

Rhabdomyosarcoma in Childhood: A Retrospective Analysis of 190 Patients Treated at a Single Institution

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ABSTRACT

Objectives: The study goal was to retrospectively review the treatment results of childhood rhabdomyosarcoma and identify prognostic factors that affect treatment outcome.

Patients and Methods: The records of 190 patients with childhood rhabdomyosarcoma treated between January 1991 and December 1999 were reviewed. The data were analyzed for clinico-epidemiological factors and the impact of potential prognostic factors on failure-free survival. Factors evaluated were age, gender, histology type, primary site, tumor size, Intergroup Rhabdomyosarcoma Study (IRS) group, surgical procedure, and the use of radiation treatment.

Results: The 5-year actuarial FFS and OS were 40% and 50%, respectively. The only significant prognostic factors as estimated by univariate analysis were histology type ($p=0.01$), primary site ($p=0.002$), tumor size ($p=0.049$), IRS-group ($p=0.003$), surgical procedure ($p=0.002$), and radiation treatment ($p=0.001$). Multivariate analysis showed that histology type ($p=0.02$), primary site, and IRS-group ($p=0.02$) were the only independent prognostic factors.

Conclusions: This analysis demonstrates that failure-free survival for rhabdomyosarcoma is dependent on several factors at the time of initial diagnosis, including histologic subtype, primary site and disease group. Our treatment results were inferior compared to IRS-studies as the patients during this period were treated on individual bases and not standardized protocol.

Key Words: Childhood rhabdomyosarcoma – Prognostic factors – Disease free survival – Chemotherapy – Radiotherapy.

INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma of childhood, representing 5% of all childhood cancers [1-2]. With

approximately 250 cases diagnosed yearly in the United States, it is the third most common extracranial solid tumor of childhood after Wilms' tumor and neuroblastoma. It is thought to arise from primitive mesenchymal cells committed to skeletal muscle differentiation and can occur in a variety of organs and tissues, including those that lack striated muscle [1]. A highly heterogenous tumor, rhabdomyosarcoma has several histologic subtypes and occurs in localized or disseminated forms [3]. Important epidemiologic, biologic, and therapeutic differences have been elucidated within the RMS family. Common sites of primary disease include the head and neck region, genitourinary tract, and extremities.

Because of the relative rarity of this disease, three pediatric cancer study groups joined in 1972 to create the Intergroup Rhabdomyosarcoma Study Group (IRSG), whose protocols now form the backbone of modern treatment for rhabdomyosarcoma throughout the United States [4]. With combined modality therapy (chemotherapy, radiation therapy, and surgery), the overall survival of children with rhabdomyosarcoma has dramatically improved from approximately 25% before 1970 to more than 75% in 2001 (IRSG IV) [5]. Despite aggressive approaches incorporating surgery, dose-intensive combination chemotherapy, and radiation therapy, the outcome for patients with metastatic disease remains poor. Future challenges include the development of less toxic therapy for patients with localized disease and new approaches for patients with metastatic disease.

In this report, we retrospectively reviewed the records of patients with childhood rhabdomyosarcoma treated at the National Cancer Institute, NCI, Cairo University, between 1991 and 1999 with the aim of identifying the prognostic factors, which may affect the treatment results.

PATIENTS AND METHODS

Patient Population:

This work was a retrospective study of the records of 190 pediatric patients with the pathological diagnosis of Rhabdomyosarcoma. They were treated at the National Cancer Institute (NCI), Cairo University, during the period from January 1991 to December 1999. The study population included patients aged 0.1 to 16 years at time of diagnosis. The period of follow-up ranged from 12 to 84 months with a median of 60 months.

Staging and Treatment:

Work-up and recommended staging studies evolved over successive trials and were individualized as a function of primary tumor site. Patients underwent one or, occasionally, more primary surgical procedures to attempt at achieving complete removal of tumor with microscopically clear surgical margins whenever feasible. Recommendations for surgical nodal sampling varied as a function of primary site.

Patients were staged following surgery based on clinically and pathologically determined extent of disease and degree of initial surgical resection, according to criteria of the IRS-clinical staging system (Table 1).

Treatment approaches to RMS incorporated surgery, radiation therapy, and chemotherapy. Radiation therapy is used to control local microscopic or gross residual disease, whereas systemic chemotherapy plays a role in primary cytoreduction as well as eradication of gross and micrometastatic disease.

Surgery: Complete surgical resection was recommended if it was not mutilating or cosmetically damaging. In cases where complete resection was not feasible, initial biopsy followed by neoadjuvant chemotherapy and definitive local control measures were taken.

Chemotherapy: All the patients received chemotherapy. It always started immediately after surgery or as upfront treatment in inoperable or metastatic patients. Many regimens of chemotherapy were utilized in this revised group of patients: VACA (vincristine, Adrimycine, cyclophosphamide, and actinomycine D), cisplatin and etoposide in addition to VACA, VAC, alternating cycles of VAC and IE (ifosfamide and etoposide). The duration of chemotherapy depended upon the stage, histology, and primary site. It ranged from 24 to 48 weeks.

Radiotherapy: It was delivered using megavoltage photon or electron beam. The irradiated volume was the pre surgical and pre chemotherapy tumor volume plus safety margin according to site. The timing of radiation therapy generally allows for chemotherapy to be given for 2 to 3 months (~W9) prior to the initiation of radiation therapy, with the exception of patients with parameningeal disease and/or evidence of meningeal extension in whom radiation therapy generally was started as soon as possible with cessation of the radiosensitizing agent dactinomycin. Patients with primary parameningeal tumors were tested for cranial nerve involvement, examined for evidence of meningeal involvement by computed tomography or magnetic resonance imaging, and underwent cytologic examination of CSF. Patients who had intra-cranial parameningeal disease without evidence of meningeal involvement received RT to the primary tumor plus a 2-cm margin.

Girls with genitourinary primaries should have their ovaries shielded, or possibly moved prior to radiation to the pelvis.

Definition of End Points and Statistical Methods:

End points for this analysis were overall survival (OS) and failure-free survival (FFS), calculated with the Kaplan-Meier method [6]. FFS was defined as time from start of treatment to first progression, relapse after response, or death from any cause. Overall survival was defined as the time from the start of treatment to death from any cause. Comparison of survival curves for different patient groups was performed with log-rank analysis [7]. Multivariate analysis was conducted with the Cox proportional hazards model. A p value ≤ 0.05 was considered statistically significant. Descriptive

statistics were presented as number and percentage (frequency distribution).

RESULTS

Patient or Tumor Characteristics:

Table (2) shows tumor and patients characteristics. The male to female ratio was 1.5:1. The age incidence of children at presentation varied between 0.1-16 years with a median age of 6 years and sixty percent were below the age of 10 years. As regards histological subtypes, the embryonal variant was the most frequent as it constituted 62% (n=118) of all cases. When analyzing the relation between histology type and primary site, we found that the orbit was the most common site of embryonal histology (27/118). The alveolar type was mainly seen in the extremities (14/31) (Table 3). The most commonly affected primary sites were head and neck (42%, n=80), trunk (15%, n=29) and extremities (15%, n=28). The orbit was the most frequent sub site and accounted for 17% (n=32). Only 30% of the patients underwent wide local or radical surgery, while seventy percent of the patients underwent only incisional or excisional biopsy. Large tumor size (>5cm) presented in 53% of cases. Lymph node involvement was absent in 80% of cases, 15% had positive LNs and in 5%, the LN status was unknown. According to the IRS grouping system, Clinical Group (CG) III was the most frequent presentation (67%).

Treatment Administered:

- 1- *Chemotherapy:* All patients received chemotherapy either radical or palliative. As shown in table (4), different regimens were used. The most common regimen used was VACA, Cisplatin, Etoposide (42%, n=80). This regimen was mostly used in stages III and IV.
- 2- *Radiotherapy:* About 63% of cases received radiation treatment, either postoperative, radical, preoperative or palliative (Table 5). The total dose differed according to the aim of radiation treatment. It was 40-50Gy in postoperative cases, 50-60Gy in radical cases and 30Gy for palliation. The dose per fraction ranged from 150cGy to 200cGy according to site and treatment volume. The overall radiation treatment time varied from less than 4 weeks up to 9 weeks with non-intended gap more than a week in 15% of patients.

Treatment Outcome:

At a median follow up of 60 months, the 5-year FFS for these patients was estimated to be 40% (95% CI 33%-48%) (Fig. 1). The 5-year overall survival was estimated to be 50% (95% CI 40% to 62%) (Fig. 2). Seventy-two failures (35 local and 37 distant) were observed among these 190 patients (Table 6).

Local Treatment Failure:

Overall, 35 of 173 patients with non metastatic disease at presentation (20%) developed local recurrence (15 patients had simultaneous distant recurrence). The lower extremity site was the most common primary site suffering from local recurrence (36%). As regards pathological type, the alveolar type was the most common type which showed local recurrence (50%) compared to non specified rhabdomyosarcoma (0%) and botryoid type (3%). Tumor size ≤ 5 cm was associated with lower incidence of local recurrence (14%) compared to tumor size > 5 cm (22%). In patients with IRS groups' I-III, local recurrence developed in 28 of 128 patients (22%) with group III, in 5 of 27 patients (19%) with group II and in 2 of 18 patients (11%) with group I. Local recurrence developed in 22 of 72 patients (31%) who did not have radiotherapy as compared to only 13 of 118 patients (11%) who did receive radiotherapy.

Distant Treatment Failure:

Overall distant metastasis developed in 20% of patients. The lung was the most common site for distant treatment failure (62%) (Table 7). As shown in table (6), lower extremity patients had the highest distant treatment failure rate (43%). Histological subtype had a significant effect on distant treatment failure. Patients with botryoid and embryonal subtypes had the lowest rate of distant treatment failure (6% and 17%, respectively), whereas patients with alveolar rhabdomyosarcoma had the highest rate (45%). Distant treatment failure was more frequent in patients with tumor size > 5 cm (24%) compared with patients with tumor size ≤ 5 cm (14%). In patients with IRS groups I-III, distant treatment failure was found in 30 of 128 patients (23%) with group III, in 5 of 27 patients (19%) with group II and in 2 of 18 patients (11%) with group I. Patients who received radiotherapy developed a lower rate of distant metastasis (18%) compared to those who did not (22%).

Prognostic Factors Associated with FFS:

The actuarial 5-year FFS rates according to age, gender, histology type, primary site, tumor size, IRS-group, LN involvement, surgical procedure, radiation treatment are detailed in table (8). The only significant prognostic factors as estimated by univariate analysis were histology type ($p=0.01$), primary site ($p=0.002$), tumor size ($p=0.049$), IRS-stage ($p=0.003$), extent of surgery ($p=0.002$), and radiation treatment ($p=0.001$).

Multivariate analysis showed that histology type ($p=0.02$), primary site, and IRS-stage ($p=0.02$) were the only independent prognostic factors affecting FFS. As regards the histologic type, the estimated 5-year FFS rate for patients with botryoid type was 80%; embryonal, 50%; pleomorphic, 35%; alveolar, 15% (Fig. 3).

According to the primary site of disease, the 5-year FFS was 85% for GU-non BP, 55% for orbital site, 50% for non-orbital non-parameningeal sites, 50% for GU-BP, 42% for extremity, 38% for trunk and 12% for retroperitoneal tumors.

IRS-group was also a prognostic factor with an estimated 5-year FFS rates: Stage I, 65%; stage II, 60%; stage III, 35%; stage IV, 10% (Fig. 4).

Table (1): IRS-post surgical grouping classification [8].

Group I	<i>Localized disease, completely resected, no microscopic residual:</i>
	A- Confined to site of origin
	B- Infiltration beyond site of origin
Group II	<i>Total gross resection:</i>
	A- Grossly resected tumors with microscopic residual tumor
	B- Regional disease, completely resected, with nodes involved, and/or tumor extension into an adjacent organ
	C- Regional disease with involved nodes, grossly resected, but with evidence of microscopic residual tumor
Group III	Incomplete resection or biopsy with gross residual
Group IV	Distant metastases present at onset

Table (2): Distribution according to patient and tumor characteristics.

	Number (%)
<i>Sex:</i>	
Male	114 (60%)
Female	76 (40)
<i>Age groups:</i>	
0.1-3 years	30 (16%)
4-6 years	49 (26%)
7-9 years	35 (18%)
10-12 years	28 (15%)
13-16 years	48 (25%)
<i>Histological subtype:</i>	
Embryonal	118 (62%)
Alveolar	31 (16%)
Pleomorphic	19 (10%)
Botryoid	13 (7%)
Non specified	9 (5%)
<i>Site:</i>	
Orbit	32 (17%)
Non orbit non parameningeal	29 (15%)
Parameningeal	19 (10%)
Trunk	29 (15%)
Retroperitoneum	19 (10%)
Extremities	28 (15%)
GU B/P	11 (6%)
GU non-B/P	23 (12%)
<i>Tumor size:</i>	
≤ 5 cm	90 (47%)
> 5 cm	100 (53%)
<i>LN-status:</i>	
Negative	152 (80%)
Positive	28 (15%)
Unknown	10 (5%)
<i>IRS-Group:</i>	
I	18 (10%)
II	27 (14%)
III	128 (67%)
IV	17 (9%)
<i>Treatment modality:</i>	
Chemo-radiotherapy	118 (62%)
Chemotherapy alone	72 (38%)
<i>Surgical procedure:</i>	
Incisional or excisional biopsy	133 (70%)
Radical	57 (30%)

GU B/P (genitourinary tract; B/P, bladder/prostate).
GU non-B/P (Para testicular, vagina, ovary, uterus).

Table (3): Relation between pathological type and primary tumor site.

Site	Embryonal	Botryoid	Alveolar	Pleomorphic	Non specified	Total
Orbit	27	1	1	2	1	32
Non orbit non parameningeal	14	1	6	5	3	29
Parameningeal	15	0	2	1	1	19
Trunk	18	0	3	5	3	29
Retroperitoneum	12	0	3	3	1	19
Extremity	13	0	14	1	0	28
GU B/P	6	4	1	0	0	11
GU non-B/P	13	7	1	2	0	23
Total	118	13	31	19	9	190

GU B/P (genitourinary tract; B/P, bladder/prostate).

GU non-B/P (Para testicular, vagina, ovary, uterus).

Table (4): Distribution of patients according to chemotherapy regimen.

Chemotherapy	Number (%)
VACA, Cisplatin, Etoposide	80 (42)
VAC	35 (18)
VACA	28 (15)
VAC/IE	22 (12)
VA	25 (13)
Total	190 (100)

Vincristine (V). Adriamycine (A). Cyclophosphamide (C). Actinomycine D (A). Ifosfamide (I). Etoposide (E).

Table (5): Distribution of patients according to radiation treatment.

Radiotherapy	Number (%)
Post operative	68 (36)
Radical	38 (20)
Palliative	9 (5)
Preoperative	3 (1)
No radiotherapy	72 (38)
Total	190 (100)

Table (6): Patterns of treatment failure in all patients.

Variables	Local relapse Number (%)	Distant metastases Number (%)
<i>Site:</i>		
Orbit	3 (9)	1 (3)
Non orbit non parameningeal	7 (24)	3 (10)
Parameningeal	3 (16)	4 (21)
Trunk	8 (28)	8 (28)
Retroperitoneum	2 (11)	5 (26)
Extremity	10 (36)	12 (43)
GU-BP	1 (9)	1 (9)
GU-NBP	1 (4)	3 (13)
<i>Pathological types:</i>		
Embryonal	20 (17)	20 (17)
Botryoid	1 (3)	2 (6)
Alveolar	10 (50)	9 (45)
Pleomorphic	4 (31)	4 (31)
Non specified	0 (0)	2 (22)
<i>Tumor size:</i>		
≤ 5 cm	13 (14)	13 (14)
> 5 cm	22 (22)	24 (24)
<i>IRS-group:</i>		
I	2 (11)	2 (11)
II	5 (19)	5 (19)
III	28 (22)	30 (23)
<i>Modality of treatment:</i>		
Chemotherapy alone	22 (31)	16 (22)
Chemo-radiotherapy	13 (11)	21 (18)

GU B/P (genitourinary tract; B/P, bladder/prostate).

GU non-B/P (Para testicular, vagina, ovary, uterus).

Table (7): Sites of distant metastasis.

Site of relapse	Number (%)
Lung	23 (62.0)
Bone	5 (14.0)
Liver	4 (12.0)
Brain	1 (3.0)
Lung and liver	2 (6.0)
Lung and bone	2 (3.0)
Total	37 (100)

Table (8): Prognostic factors estimation by univariate analysis.

Variables	% 5-yr FFS (95% CI)	Significance
<i>Age:</i>		
<6 years	45 (25-65)	NS
≥6 years	36 (21-56)	
<i>Gender:</i>		
Male	39 (21-60)	NS
Female	45 (25-64)	
<i>Histological subtype:</i>		
Botryoid	80 (69-94)	S <i>p</i> <0.01
Embryonal	50 (30-74)	
Pleomorphic	35 (18-51)	
Alveolar	15 (5-24)	
Non specified	20 (5-35)	
<i>Site:</i>		
Orbit	55 (34-77)	S <i>p</i> <0.002
Non orbit non parameningeal	45 (27-75)	
Parameningeal	40 (25-57)	
Trunk	35 (21-60)	
Retroperitoneum	12 (1-25)	
Extremity	30 (20-66)	
GU-NBP	80 (78-93)	
GU-BP	50 (25-77)	
<i>T-stage:</i>		
T1 ≤ 5 cm	51 (27-74)	S <i>p</i> <0.049
T2 > 5 cm	30 (12-52)	
<i>LN involvement:</i>		
Negative	52 (28-77)	NS
Positive	35 (25-47)	
<i>IRS-group:</i>		
I	65 (44-85)	S <i>p</i> <0.003
II	60 (50-73)	
III	35 (22-50)	
IV	10 (1-20)	
<i>Surgical procedure:</i>		
Non radical (incisional or excisional bx)	29 (15-46)	S <i>p</i> <0.002
Radical	52 (25-76)	
<i>Treatment modality:</i>		
Chemotherapy alone	26 (18-42)	S <i>p</i> <0.002
Chemo-radiotherapy	54 (22-79)	

S : Significant *p*≤0.05.
NS : Insignificant.

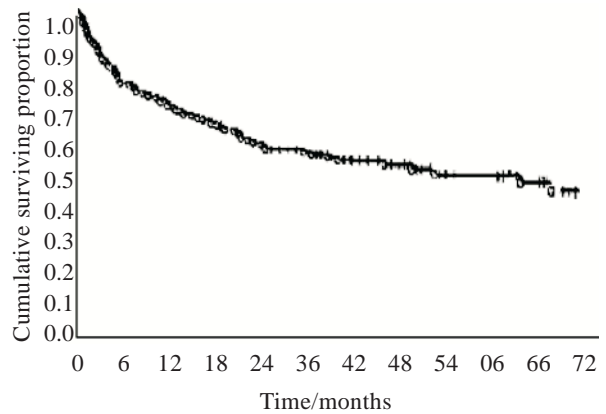


Fig. (1): Failure-free survival for all patients.

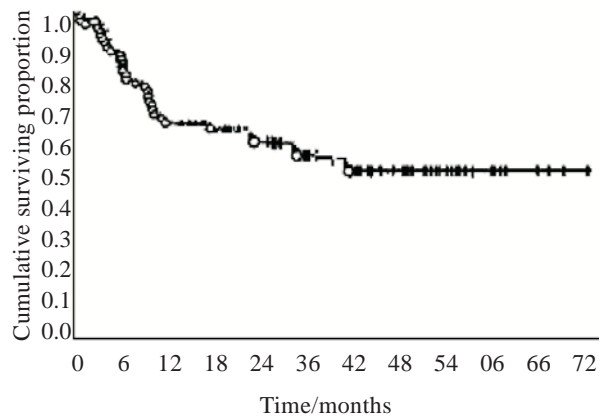


Fig. (2): Overall survival for all patients.

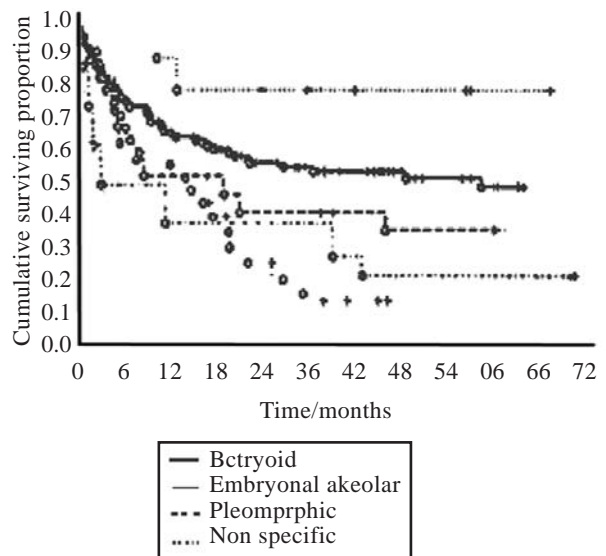


Fig. (3): Failure-free survival according to histology subtype.

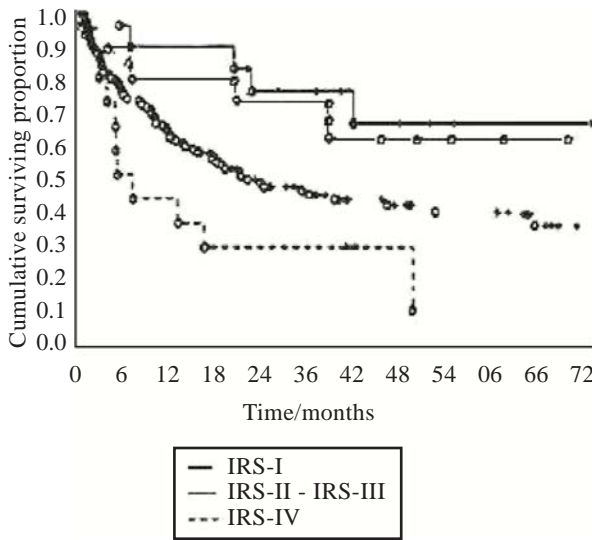


Fig. (4): Failure-free survival according to IRS-group.

DISCUSSION

Rhabdomyosarcoma is one of the most common soft tissue sarcomas of childhood, as it constitutes 5-8% of all childhood malignancies [1]. In the National Cancer Institute, Cairo University, soft tissue sarcomas represent 3.75% of total malignancy and 26.7% of those occurring in the pediatric age group. Soft tissue sarcomas are the second common malignancy after lympho-hemopoietic malignancies in pediatrics. Rhabdomyosarcoma, fibrosarcoma and malignant fibrous histiocytoma are the most common 3 sarcomas representing 24%, 18.4%, and 15.7%, respectively [9].

In our study, the male to female ratio was 1.5:1. In the IRS-IV, the male to female ration was 1.6:1 [5]. The median age of patients was 6 years and sixty percent were below the age of 10 years. This was similar to that reported in IRS-IV study where 70% of cases were below 10 years and the median age was 5 years [5].

The most frequent site was the head and neck region, which accounted for 42% (orbit 17%, non orbit non parameningeal (16%), and parameningeal (9%). This was comparable to a Turkish study, where the head and neck region was the most frequent site (49%) [10]. In the IRS-III, the orbit constituted 10%, non orbit non parameningeal 10% and parameningeal 15% [11].

Embryonal RMS was the most frequent histological subtype in our study (62%). In IRS-

V, the embryonal variant accounted for 70% of cases [5], and it presented 56% in IRS-I [8]. The embryonal variant accounted for 70% of the head and neck region. Similarly, it represented 72% in IRS-I [8]. The embryonal variant including the botryoid type was also prevalent in genitourinary sites (88%). It was 79% in IRS-I [8] and 72% in the study reported by Wijnaedt et al. [12].

As regards the extent of surgery, 70% of the patients had only a biopsy either incisional or excisional. This was similar to IRS-II study, where 64% of the patients had only a biopsy [13]. Tumor size >5cm was more frequent in our study (52%) and this was similar to that of IRS-IV in which 51% of tumors were >5cm [5]. CG III was the most frequent stage in our group of patients as it constituted 66% of cases which was similar to that reported in IRS-IV trial (62%) [5] and was different from findings in IRS-III (55%) [11]. This reflected that most of our patients presented with advanced disease.

Five-year overall survival (OS) and failure-free survival (DFS) were 50% and 40%, respectively, in our study. These results are inferior to the results of IRS-studies; 5-year event-free survival (EFS) was 55% in IRS-I [8], 63% in IRS-II [13], 65% in IRS-III [11], and improved to 76% in IRS-IV [5]. This can be explained by improvement of early diagnosis, staging work-up and better chemotherapy regimens. In a prospective trial done recently in our NCI, Mehani [14] treated 45 patients with non metastatic RMS according to SIOP 75. The 2-year OS and DFS rates were 79% and 51%, respectively. The results of SIOP (MMT89) was less than IRS-IV, whereas the 5-year OS and EFS were 71% and 57%, respectively [15].

On multivariate analysis, we found that primary site, histology, and IRS-group were independent prognostic factors affecting FFS. These factors were in agreement with other published reports [5,8,10,13,15].

Patients with GU-non BP had the best 5-year FFS (85%) while extremities, trunk and retroperitoneal sites had the worst results which are attributed to advanced disease at presentation and predominance of unfavorable histology as alveolar subtype which constituted more than half the tumors in these sites. In IRS-III, 5-year FFS was 84% for genitourinary (non bladder

non prostate) sites. On the other hand, extremities showed better results than our study as the 5-year-FFS was: 47% in IRS-I [8], 43% in SIOP [16] and 66% in IRS-III [11]. In our study, the 5-year FFS for orbital site was 50%. This result was similar to the 5-year EFS (53%) of SIOP (MMT89) [15] and inferior to that reported in other series as it was 91% in the final report of IRS-I and II [17] and 93% in IRS-IV [5]. This is attributed mainly to the unfavorable predominance of large tumors and more advanced disease stage in our patients.

Histological variant is a strong prognostic factor. Patients with favorable histological subtypes as botryoid and embryonal showed 5-year FFS of 80% and 50%, respectively, while unfavorable histological variants as pleomorphic and alveolar showed 5-year FFS of 32% and 12%, respectively. Comparing the results to IRS-II, the 5-year FFS was 65% for botryoid, 64% for embryonal, 51% for pleomorphic and 53% for alveolar type [13]. Patients with embryonal rhabdomyosarcoma have not always enjoyed excellent survival in IRS studies. Those patients with unfavorable primary sites who received IRS-I/II therapy had significantly higher distant treatment failure rates as compared with those with favorable primary sites. Changes in systemic therapy on IRS-III/IV led to significant decreases in distant relapse rates with improved cure rates. The most significant improvement was on the most recent IRS-IV study [5], in which chemotherapy for patients with embryonal histology tumors was changed from primarily two-drug therapy with VA to three-drug regimens (VAC/VA - ifosfamide/VI - etoposide) using cyclophosphamide (Cytosan; Bristol-Myers Squibb Co, Princeton, NJ) ($2.2\text{g}/\text{m}^2$) or the ifosfamide equivalent. With these changes, 97% of patients were alive at 5 years, and the negative influence of unfavorable primary site in outcome disappeared.

When prognosis was analyzed by IRS-group, patients with group I or II tumors fared better than those with group III or IV tumors ($p < 0.003$). The 5-year FFS of group I, II was 65%, which was lower than reported in IRS-I (group I 80% and group II 72%) [8], in IRS-II (group I 80% and group II 74%) [13] and in IRS-III (group I 83% and group II 77%) [11]. In the IRS-IV study, they reported the 3-year FFS for group I and II as 82% and 86% respec-

tively [5]. Patients with group III constituted the majority of our patients and they had low 5-year FFS (36%). The 3-year event-free survival (EFS) for stage III in SIOP (39%) was in agreement to our results [16]. On the other hand, this group of patients who enrolled in IRS clinical trials benefited from more intensified therapy and the 5-year FFS was 48%, 58%, 66% in IRS-I, IRS-II and IRS-III, respectively [11]. In IRS-IV, group III achieved better results with 3-year FFS of 73%. The presence of metastatic disease is the strongest predictor of clinical outcome in patients with RMS. The 5-year FFS in our study was 10%. In IRS-IV, despite aggressive multimodality treatments, these children fared poorly; only 25% were free of disease 3 years after diagnosis. They showed more favorable results if they had two or fewer metastatic sites and embryonal histology. This favorable subset of patients had outcomes approaching those observed in selected patients with localized, non metastatic disease [5]. Similarly, analysis of another series of patients with metastatic RMS from the European Cooperative Group Studies found favorable outcomes in subsets of patients with metastatic disease [18]. The overall FFS in those patients was only 15% but was better in patients with GU-NBP primary sites (50%) and in those who had single rather than multiple sites of metastasis. Embryonal histology also was associated with improved survival in that series.

Patients who did not receive radiation treatment fared poorly than patients who did receive radiation treatment (5-year FFS was 32% vs. 51% respectively). The use of radiotherapy has been investigated for patients with RMS in all IRS-studies. They came to the conclusion that radiotherapy improves FFS and OS in CG II and III. In CGI, RT is not recommended except for unfavorable histology (alveolar and undifferentiated). On IRS-I and II, patients with alveolar or undifferentiated sarcoma who received RT compared with those who did not receive RT had greater 10-year FFS rates (73% v 44%, respectively; $p < 0.03$) and overall survival rates (82% v 52%, respectively; $p < 0.02$).

Conclusion:

Rhabdomyosarcoma is a heterogeneous disease that may arise in virtually any organ or tissue except bone. Meticulous diagnostic imaging of both the primary tumor and sites of

potential local, regional, and distant metastatic spread is crucial to the selection of appropriate therapy. Our treatment results were inferior compared to IRS-studies as the patients were treated on individual bases and not standardized protocol. Treatment according to the results of IRS-IV would achieve better results.

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