ORIGINAL ARTICLE

Childhood orbital rhabdomyosarcoma: Report from Children's Cancer Hospital-57357-Egypt

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Abstract

Background: Rhabdomyosarcoma (RMS) in the head and neck especially orbit represents a major anatomic site for this tumor in pediatrics. Orbital RMS is the most common primary orbital malignancy in children with approximately 35 new cases per year.

Objectives: The aim of this work is to study cases of orbital RMS and assess epidemiology, clinical and pathological characteristics as well as survival outcomes.

Methods: Patients diagnosed with orbital RMS between July 2007 and July 2012 follow-up till July 2014. They were treated according to IRS-IV and IRS V protocols. Case report forms were analyzed and treatment outcome, OS and FFS for patients were analyzed.

Results: Seventeen orbital RMS patients were diagnosed at the mentioned period. Complete remission was identified in 7 (41.2%) cases, Partial remission in 4 (23.5%) cases and progressive disease in 4 (23.5%) cases while 2 cases died before evaluation. Three patients had experienced different management-related ophthalmic sequelae. Only one patient died due to chemotherapy-associated toxicity. The 4-years OS and 4-years FFS were 94.1 ± 5.7% and 65.4 ± 1.5% respectively.

Conclusion: The current study demonstrated that RMS cases that present with orbit involvement are associated with better clinical outcome. Future treatment of patients with non-metastatic orbital RMS will focus on adjustments in therapy to reduce acute and late adverse effects while maintaining their excellent treatment outcome. New therapeutic approaches are required for the patients whose present outcome is less than optimal.

Key words

Orbital rhabdomyosarcoma, Clinical outcome, Sarcoma prognostic significance

1 Introduction

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma of childhood, representing 5% of all childhood cancers [1]. It represents 4% of all solid tumors in children. Orbital RMS is the most common primary orbital malignancy in children with approximately 35 new cases per year [2].

Primary Orbital RMS is mainly a disease of young children, where 90% of cases present before the age of 16 years old. The mean age of onset is 5-7 years old [3]. Orbital RMS usually presents as a space-occupying lesion in the orbit during the first decade and may mimic other neoplastic or inflammatory masses [4]. While presentation within this age group is the most common, case reports have documented newborns and elderly patients with orbital RMS. There is a slight male to female predilection with a male: female ratio of 5:34. Primary orbital RMS involves the orbit, eyelid, conjunctiva, or rarely, the uveal tract. Additionally, RMS can directly extend to orbit from the paranasal sinuses or nasopharynx and infrequently, metastasize to the orbit from distant sites.

The typical presentation for primary orbital RMS is the rapid onset of unilateral proptosis and inferior or inferiotemporal displacement of the globe. Otherwise, patients may have a history of worsening eyelid edema and erythema, chemosis, ophthalmoplegia, blepharoptosis, or a palpable mass [1].

Paranasal sinus RMS with secondary orbital invasion frequently presents similar to primary orbital RMS but with additional symptoms including nasal or sinus congestion and epistaxis. Rarely, nasopharyngeal RMS can invade the orbital apices with resultant rapid, bilateral visual loss secondary to optic nerve compression.

The orbit is a favorable site which occasionally is in the form of embryonal variant [3]. Other institutional soft tissue sarcoma study team has recommended utilizing the preoperative tumor, node, metastasis (TNM) classification system to aid in the staging of RMS. The best diagnostic aid is a high index of suspicion whenever one sees a rapidly progressive exophthalamos in a child. Orbital RMS is almost always of the embryonal type, believed to originate in the orbital soft tissues from undifferentiated pluripotential embryonic mesenchyme [5].

Metastatic spread of orbital RMS is uncommon, however if left untreated has a tendency to metastasize to the lung, bone and bone marrow mainly via hematogenous spread (because orbital lymphatics are scarce). Locally, orbital RMS can invade the orbital bones and can extend intracranially. Metastatic orbital RMS has an unfavorable prognosis when compared to localized disease; however in a joint European-North American pooled analysis orbital site proved to be favorable [3].

The intensity of treatment depends on the estimated relapse risk, thus treatment is risk adapted. Extent of disease, primary tumor site, clinical group and histology has been associated consistently with prognosis.

Patients with nonmetastatic RMS have an overall survival rate of about 71% with combined modality therapy (chemotherapy, radiation therapy, and surgery). The prognosis of children with RMS is determined by clinical group, stage, histology, and age at presentation [3].

Histopathology also plays an important role in prognosis. It is classified according to histopathology into embryonal and alveolar subtypes with the embryonal subtype being of better prognosis. There is a definite survival advantage to the embryonal variant compared to the alveolar variant of orbital RMS. A review of orbital RMS in the IRSG studies show a 94% and 74% 5-year survival for the embroyonal and alveolar variants, respectively. Orbital RMS presenting in infants less than one year of age follows a more aggressive course with poor survival rates of 54% Survival rates for paranasal RMS that secondarily invades the orbit is considered lower than for primary orbital RMS. Survival of orbital RMS has improved due to advances in chemotherapy and radiotherapy. Post treatment complications, including side effects of radiotherapy and secondary orbital malignancies, as well as visual dysfunction, occur more often and present new challenges due to improved long-term survival [6].

Although most of the orbital RMS cases are referred initially to ophthalmologist; its management necessitates cooperation between multiple teams including pediatric oncology, radiation therapy, radiology, ophthalmology and surgery.

The aim of this work is to study orbital RMS and different risk factors. Assess epidemiology, clinical presentation, and pathological subtype to the treatment outcome. The outcome was studied based on Overall Survival (OS) and Failure Free Survival (FFS).

2 Methods

2.1 Patients

This is a retrospective study representing first five years' experience with newly diagnosed orbital RMS patients presented at the Children's Cancer Hospital during the period from July 2007 till July 2012. Patients were followed up till July 2014. Informed consent was obtained at presentation from the parents/guardians of all children who were treated on this protocol.

Investigations at diagnosis included the following: physical examination, evaluation of local tumor extent with computerized tomography (CT), and/or nuclear magnetic resonance imaging (MRI). CT and MRI images are fundamental in the preoperative evaluation to determine location and size, but they are also important in evaluating residual or recurrent disease [7, 8]. Particular attention should be given to the presence of bone erosion and intracranial extension. Assessment of the metastatic lesions was done by conventional chest CT scan, bone scan, and bone marrow aspirates/biopsy, PET/CT. CSF analysis was done in parameningeal lesions.

Pathological and immunohistological studies:

Pathological studies were done for every patient and initial consultation of surgery for complete resection if feasible and none mutilating versus biopsy. In all patients, histological sections were prepared from formalin-fixed paraffin embedded tissue and stained with hematoxylin and eosin, and a marker study using desmin and myogenin markers was done. Histopathology was determined as embryonal (including spindle cell and botryoid subtypes), and non-embryonal histology that included alveolar subtype.

Staging and classifications:

Classification was done based on the Intergroup Rhabdomyosarcoma Study (IRS) pretreatment TNM staging and surgical grouping system shown in Tables 1 and 2. Histology was determined as embryonal (including spindle cell and botryoid subtypes), and non-embryonal histology that included alveolar subtype. The site was assigned as a favorable site as we reported only orbital RMS.

Table 1. Intergroup Rhabdomyosarcoma TNM Staging Classification

Stage	Sites	T-invasiveness	T-size	N	M
1	Orbit, Head and neck*, Genitourinary#	T1 or T2	a or b	N0 N1 or Nx	M0
2	Bladder/prostate, Extremity, Cranial parameningeal, Other†	T1 or T2	a	N0 or Nx	M0
3	Bladder/prostate, Extremity, Cranial parameningeal, Other†	T1 or T2	a b	N1 N0 N1 or Nx	M0
4	All	T1 or T2	a or b	N0 or Nx	M1

Note. T (tumor): T1, confined to anatomic site of origin; T2, extension; a≤ 5 cm in diameter; b>5 cm in diameter. N (regional nodes): N0, not clinically involved; N1, clinically involved; Nx, clinical status unknown. M (metastases): M0, no distant metastases; M1, distant metastasis present.

*Excludingparameningeal.#Non bladder-non prostate.†Includes trunk, retroperitoneum, *etc*.

Table 2. Intergroup Rhabdomyosarcoma Clinical Group Stage System

Clinical Group	Extent of Disease and Surgical Result
IA	Localized tumor, confined to site of origin, completely resected
B	Localized tumor, infiltrating beyond site of origin, completely resected
IIA	Localized tumor, gross total resection, but with microscopic residual disease
B	Locally extensive tumor (spread to regional lymph nodes), completely resected
C	Extensive tumor (spread to regional lymph nodes), gross total resection, but with microscopic residual disease
IIIA	Localized or locally extensive tumor, gross residual disease after biopsy only
B	Localized or locally extensive tumor, gross residual disease after major resection (= 50% debulking)
IV	Any size primary tumor, with or without regional lymph node involvement, with distant metastases, irrespective of surgical approach to primary tumor

2.2 Treatment

The global strategy for nonparameningeal RMS remained fairly uniform over time. Initial surgery was only recommended for small orbital tumors when complete resection was expected, especially for eyelid primaries. For all other tumors, biopsy was mandatory at diagnosis. Baseline strategy consisted of first-line neo-adjuvant chemotherapy to reduce tumor volume and evaluate tumor response.

Therapy was assigned based on the COG- IRS-IV and VRMS risk group classification. Ten patients were enrolled on IRS-IV while 7 were enrolled on IRS-V.

Orbital RMS Patients were classified according to the stage, clinical group and histological subtype into:

Cases assigned to IRS-IV classified into low and high (10 cases).

Low risk group: Included patients with embryonal RMS or botryoid who had: Non-metastatic tumors, clinical group I, II, or III (orbital cases without parameningeal extension).

High risk group: Included orbital cases with parmeningeal extension, orbital cases with unfavourable histology (alveolar type) or metastatic patients with stage IV.

Cases of orbital RMS assigned to study based on COG study IRS-V (7 cases)

a) Low risk group: Included patients with embryonal RMS or botryoid who had: Non-metastatic tumors, clinical group I, II, or III(orbital cases without parameningeal extension)

b) Intermediate risk group: Included patients with: Alveolar RMS, Non-metastatic tumors, clinical group I, II, or III or embryonalor orbital cases with parameningeal extension clinical group II and III

c) High risk group: Included all metastatic patients with stage 4

2.3 Chemotherapy

Treatment protocol for low risk patients based on IRS-IV shown in Table 3 while intermediate and high risk group based on IRS-IV (see Table 4).

Table 3. Roadmaps for RMS treatment

Weeks	1	2	3	4	5	6	7	8	9	10	11	12	13
	VAC	V	V	VAC	V	V	VAC	V	V	AC	**	**	VA
Weeks	14	15	16	17	18	19	20	21	22	23	24	25	26
	V	V	VA	V	V	VA	V	V	A	**	**	VA	V
Weeks	27	28	29	30	31	32	33	34	35	36	37	38	39
	V	VA	V	V	VA	V	V	A	**	**	VA	V	V
Weeks	40	41	42	43	44	45	46	47					
	VA	V	V	VA	V	V	VA	**					

Note. Vincristine (V): 1.5 mg/m^2 (max. 2 mg) IV push. Actinomycin (A): 0.045 mg/kg (max. 2.5 mg) IV push. Cyclophosphamide (C): 1.2 mg/m^2 IV infusion over 60 min with hydration and MESNA.

*give (A) before radiation therapy. ** omit week 16, 19 (A) during radiation therapy.

Table 4. Roadmaps for IR and HR RMS treatment

Weeks	0	1	2	3	4	5	6	7	8	9	10	11	12
	VAC	V	V	VAC	V	V	VAC	V	V	VAC	V	V	VAC**
Weeks	13	14	15	16	17	18	19	20	21	22	23	24	25
	---	---	VC	---	---	VC	V	V	V	VAC	V	V**	VAC
Weeks	26	27	28	29	30	31	32	33	34	35	36	37	40
	V	V	VAC	---	---	VAC	V	V	VAC	V	V	VAC	**

Note. Vincristine (V): 1.5 mg/m^2 IV push. Actinomycin (A): 1.35 mg/m^2 IV push. Cyclophosphamide (C): 1.5 mg/m^2 at weeks 0 and 3 to be increased to 1.8 mg/m^2 if tolerated, given IV infusion over 2 hours with MESNA and fluids.

*give (A) before radiation therapy. ** omit week 16, 19 (A) during radiation therapy.

2.4 Local control

Most of cases in our study received local control in the form of radiotherapy.

2.5 Radiotherapy

Timing of radiotherapy varied according to protocol used and according to risk criteria. Patients were scheduled to protocol based on IRS IV received radiotherapy at W12 in addition to high risk and low risk patients scheduled for protocol based on IRS V. Only patients' intermediate risk based on IRSV received raditherapy in W4.

The gross tumor volume (GTV) was defined as the pre-treatment visible and for palpable disease detected by physical examination, operative findings, CT or MRI including any involved lymph nodes. For all clinical groups, the clinical target volume (CTV) was defined by adding one cm safety margin to GTV. Those who have clinical group III disease who do not undergo a second look operation may have a second CTV defined for a core down boost. The planning tumor volume (PTV) is created by adding safety margins that deals with the setup position uncertainties. Clinical group II without nodal involvement received 36 Gy, while those with nodal involvement (N1) received 41.4 Gy. Clinical group III received 45 Gy. Patients received radiotherapy to metastatic sites which can be localized and imaged (*i.e.* excluding the bone marrow).

2.6 Surgery

Cases were assessed initially by surgery to assess respectability and improve clinical grouping. We did not encourage in our study the second look surgery.

2.7 Evaluation criteria

Complete Response (CR): complete disappearance of the tumor confirmed at > 4 weeks

Partial Response (PR): at least 64% decrease in volume compared to the baseline

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Progressive Disease (PD): at least 40% increase in tumor volume compared to the smallest measurement obtained since the beginning of therapy

Stable Disease (SD): neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD taking as reference the smallest disease measurement since the treatment started

Relapse/recurrence(R): appearance of new lesions or reappearance of old lesions for patients in CR

2.8 Data management and statistical analysis

Study data were collected and managed using REDCap electronic data capture tools hosted at Children's cancer hospital - Egypt.

Patients' demographics and initial data were analyzed using SPSS statistical package (20) for Windows. Qualitative data were expressed as frequency and percentage, while quantitative data were expressed as mean ±SD and median. The chi-square test and Fisher Exact test were used for comparative analysis. Statistically significant level was considered at $p \leq .05$.

Survival estimates were calculated using the Kaplan-Meier. The differences between curves were tested for statistical significance using the log rank test.

FFS was defined as the time from the start of treatment to disease progression, recurrence, or death as a first event. OS was defined as the time from start of treatment to death.

3 Results

3.1 Patient characteristics

The study included 17 newly diagnosed orbital RMS patients representing 9.18% of the total RMS cases presented to CCHE from July 2007 till July 2012 and followed up till July 2014. Ten patients were enrolled on IRS-IV while 7 were enrolled on IRS-V. Seven (41.18%) cases came from Upper Egypt, 6 (35.29%) from Nile Delta and three (17.65%) cases from Cairo and Giza.

Orbital RMS cases presented with a median age of 5.04 years (mean 5.546 ± 4.23, range 4 months -14.7 years). The male to female ratio was 2.4:1. Three patients (17.65%) presented with an age younger than 1 year, 12 (64.71%) between 1 and 10 years, and 3 (17.65%) older than 10 years. Male mean age at presentation was higher than female (6.55 years old versus 3.14 years old) although it was not a statistically significant (*p*-value >.05).

Ten patients presented with proptosis (58.82%), while eye displacement was found in 8 (47.04%) cases and lid swelling in 9 (52.94%) cases. Other reported symptoms were lacrimation (one patient) and redness in another patient. Duration of symptoms ranged between 0.6 and 6 months with mean of 1.853 months (median 1 month). Duration of symptoms was slightly shorter in females with mean of 1.4 months, males 2.02 months; this was not statistically significant which may be due to the small sample size.

3.2 Tumor characteristics

Regarding laterality, the left side orbit was affected in 11 (64.71%) cases while it was the right side in 6 (35.29%) patients.

Radiological assessment revealed medially located tumor in 12 (70.6%) of the cases, central in 4 (23.5%) and lateral in 1 (5.9%) on the horizontal plane. Vertically, most of the tumors were inferior 8 (47.1%), superior in 6 (35.3%) and central in

3 (17.6%) cases. On the third plane, 10 (58.8%) of the cases has posterior located tumors while 7 (41.2%) cases had anterior tumors. Three cases (17.65%) showed intra-cranial extension.

Tumor was intraconal in 3 cases (17.65%), definite extraconal in 7 (41.18%) cases while another 2 (11.76) cases were probably extraconal, and extraconal with intraconal extension in one case, tumor relation to muscle cone couldn't be assessed in two cases and was not reported in another two cases.

Lid was involved in 5 (29.5%) cases; in 4 cases the tumor involved the canthi and lids without further extensions while it involved postseptal structures in one case. Nearby air sinuses and parapharyngeal spaces were affected in 6 (35.4%) cases. Bone destruction was reported in 6 cases included 4 destructing lamina papyrecia of ethmoid air sinus. Muscles were invaded radiologically in 5 (29%) cases, not invaded in 7 (41%), couldn't be assessed in two cases and not reported in three cases. Optic nerve was compressed in 9 (52.92%) cases, not involved in 6 (35.29%) cases and not reported in two cases.

Pathological examination of the tumors revealed embryonal histotype in 13 (76.5%) and alveolar type in 4 (23.5%) cases.

For tumor staging, Stage T2a tumor was reported in 15 (88.2%) cases, T2b in 1 (5.9%), and unknown in 1 (5.9%). Regional nodal metastasis (N1) occurred in 2 (11.8%), while distant metastasis (M1) in 2 patients (11.8%). For the two distant metastatic tumor patients, the sites of spread were bone in one patient and another one presented with lung nodules. IRSG stage distribution was: Stage 1 in 14 (82.35%), Stage 2 in 1 (5.88%), and Stage 4 in 2 (11.76%). Clinical group classification was I in 4 (23.52%), II in 3 (17.64%), III in 8 (47.05%) and IV in 2 (11.76%). Nine patients (52.94%) were categorized as low risk, 6 (35.29%) as intermediate risk, and 2 (11.76%) as high risk.

3.3 Treatment management and outcome

Local control

Radiotherapy was the sole method of local control in 7 (41.2%) cases. Both Surgery and Radiotherapy shared in local control of another 7 (41.2%) cases, while surgery alone controlled two tumors (11.8%) while one patient didn't get surgery or radiotherapy because he died before time of local control. Three cases received a radiotherapy dose of 4,500 cGy, other 5 received a dose of 5,040 cGy, one case received 3,600 cGy and another one received 5,940 cGy. Three cases were not eligible for radiation therapy as per treatment guidelines; two were clinical group 1 while the other one was less than one year of age. Radiotherapy was conducted using conformal technique in 10 cases and Intensity modulated in 4 cases.

Surgery was conducted in 9 (58.8%) of the cases. Four of them underwent complete resection, 3 completely resected with microscopic residue while 2 had gross residue after major resection. Surgery entitled exenteration in one case where globe and optic nerve was extensively involved by the tumor. Another one patient had a delayed surgery.

Treatment outcome and survival functions

Median follow-up time was 45.9 months (mean 41.67 months, range 0.93-79.43 months).

Institutional RMS study team discussions evaluated the cases and considered their response to first line treatment as complete remission in 7 (41.2%) cases, partial remission in 4 cases (23.5%) and progressive disease in 4 cases (23.5%). 2 cases (11.8%) were not applicable to this outcome classification. Patients who experienced relapse included two with local relapse and suffered from a superior orbital extra-ocular soft tissue mass. The other two had distant relapse in cervical lymph nodes in one case and abdominal, pelvic, parotid and cervical lymph nodes in the other case.

Three patients had experienced management-related ophthalmic sequelae. The first patient has cataract, choroiditis which followed by retinal detachment and atrophiabulbi. The second patient had devitalized cornea and was enucleated due to

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extensive involvement by the tumor. The third patient complained of dropping of eyelashes and brows with skin pigmentations at radiotherapy target site.

Only one patient died due to chemotherapy-associated toxicity before scheduled time of local control. 4-years OS and 4-years FFS were 94.1 ± 5.7% and 65.4 ± 1.5 % respectively in Figures 1 and 2.

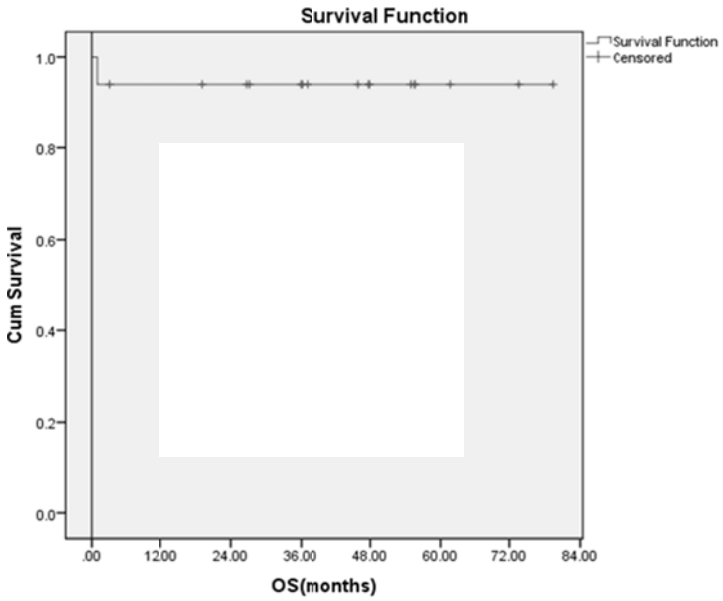

Figure 1. Overall survival of the studied rhabdomyosarcoma patients

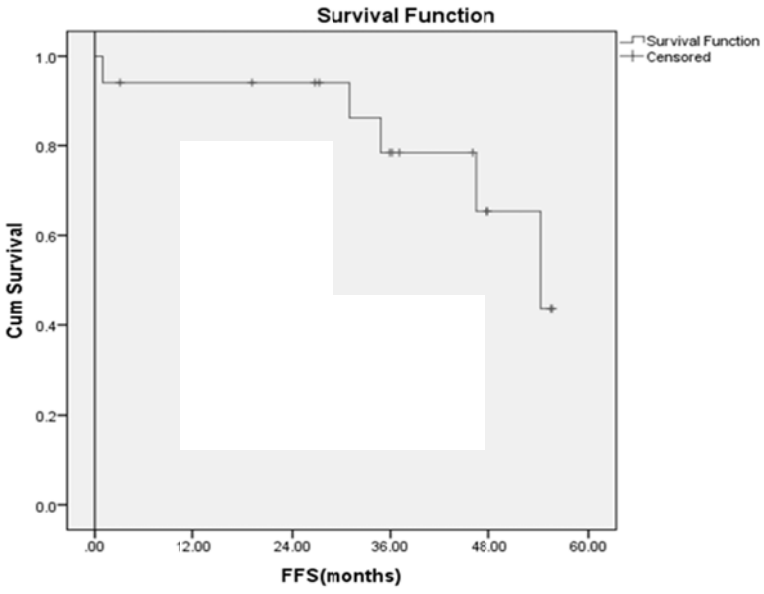

Figure 2. Failure Free survival of the studied rhabdomyosarcoma patients

There was non-significant effect of group, stage or pathological subtype on OS and FFS. There was a significant effect of method of local control (p-value<.05) where patients who took both surgery and radiotherapy had a 4-years FFS of

41.7±3.04%, those with surgery 50%±3.54% and those who took radiotherapy only had a 4-years FFS of 100% (see Figure 3).

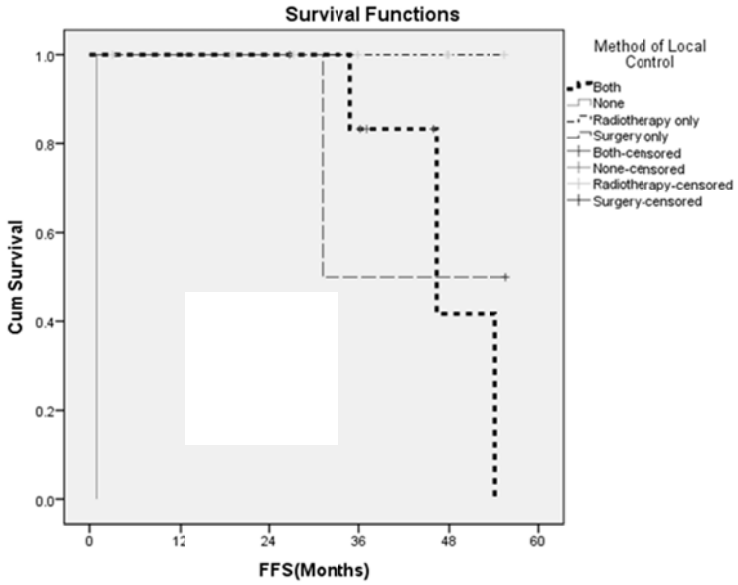

Figure 3. Failure free survival in relation to type of local control

4 Discussion

Orbital-RMS originate from the developing muscles of the orbit. The incidence of malignant orbital tumors in general has been increasing. In a study of population based incidence and survival in head and neck RMS reported an annual percentage increase of 1.16% and a statistically unchanged 5-year survival over the past 30 years [9].

Orbital RMS patients represented 9.18% of the total RMS cases presented to CCHE in the study period. It is stated that Orbital RMS constituted 9% of RMS cases [10]. Orbital RMS is one of the favorable sites for RMS. Our study representing first five years' experience with newly diagnosed orbital RMS patients presented at the Children's Cancer Hospital during the period from July 2007 till July 2012. Patients were followed up till the end of June 2013. Seventeen cases were studied epidemiological, clinical and management. Different prognostic factors were studied in relation to survival.

Primary Orbital RMS is mainly a disease of young children, with 90% occurring before the age of 16 years old with a mean age of onset of 5-7 years old. While presentation within this age group is the most common, In the current study cases presented with a median age of 5.04 years (mean 5.546 ± 4.23, range 4 months -14.7 years), there was no significant in FFS between patient age categories (<1, 1 to 10, >10) This may be explained by the small number of cases.

There is a slight male to female predilection with a male: female ratio of 2.4:1 in contrast to 5:3. Most authors agree that there is no racial predisposition to malignancy [11].

Embryonal and alveolar pathological subtypes are the main subtypes that present in RMS children, while pleomorphic type is the predominant one in adulthood.

The vast majority of orbital rhabdomyosarcomas are of the embryonal sub type 17-19. Previous studies have found 90% embryonal and 10% alveolar subtype compared to 76.5% and 23.5% respectively in our report. The higher percentage of alveolar cases may be explained by the smaller number of the cases.

Contrary to early belief, these tumors do not arise from the extraocular muscles, but rather develop from primitive mesenchymal cells that go on to differentiate into striated muscle cells [12-14].

The presenting symptoms were mainly proptosis (58.8%), eye displacement (47%), eyelid swelling (52.94%) and blepharoptosis. Symptoms are usually rapid due to limited space in the bony orbital. We didn't diagnose any patients with intra-ocular RMS. Extra-ocular retinoblastoma patients were regularly examined for immunohistochemical markers of RMS to avoid such misdiagnosis.

In contrary to previous studies, the reported tumors were mostly medial, inferior and posteriorly located in 40%, and superiorly located in 35% of the cases only.

Moreover, medially located tumors with inferior and posterior extensions were associated younger age. With considering all planes, infero-medial posterior tumors represented about 40% of the cases followed by superior, horizontally centered and anterior tumors.

In our series we reported extraconal tumors in about 53% of cases which correlate with 60% reported in other papers. Bone erosion was reported in 35.3% which could be identified by CT studies.

The collaborative efforts of Intergroup Rhabdomyosarcoma Study Group (IRSG) which became Soft Tissue Sarcoma Committee of the Children's Oncology Group (COG) later resulted in major advances in diagnosis, differentiation (IRS-I&II), prognosis and prediction of outcome in four consecutive clinical trials.

Group I patients of embryonal histopathology who underwent complete resection was identified to have better prognosis better that alveolar subtype.

Orbital tumors represented a better prognostic criterion in Group III patients with postoperative gross residual.

Our results were comparable to what was published by IRSG in 1997 regarding the group of patients. We reported group I in 4 (23.5%) while it was 3% in IRSG report, II in 3 (17.64%) compared to 20%, III in 8 (47.05%) compared to 74% and IV in 2 (11.76%) compared to 3% in IRSG series. Nine patients (52.94%) were categorized as low risk, 6 (35.29%) as intermediate risk, and 2 (11.76%) as high risk.

Local control using surgery and/or radiotherapy with chemotherapy are the main lines of management of the disease. Radiotherapy was the sole method of local control in 7 (41.2%) cases. Both Surgery and Radiotherapy shared in local control of another 7 (41.2%) cases, while surgery alone controlled two tumors (11.8%). Three cases received a radiotherapy dose of 4,500 cGy, other 5 received a dose of 5,040 cGy, one case received 3,600 cGy and another one received 5,940 cGy. Three cases were not eligible for radiation therapy as per treatment guidelines; two were clinical group 1 while the other one was less than one year of age. Radiotherapy was conducted using conformal technique in 10 cases and Intensity modulated in 4 cases.

Surgery was conducted in 9 (58.8%) of the cases. Four of them underwent complete resection, 3 completely resected with microscopic residue while 2 had gross residue after major resection. Surgery entitled exenteration in one case globe and optic nerve was extensively involved by the tumor. Another one patient had a delayed surgery. One patient didn't get surgery because he died before time of local control.

In literature nonmetastatic RMS have an overall survival rate of about 71% with combined modality therapy (chemotherapy, radiation therapy, and surgery). The prognosis for RMS, including primary orbital RMS, has improved significantly in the past 30 years Survival has changed drastically over the years, from 30% in the 1960's to 90% presently, with the advent of new diagnostic and therapeutic modalities [15].

Survival rates when utilizing surgery alone, primarily exenteration, were as low as 30% for primary orbital RMS With the recommendations based on post-operative staging for primary orbital RMS, the IRS-IV study showed a 3-year failure-free survival rate of 91%, 94%, and 80% for group I, II, and III disease respectively [16].

In the current study, 5-years OS and 5-years FFS were 94.1% ± 5.7% and 43.6% ± 2.05 % respectively. FFS was higher in those who had radiotherapy (36.3% ± 2.7%) compared to those who didn't had (33.3% ± 2.7%) and it was not statistically significant but this may be debated for the small number of patients and ineligibility of those 3 patients to radiotherapy.

In conclusion, the current study demonstrated that RMS cases that present with orbit involvement are associated with better clinical outcome. The small number of patients limited the study findings significant prognostic factors in that group of patients.

Future treatment of patients with non-metastatic RMS whose present outcome is favorable will focus on adjustments in therapy to reduce acute and late adverse effects while maintaining their excellent treatment outcome. New therapeutic approaches are required for the patients whose present outcome is less than optimal.

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