4)	0 (0)		-	-		0.8	0 (0)	
No	37 (95)	19 (51)		26 (96)	19 (73)		16.4	6 (32)		5.4	10 (27)	
CD13			0.275			0.777			0.291			0.986
Yes	100 (86)	48 (48)		80 (84)	48 (60)		13.5	21 (44)		6.7	33 (33)	
No	16 (14)	10 (63)		15 (16)	10 (67)		8.6	3 (30)		3.7	4 (25)	
CD 14			0.800			0.786			0.827			0.770
Yes	22 (30)	11 (50)		20 (30)	11 (55)		13.5	5 (45)		6.4	10 (45)	
No	52 (70)	28 (54)		46 (70)	28 (61)		12.8	13 (46)		6.7	18 (35)	
CD 19			0.238			0.152			-			0.050
Yes	2 (2)	0 (0)		2 (2)	0 (0)		-	-		1.2	0 (0)	
No	109 (98)	54 (50)		88 (98)	54 (61)		11.2	22 (41)		6.4	34 (31)	
CD33			0.809			0.432			0.096			0.365
Yes	94 (81)	48 (51)		76 (80)	48 (63)		13.5	23 (48)		6.7	34 (36)	
No	22 (19)	10 (45)		19 (20)	10 (53)		8.6	1 (10)		4.0	3 (14)	
CD 61			0.363			0.298			0.879			0.504
Yes	5 (5)	1 (20)		4 (5)	1 (25)		-	1 (100)		2.5	1 (20)	
No	92 (95)	44 (48)		73 (95)	44 (60)		12.8	18 (41)		5.6	29 (32)	

abbreviations : N=number, mo=months, ind chemo=induction chemotherapy

Table 3. Results of multivariate analyses

Variable	Relative risk(95% CI)			
	Failure to achieve CR		Relapse	Death
	Total patients (N=132)	Patients given ind chemo (N=108)		
Age(yr)				
35 or younger				
36-55	1.09(0.44-6.67)	0.87(0.33-2.29)	0.41(0.16-1.05)	0.80(0.45-1.42)
> 55	3.33(1.22-25.00)*	3.13(1.09-9.01)*	1.12(0.43-2.88)	1.95(1.11-3.43)*
Sex				
Male				
Female	0.42(0.19-0.91)*	0.41(0.18-0.98)*	1.05(0.47-2.33)	0.73(0.47-1.13)
PS				
50 or less				
60	0.32(0.08-1.25)		0.46(0.13-1.68)	0.88(0.46-1.71)
70-80	0.46(0.22-1.19)		0.18(0.05-0.60)*	0.60(0.34-1.08)
90	0.25(0.05-1.18)		0.11(0.01-0.64)*	0.47(0.18-1.23)
WBC($\times 10^3/\mu l$)				
< 1.0				
1.0-99.9	3.23(0.68-16.67)			
100 or over	5.88(0.82-50.00)			
FAB subtype				
M0-M2				
M3			0.19-(0.04-0.88)*	
M4-M5			1.54(0.63-3.76)	
M6-M7			1.77(0.20-15.63)	
% BM blast (%)				
< 50				
50-79				1.40(0.81-2.43)
80 or over				1.86(1.03-3.37)*

* $P < 0.05$

** Abbreviations : CI=confidence interval, ind chemo=induction chemotherapy, yr=year, PS=Karnofsky performance status, % BM blast=percentage of blast in the bone marrow

duration with patients who are over 55 years of age having significantly shorter median durations of CR (5.4 vs 7.8 and 14.4 months, Table 1A). However, after multivariate analysis, the age of the patients was less apparent than performance status of the patients or FAB subtype of AML (Table 3). One of the most obvious factors that may explain poor outcome of elderly AML patients is the inability of many of these patients to withstand the rigors of intensive chemotherapy and its expected complications. Many of these patients may also have subclinical organ dysfunction which may manifest after the stress of chemotherapy. Further studies with larger patient populations are necessary to ascertain whether elderly patients have inherently more chemotherapy resistant leukemia.

Median duration of CR in our study was 11.2 months (Fig. 1) which was comparable to other reported data (Cassileth et al., 1992 ; Wiernik et al., 1992). For the duration of CR, univariate analysis showed that the age of the patients, performance status of the patients, percentage of blast in the peripheral blood, hemoglobin level, percentage of blast in the bone marrow, and FAB subtype were significant variables (Table 1A, 1B, and 1C).

Multivariate analysis showed that performance status of patients and FAB subtype were only independent variables predicting the duration of CR (Table 3). Patients with acute promyelocytic leukemia (APL)(FAB subtype M3) had significantly longer CR duration when compared to other types of AML. In our series, there were 19 cases of APL comprising 14% of all cases of AML. Of 10 patients with APL who achieved CR, only 2 patients relapsed. Median duration of CR has not been reached (Table 1B). It is well known that patients with APL has several distinct clinicopathologic characteristics among patients with AML, which include younger age, lower initial WBC count, bleeding tendency due to disseminated intravascular coagulation, and longer du-

ration of disease free survival (Stone and Mayer 19 90 ; Kim et al., 1993 ; Lee et al., 1994 ;). The results of multivariate analysis in our study suggest that longer CR duration observed in patients with APL is due to inherent biologic nature of the disease and not due to compounding variables such as younger age of patients at the presentation or low initial WBC count.

Median duration of survival of all 132 patients was 6.7 months (Fig. 2). Survival time in our report is shorter than those from reports of chemotherapy trials because of inclusion of patients who were treated with supportive cares only in our study (Berman et al., 1991 ; Cassileth et al., 1992 ; Wiernik et al., 1992). There are two reports which analyzed survival of Korean patients with AML. Ko et al.(19 83) analyzed 141 cases of AML diagnosed between July, 1976 and June, 1980. Mean survival time from the diagnosis was only 0.3 months. Kang et al.(1992) reported median survival time of 3 months among 271 patients with AML seen between January, 1981 to December, 1991. It is interesting to note that the survival times of Korean patients with AML increase over time, which is probably due to the improvement in the quality of chemotherapy and supportive care i.e. antibiotics and transfusion support given to these patients. Earlier diagnosis of AML in the course of the disease may be another factor that explains increasing survival of patients after diagnosis. Univariate analysis in our study showed that the age of the patients, the performance status of the patients, ABC in the peripheral blood, bone marrow cellularity, the percentage of blast in the bone marrow, and CD5 marker positivity were significant variables which predict survival time of patients (Table 1A, 1B, 1C and 2). After the multivariate analysis, the age and the percentage of the blast in the bone marrow remained significant (Table 3).

In our study, 5 to 34% of AML leukemic cells were positive for T cell markers (CD2, CD5, and CD7) and can be classified as biphenotypic. Patients with leukemic cells with these features showed poorer prognosis in our study, which is consistent with the results from other studies (Table 2) (Foon et al., 1986 ; del Vecchio et al., 1989 ; Park et al., 19 91 ; Park et al., 1992). Patients with B cell marker (CD19) positive leukemic cells may also have worse prognosis but this could not be confirmed in our study due to small number of patients. TDT marker positivity did not influence the prognosis of patients with AML.

In conclusion, our study showed that patients with AML have variable duration of survival. The age of patients and the percentage of blast in the bone marrow were the significant independent pretreatment variables which predict survival duration of patients. Further studies utilizing cytogenetic and molecular characteristics of leukemic cells in larger number of patients are warranted to better define the prognostic factors of patients with AML.

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