Pattern of Pediatric Soft Tissue and Bone Sarcomas at South Egypt Cancer Institute, Retrospective Study

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Abstract

Background: Sarcomas are malignant tumors that arise from mesenchymal tissue and represent an important group of childhood tumors. This study aimed to describe the pattern of pediatric sarcoma at our locality.

Methods: A retrospective descriptive study conducted at Pediatric Oncology Department, South Egypt Cancer Institute. It included all pediatric patients up to 18 years with De novo histologically confirmed soft tissue or bone sarcoma between January 2013 and December 2018. Data collected from patients' files were demographic data, clinical presentation and diagnostic criteria. Patients stratified into two groups, soft tissue (group I) and bone sarcoma (group II).

Results: Histologically confirmed pediatric soft tissue and bone sarcoma were reported in seventy nine patients representing 6.5% (79 out of 1200) of all recorded malignant pediatric tumors at our department during the same period. Soft tissue sarcoma (STS) recorded in 34 (43.1 %) patients and bone sarcoma in 45 (56.9 %) patients. Twenty three (67.6%) were younger than 10 years in STS group, while 37(82.2%) of bone sarcomas group were older than 10 years. Swelling was the most common presentation in both study groups; 61.8% in STS group versus 75.6% in bone sarcoma group. The majority of patients presented with large sized tumors (53%, and 68.9%) in STS and bone sarcomas respectively. High grade pathology (70.6% and 93.3%) reported in STS and bone sarcoma respectively .Distant metastasis in 18 (40%) of bone sarcoma patients and only in 4(11.8%) of STS Patients. Stage III was the most common (58.8**%)** in STS group.

Conclusion:

Misdiagnosis and late presentation were resulted in presentation of most our patients with large sized tumor and advanced stage (III or IV), that may reduce the chance of curative treatment. Studying of the impact of clinical and tumor characteristics on survival outcome is planned in the future .

Key words: Sarcomas, Rhabdomyosarcoma, Non Rhabdomyosarcoma, Osteosarcoma, Ewing sarcoma, descriptive study

Introduction:

Sarcomas are mesenchymal malignancies that affect people of all ages but are relatively more abundant in children than adults, arising within embryonic mesenchymal tissues during the process of differentiation, they have been classically categorized by histology and primary location into bone versus soft tissue sarcoma (STS) [1] .

Sarcoma constitute 6% to 8% of all cancers in children less than 15 years of age. The most frequent childhood STS is Rhabdomyosarcoma (RMS), constituting more than 50% of patients. Non-RMS soft tissue sarcomas (NRSTS) represent biologically and clinically heterogeneous tumors. Distribution of subgroups of STS is age linked; RMS predominates in children less than 10 years of age whereas NRSTS are more common in older age groups. There are variety of primary sites and many histologic types for STS in childhood. [2].

Primary malignant bone tumors are relatively uncommon, accounting for 3% of all childhood malignancies. Of these, osteosarcoma (OS) and Ewing sarcoma (ES) are the most common and comprise 90% of pediatric malignant bone tumors .These tumors are broadly classified according to their cytological features into those that produce osteoid and those that do not [3].

Patients with sarcoma can present with an asymptomatic mass or with signs and symptoms that are associated with the primary tumor site and are related to mass effect or complications that are secondary to the tumor [4].

Imaging studies should include computed tomography (CT) scan or Magnetic Resonance Imaging (MRI) of the primary tumor to determine the size and possible involvement of vital organ structures. Obtaining adequate tissue for histology and immunohistochemistry is very important for adequate diagnosis [5].

Metastatic evaluation includes bone marrow biopsy and technetium methylene bisphosphonate bone scintigraphy for detection of marrow involvement and bone metastases, respectively. CT scan of the chest is performed to evaluate for the presence of lung metastasis or thoracic lymph node involvement [6].

Treatment of STS depends mainly on risk stratification of the patients and focused on multimodality therapy, which has improved the prognosis over the past two decades. Current regimens focus on decreasing treatment for low-risk patients to decrease the long-term side effects while maximizing therapy for patients with metastatic disease for better survival [7].

Chemotherapy plays an important role in the management of OS and ES, with surgical resection of the primary tumor necessary for curative treatment in OS, whereas either surgery, radiation therapy or both are commonly considered for treatment of the primary site in ES [8].

Our Pediatric Oncology Department at South Egypt Cancer Institute (SECI) is the largest tertiary referral center in the Upper Egypt. Pediatric sarcomas represent about 4% of childhood tumors at our Department [9].

Management is guided through treatment protocols adapted from large pediatric oncology clinical trials group (Children's Oncology Group and the International Society of Pediatric Oncology), with therapy modified on the basis of available chemotherapy , surgical and radiation therapy resources [9].

The objective of this study was to describe the pattern of pediatric sarcoma at our Pediatric Oncology Department.

Patients and Methods:

A retrospective descriptive study conducted at Pediatric Oncology Department, SECI. The study included all pediatric patients up to 18 years with De novo histologically confirmed sarcoma (STS and bone sarcoma) between January 2013 and December 2018 after approval by Ethical Committee at SECI.

Data were collected from patients' files during the study period included**:** Demographic and clinical data at presentation (site and size of the primary tumor and metastatic sites). Diagnostic work up including imaging studies, histopathological examination and risk stratification. Data analyzed regarding STS as (group I) and bone sarcoma as (group II).

Statistical analysis:

The statistical analysis was performed using SPSS, version 23.0. Numerical data were described with median and range. Categorical data were described with number and percentage.

Results:

Seventy nine eligible patients of histologically confirmed STS and bone sarcoma were included in the analysis. They represent 6.5% (79 out of 1200) of all recorded malignant pediatric tumors during the same period. During collection of patients' data and revision of their history about their complaint and presentation to our SECI, we recorded wide range of time lag until presentation and diagnosis (range 2 to 9 months) which was more among bone sarcoma patients. Thirty four patients were STS and 45 were bone sarcoma (56.9 %). The majority, 61 (77.2%) were from Assiut (STS 23 and bone sarcoma 38), Sohag 4(STS 2 and bone sarcoma2), Elminia8 (STS 6 and bone sarcoma2), patients and Quena 5(STS 3 and bone sarcoma 2) patients.

Group I (Soft Tissue Sarcoma)

A total of 34 (43.1 %) patients of histologically confirmed STS were reported (15 (44.1 %) RMS and 19 (55.9 %) NRSTS). There was a slight overall male predominance (52.9%). The median age was 8 years; most patients (67.7%) were younger than 10 years of age. Table 1 lists clinical and tumor characteristics.

Most patients presented with a painless swelling (61.80%). The commonest site was the trunk (32.3%) followed by the extremities (29.4%) and head &Neck (23.5%). 18 (53%) patients presented with large tumors size (> 5cm). Incisional biopsy was done to 19 (55.9%) patients, 24 (70.6%) patients had high grade pathology.

Majority of patients (88.2%) had localized disease at time of presentation and stage III was recorded in (58.8%) and eleven patients (32.3%) were intermediate risk Table 1.

Table (1): Clinical and tumor characteristics of group I (soft tissue sarcoma)

Variable	No. (=34)	%
Age groups		
Age < 10 years	23	67.60
Age ≥10 years	11	32.40
Sex		
Male	18	52.94
Female	16	47.06
Presentation		
Swelling	21	61.80
epistaxis	1	2.9
hematuria	3	8.80
local pain	1	2.90
abdominal distention	4	11.80
bilateral LL weakness	1	2.90
limping	2	5.90
headache	1	2.90
Site		
Head & Neck (favorable site)	5	14.71
Head & Neck (Unfavorable site)	4	11.76
Genitourinary	4	11.76
Extremity	10	29.41
Trunk	11	32.35
Metastasis		
No	30	88.20
Yes	4	11.80
Size of tumor (cm)		
≤ 5cm	16	47
> 5cm	18	53
Pathology (grade)		
High grade	24	70.60
Intermediate grade	10	29.40
Risk stratification		
High Risk	17	50.40
Intermediate Risk	11	32.35
Low Risk	6	17.65

Demographic data and clinicopathologic characteristics of group I subtypes

Rhabdomyosarcoma

Fifteen (44.1 %) patients had RMS .The median age was 6 years (range, 14months to 13 years). Eight patients (53%) were under 5 years and 7 patients (46.7%) were males Table (2)

Swelling was the most common presentation in 9 patients (60%). The most common sites were head and neck (5 patients, 33.3%) (2 non parameningeal and 3 meningeal), followed by the genitourinary sites & extremities (4 patients, 26.7% each) and trunk in two patients (13.3%). Twelve patients (80%) had unfavorable site and 8 patients (53.3%) had tumor size more than 5 cm. Embryonic histology was diagnosed in 12 cases (80%) and alveolar histology in 3 cases (20%). Eight patients (53.3%) were high grade and 7 patients (46.7%) were intermediate grade. Eight patients (53.3%) were clinical group III and 2 (13.3%) patients clinical group IV, Regarding stage, 10 (66.7%) patients were stage III, 3 patients (20%) were stage II and 2 patients (13.3%) were stage IV (one had bone metastasis and the other had bone marrow metastasis). Three patients stratified as low risk, 9 patients were intermediate risk and 3 patients were high risk.

Non Rhabdomyosarcoma

Nineteen (55.9 %) patients had NRSTS. The median age was 8 years (range, 2.5- 16 yrs). Seven patients (36.8%) were less than 5 years of age, and 11 patients (57.8%) were males Table (2)

Swelling was the main presentation in 15(78.9%) patients. The most common site was extremities in 8 patients (42.2%), trunk in 7 patients (36.8%) and head and neck in 4 patients (21%).Ten patients (52.6%) had tumor size more than 5 cm. High grade pathology in 16(84.2%) and 3 patients (15.8%) had intermediate grade pathology. Stage III was the most common reported in 15(78.9%) patients and two patients had lung metastasis (11.1%). Sixteen (84.2%) patients were stratified as high risk, and 3(15.8%) patients were intermediate risk.

Group II (bone sarcomas)

A total of 45 (43.1 %) patients of histologically confirmed bone sarcoma were reported .Twenty nine (64.44%) patients had OS and 16 (35.56 %) patients had ES Table (3).

There was a slight male predominance (51.11%). Majority of patients (82.2%) were older than 10 years of age. Most patients presented with a painless swelling (75.56%) and local pain in (15.56%).The commonest site was the extremities (41%), the lower extremities (64.4%) followed by upper extremities (17.8%). Most patients presented with large tumors (> 8 cm in 68.9%).

A high proportion of patients presented with metastatic disease (OS (31.03%) and ES (56.25%), the lung being the most common site of distant metastasis in 10 patients (22.2%). High grade pathology was found in 42(93.3%) and the remaining were intermediate grade. Table (3).

Table (2): Demographic data and clinicopathologic characteristics of group I subtypes

Variable	RMS (n=15)	NRSTS (n=19)
Age		
Median	6yrs	8yrs
Range	14months-13yrs	2.5-16yrs
Gender		
Males	7 (46.7%)	11 (57.8%)
Females	8 (53.3%)	8 (42.2%)
Presentation		
Swelling	9 (60%)	15 (78.9%)
Primary site		
Head&neck	5 (33.3%)	4 (21%)
Extremities	4 (26.7%)	8 (42.2%)
Trunk	2 (13.4%)	7 (36.8%)
Size of tumor (> 5cm)	8 (53.3%)	10 (52.6%)
Grade		
High	8 (53.3%)	16 (84.2%)
Intermediate	7 (46.7%)	3 (15.8%)
Stage		
II	3 (20%)	2 (10%)
III	10 (66.7%)	15 (78.9%)
IV	2 (13.3%)	2 (11.1%)

Abbreviations: RMS, rhabdomyosarcoma; NRSTS, non rhabdo soft tissue sarcoma,

Table (3): Clinical and tumor characteristics of group II (bone sarcoma)

Variable	No. (=45)	%
Age groups		
Age < 10 years	8	17.78
Age≥10 years	37	82.22
Sex		
Male	23	51.11
Female	22	48.89
Presentation		
Swelling	34	75.56
local pain	7	15.56
Limping	2	4.44
Headache	0	0.00
Respiratory distress	1	2.22
Pathological fracture	1	2.22
Site		
Head &Neck	1	2.22
Extremity	37	82.22
Trunk	7	15.56
Metastasis site		
No	27	60.00
Yes	18	40.00
Bone Marrow	+3	6.67
Chest	10	22.22
Bone Marrow +bone	2	4.44
Chest +bone	3	6.67
Size of tumor (cm)		
≤8cm	14	31.1
>8cm	31	68.9
Pathology (grade)		
High grade	42	93.3
Intermediate grade	3	6.7

Demographic data and clinicopathologic characteristics of group II subtypes

Ewing sarcoma

Sixteen patients were reported to have ES. The median age was 8 years (range, 6-16). 12 patients (41.4%) were above 10 years old, the sex equally distributed, 12 patients (75%) had tumor size more than 8 cm Table (4)

The extremities were affected in 9 (56.25%) patients and trunk was in 7 (43.75%) patients. The most affected sites were as follow: the pelvic bones (4), Femur (2), humerus (3), tibia (1), fibula (2), ulna (1), spine (2) and chest wall in one patient. Regarding stage, 9 (56.25 %) patients were stage IV (3 patients had bone marrow metastasis, 2 lung and 4 had both bone combined with B.M (2 patients) or lung (2 patients)). All patients had high grade pathology.

Osteosarcoma

Twenty nine patients were reported to have OS. The median age was 10 years (range, 4- 17). 25 patients (83%) were 10 years or above. The sex was 15 males (51.7%) and 14 females (48.3%) Table (4)

Nineteen patients (65.5%) had tumor size more than 8 cm. The presenting site was extremities in all patients except one who presented in the head. The most affected sites were as follow: lower limbs in 24 patients (Femur (13), tibia (10) and fibula in one patient) and humerus in 4 patients. Nine patients (31.03 %) were stage IV (8 patients had lung only and 1 had combined lung& bone metastasis. The pathology was had high grade in 26 (89.7%) patients and intermediate grade in 3 (10.3%) patients.

Table (4): Demographic data and clinicopathologic characteristics of group II subtypes

Variable	ES (n=16)	OS (n=29)
Age		
Median	8 yrs	10 yrs
Range	6-16 yrs	4-17 yrs
Gender		
Males	8 (50%)	15 (51.7%)
Females	8 (50%)	14 (48.3%)
Presentation		
Swelling	12 (75%)	19 (65.5%)
Primary site		
Head & neck	--	--
Extremities	9 (56.25%)	1 (3.4%)
Trunk	7 (43.75%)	28 (96.6%)
Size of tumor (> 8cm)	12 (75%)	19 (65.5%)
Grade		
High	16 (100%)	26 (89.7%)
Intermediate	--	3 (10.3%)
Stage		
II	1 (6.25%)	1 (3.45%)
III	5 (31.25%)	19 (65.52%)
IV	9 (56.25%)	9 (31.03%)

Abbreviations: ES Ewing sarcoma, OS Osteosarcoma

Discussion:

Sarcoma has aggressive behavior, accounts for a disproportionate amount of morbidity and mortality in affected children. It constitutes approximately 10% of all childhood malignancies [10]. Here, in our study, pediatric sarcoma represents 6.5% of all pediatric cancers less than 18 years of age, which increased more than the previous incidence (4%) at our department from 2003 to 2013 [9]. This can be explained by the advances in diagnostic facilities and the cooperation between health insurance center and SECI recently. We performed this study to describe the pattern of pediatric sarcoma at our department. Although the difference in percentage of whole STS and bone sarcomas, embryonal RMS, OS and ES are the most common pediatric sarcomas in all studies allover [10, 11]. The residence is not affecting the pattern of presentation

In this study the incidence of patients in group I (43.1 %) was less than to that reported in the literature as STS accounts for 50-60% of all pediatric sarcoma in children less than 15 years [2]. Also, our findings were less than what found by Swillis and his colleagues in Tanzania as (66%) of the their sarcoma patients were STS, (74.1%) RMS (ERMS (74%) and ARMS (26%) and (25.9%) were NRSTS [11] this can explained by difference in patients number in two studies (34 versus 89). Group II represented 56.9 % (64.4% OS and 35.6 % ES) which is more than the study done by Siwillis and his colleagues as 34% were bone sarcoma, (87% OS and 13% ES) [12].

Swelling was the most common presentation in both study groups,(61.8% in STS group and 75.6% in bone sarcoma group), which is comparable to which reported in other studies [12, 13,14,15,16].

Majority of patients with RMS presented with swelling (60%) while in study done by Badr and his colleagues they reported 36% of their cases presented with swelling [13]. All patients with NRSTS presented with swelling which is more than what found by Spunt et al. as they found that 85% of their patients presented with swelling [14]. Regarding patients with ES, we found 75% of them presented with swelling while in study by Ginsberg et.al. they reported 50% presented with swelling [15]. Also 65.5% of our OS patients had the same presentation which was different from what found in study by Kim et al. as 39% of their cases presented with swelling [16] and matched with Egyptian study this may be explained by late presentation due to either lack of awareness among our population or misdiagnosis [17].

Regarding the Common primary tumor site, in patients with group I, we found that most of them were in the trunk (32.3%) followed by extremities (29.4%) with lower frequency of head and neck region (14.7%). While in Indian study done by Kachanov and his colleagues, they found that most of cases were in extremities and head and neck region (25% for each site) [18]. In our RMS patients, the common primary tumor site was head and neck (33.3%) which is different from what found in Badr et al. (29% in extremities and 15% in the trunk) [13]. Also in our

NRSTS cases, 42.1% were in the extremities and 52.6% in the trunk, Spunt et al. reported 41% of their cases in the extremities and 26% in the trunk [14].

The extremities were the most common site among group II patients (55.54% in ES and 96.55% in OS) which is similar to study done by Nedelcu and his colleagues that reported predominance of extremities in most cases of bone sarcoma (55.5% in ES and 93.75% in OS) [19].

Regarding size of the mass in patients with group I, the long diameter was less than or equal 5 cm in 47% patients which is similar to study of Siwillis and his colleagues as 42.7% of their STS cases were less than 5 cm [11] but in a study done by Carneiro and his colleagues, they found that the long diameter was less than 5cm in 28% of patients [20]. This controversy could be attributed to the difference in number of study group, where Carnerio et al. studied a larger group of patients than our study (239 versus 34).

Most of group II presented with a mass size more than 8 cm (68.9%) which was higher than what found by Siwillis et al. (52.2%) [11]. This difference could be attributed to the latency of presentation happened in our patients.

Regarding histopathological tumor grade, our study revealed that 70.6% of group I were high grade and the rest were intermediate grade. While in a study done by Carneiro and his colleagues, most of their patients were high grade (90%) [20]. Group II ,93.3% were high grade and only 6.7% were intermediate grade which was quite similar to study done by Heare and his colleagues as about 85 % of their cases had high grade disease [21].

In group I, 88.2% of cases had localized disease and 11.8% had metastatic disease at time of presentation with no predominant site of metastasis. While in study by Weiss and his colleagues, they reported distant metastases between 15% to 25% of newly diagnosed patients , lung was the most frequent site of metastasis [1]. Also in study by Siwillis and his colleague , (39.3%) had metastatic disease at presentation and most of them had pulmonary metastasis [11]. In our RMS cases, metastasis reported in (13.33%) which is slightly more than study done in 57357 Egypt by El Nadi and his colleague, about (11.3%) had metastatic disease [22]. Also in our NRSTS cases, metastasis reported in (11.1%) which is less than study by Fleming et al. (18%) had distant metastasis [23].

On the other hand, metastatic disease in group II was more prominent than in group I (40% in bone sarcoma, ES (56.25%) and OS (31%) with 66.7% of them were pulmonary metastasis. This is different from a study done by Barros and his colleagues that reported metastasis in about 30% of their patients (28% in ES and 33% in OS) most of them had pulmonary metastasis [15]. Also, our findings is higher than what mentioned by Nedelcu and his colleagues as 27.7% had stage IV [19]. This could be explained by time lag until presentation and diagnosis which could be explained by misdiagnosis by healthcare providers as infection or fracture which finally lead to delay in diagnosis.

Stage III was the most common tumor stage in group I patients, 58.8%) which is similar to study of Hawkins and his colleagues as stage III disease represented most of their cases [24]. Intermediate risk was the most common stratification in group I (45.8%) which is quite similar to what found in Hawkins et al. as about 52% were intermediate risk [24].

There are several limitations in this study, including that is a retrospective review over a relatively short time , few number of patients and the data were collected from one cancer institute at upper Egypt , which may not be representative of the entire country.

In conclusion, misdiagnosis and late presentation were resulted in presentation of most our patients with large sized tumor and advanced stage (III or IV), that may reduce the chance of curative treatment. Studying of the impact of clinical and tumor characteristics on survival outcome is planned in the future.

Abbreviations

CTS: Compute Tomography Scan
MRI: Magnetic Resonance Imaging
STS: Soft Tissue Sarcoma
RMS: Rhabdomyosarcoma
ERMS: Embryonal RMS
ARMS: Alveolar RMS
NRSTS: Non-Rabdo Soft Tissue Sarcomas
PNET: Primitive Neuroectodermal Tumor
OS: Osteosarcoma
ES: Ewing sarcoma
SECI: South Egypt Cancer Institute
COG: Children Oncology Group
TNM: Tumor size, Nodal involvement, Metastasis

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