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Original Article

Childhood soft tissue tumors, one center experience

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Abstract

Aim: Studies on childhood soft tissue tumors have generally been conducted with malignant tumors. There are few studies in the literature comprising all soft tissue tumors. The current study aimed to examine the incidence of all benign and malignant soft tissue tumors during childhood in East Mediterranean region.

Materials and Methods: This study retrospectively analyzed the data gathered from patients diagnosed with soft tissue tumors according to the WHO 2020 classification. It focused on those aged 0–18 years that underwent excisional biopsy at Adana City Training and Research Hospital (Adana, Turkey) between 2014 and 2020.

Results: Of the total patients, 47.5% were female and 52.5% male. Of these, 87.2% of the cases were benign, 9.2% malignant, and 3.6% intermediate. Hemangioma (55%) was the most common benign soft tissue tumor, and the most common location was the head–neck. Other benign soft tissue tumors were neurofibroma (8.8%), lipoma (6.1%), schwannoma (5.1%), and neuroma (4.4%). Rhabdomyosarcoma (53.2%) was the most common malignant soft tissue tumor. The embryonal subtype was the most common (36.6%). Other malignant soft tissue tumors were extra-osseous PNET/Ewing's sarcoma (16.6%), synovial sarcoma (13.3%), and leiomyosarcoma (3.3%).

Conclusion: Similar to the literature, in this study, the most common benign soft tissue tumor in children was hemangioma, and the most common malignant soft tissue tumor was rhabdomyosarcoma. It is hoped that this study will contribute to the literature as it is the first study to cover all childhood soft tissue tumors at national and regional scale.

Keywords: Childhood; neoplasms; soft tissue

INTRODUCTION

Soft tissue neoplasms are rare and heterogeneous tumors that originate from mesenchymal tissue and consist of many subgroups. Soft tissue sarcomas, mostly seen in adults, constitute 1% of all malignancies (1). It is the fifth most common disease among all childhood malignancies, with a rate of 4% (2). Pleomorphic sarcoma is mostly seen in adults, whereas rhabdomyosarcoma is more common in children. According to the World Health Organization (WHO) 2020 classification, soft tissue tumors are classified into four categories: (i) benign, (ii) malignant, and in some subgroups, (iii) intermediate locally aggressive and (iv) intermediate rarely metastasizing tumors (1).

Studies on childhood soft tissue tumors have generally been conducted with malignant tumors. In the literature review, no regional or national study on the incidence and distribution of benign and malignant soft tissue tumors in childhood was found. Using the data of Adana City Training and Research Hospital (Adana, Turkey), which has a large pathology archive of soft tissue tumors and serves a wide geography, this study aimed to evaluate the data on this subject.

MATERIALS and METHODS

This study retrospectively analyzed the data gathered from patients diagnosed with soft tissue tumors according to the WHO 2020 classification. It focused on those aged 0–18 years that underwent excisional biopsy at Adana City Training and Research Hospital between 2014 and 2020. Childhood tumors such as hematological malignancies, epithelial tumors, bone tumors, central nervous system tumors, neuroblastomas, and Wilms' tumors were excluded. The study was approved by the Ethics Committee of Adana City Training and Research Hospital, Health Sciences University (decision number: 983).

The distribution of the patients in terms of age, gender, pathological diagnosis, size, localization, tissue originating from the tumor, and behavioral characteristics was evaluated. Age was measured in years. The patients were grouped into men and women. Tumor size was measured in centimetres. Localization was grouped as the head–neck, trunk, and skeletal systems. The histological origins of adipocytic, fibroblastic/myofibroblastic, fibrohistiocytic,

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smooth muscle, pericytic (perivascular), skeletal muscle, and vascular tumors of soft tissues and tumors with indeterminate differentiation and undifferentiated/unclassified sarcomas were classified. Behavioral characteristics were grouped as benign, intermediate, and malignant.

RESULTS

In this study, the age of the patients ranged between 0 and 18 years, and the median age was 12 years. Of the total patients, 47.5% were female and 52.5% male. Tumor size varied between 0.1 and 20.0 cm, and the median size was 1.3 cm. Clinical and pathological features are presented in Table 1.

Table 1. Clinicopathological features of childhood soft tissue tumors

Variable	n(%)
Age(yrs median)	12
Gender	
Female	160(47.5)
Male	177(52.5)
Tumour size(cm, median)	1.3
Localization	
Head and neck	150(44.5)
Trunk	73(21.7)
Skletal system	114(33.8)
Orgin	
Vascular tumours of soft tissue	177(52.5)
Nerve sheath tumours	59(17.5)
Adipocytic tumours	25(7.4)
Fibrohistiocytic tumours	21(6.3)
Skeletal muscle tumours	16(4.7)
Tumours of uncertain differentiation	16(4.7)
Fibroblastic / myofibroblastic tumours	11(3.3)
Smooth muscle tumours	6(1.8)
Pericytic (perivascular) tumours	6(1.8)
Gastrointestinal stromal tumours	1(0.3)
Behaviour	
Benign	294(87.2)
Intermediate	12(3.6)
Malign	31(9.2)

Of the cases, 87.2% were benign, 9.2% malignant, and 3.6% intermediate. The clinical and pathological features of the tumors according to their behavioral characteristics are summarized in Table 2.

Benign tumors were listed as hemangioma (55%), neurofibroma (8.8%), lipoma (6.1%), schwannoma (5.1%), and neuroma (4.4%) in the order of frequency. The distribution of benign tumors is provided in Table 3.

Table 2. Clinicopathological features of childhood soft tissue tumors in terms of behavior patterns

	Benign n(%)	Intermediate n(%)	Malign n(%)
Gender			
Female	143 (89.4)	6 (3.8)	11 (6.9)
Male	151 (85.3)	6 (3.4)	20 (11.3)
Localization			
Head and neck	144 (96.0)	2 (1.3)	4 (2.7)
Trunk	55 (75.3)	2 (2.7)	16 (21.9)
Skletal system	95 (83.3)	8 (7.0)	11 (9.6)
Orgin			
Vascular tumours of soft tissue	175 (98.9)	1 (0.6)	1 (0.6)
Nerve sheath tumours	59 (100)	-	-
Adipocytic tumours	23 (92)	1 (4)	1 (0.4)
Fibrohistiocytic tumours	18 (85.7)	3 (14.3)	-
Skeletal muscle tumours	-	-	16 (100)
Tumours of uncertain differentiation	5 (31.3)	1 (6.3)	10 (62.5)
Fibroblastic / myofibroblastic tumours	4 (36)	6 (55)	1 (9)
Smooth muscle tumours	5 (83)	-	1 (17)
Pericytic (perivascular) tumours	6 (100)	-	-
Gastrointestinal stromal tumours	-	1 (100)	-

Table 3. Distribution of the most common benign soft tissue tumors in childhood

Benign soft tissue neoplasms	n(%)
Hemangioma	161(55)
Neurofibroma	26(8.8)
Lipoma	18(6.1)
Schwannoma	15(5.1)
Neuroma	13(4.4)
Lyphangioma	11(3.7)
Fibroma	11(3.7)
Tenosynovial giant cell tumour	5(1.7)
Granular cell tumour	5(1.7)
Glomus tumour	4(1.3)
Dermatofibroma	4(1.3)
Myxoma	4(1.3)

Table 4. Clinicopathological features of most common malignant soft tissue tumors

Diagnosis	n(%)	Age (mean)	Gender n(%)		Localization n(%)		
			Male	Female	Head and neck	Trunk	Skletal system
Rhabdomyosarcoma	16(53.2)	7.3	10(62.5)	6(37.5)	2(12.5)	10(62.5)	4(25)
PNET / EWING Sarcoma	5(16.6)	11.8	5(100)	-	1(20)	1(20)	3(60)
Synovial Sarcoma	4(13.3)	14.25	3(75)	1(25)	-	1(25)	3(75)
Leiomyosarcoma	1(3.3)	18.0	-	1(100)	-	1(100)	-
Liposarcoma	1(3.3)	16.0	1(100)	-	-	-	1(100)
Low-grade fibromyxoid sarcoma	1(3.3)	12.0	1(100)	-	-	-	1(100)
Epithelioid haemangioendothelioma	1(3.3)	11.0	-	1(100)	-	-	1(100)
Alveolar soft part sarcoma	1(3.3)	13.0	1(100)	-	1(100)	-	-

The most common malignant tumors were rhabdomyosarcoma (53.2%), extra-osseous PNET/Ewing's sarcoma (16.6%), synovial sarcoma (13.3%), and leiomyosarcoma (3.3%). The rate of embryonal rhabdomyosarcoma was 69%, and that of alveolar rhabdomyosarcoma was 31%. The malignant adipocytic tumor subtype was myxoid liposarcoma. The distribution of malignant tumors is given in Table 4.

DISCUSSION

Soft tissue tumors are mostly heterogeneous with benign behavior. They constitute 1% of all malignancies (1). They are usually seen in adults, with only 15% of them in children and adolescents. In the United States of America, 6,000 soft tissue sarcomas are diagnosed in adults and 600 in the pediatric age group each year (3). In Europe, malignant soft tissue sarcomas constitute approximately 12% of pediatric cancers (4). In a study conducted in Turkey between 2002 and 2008, soft tissue sarcomas constituted 6.4% of all malignant tumors in the pediatric age group (5). However, clear data could not be found in the literature on the distribution of benign soft tissue tumors in East Mediterranean region and Turkey.

Most soft tissue tumors grow spontaneously, and although the etiology is unknown, genetic and environmental effects have been described in various tumors. The diagnosis is based on clinical, radiological, and histological features. In the past, limited techniques were used in diagnosis, but now, with advances in pathology, immunohistochemistry and molecular techniques are used significantly in both diagnosis and classification (1). In addition, advanced genetic and molecular studies are widely used in understanding the pathogenesis and treatment of soft tissue tumors (6). Patients usually present with swelling. It is important to evaluate the clinical history, physical examination, radiology, and histological examination together to arrive at a diagnosis (7). Clinical features such as age, location of the tumor, and growth time of the lesion are very important in histopathological examination. Radiological findings, especially magnetic resonance imaging, can also be helpful. Diagnostic biopsies can be performed in different ways depending on the location of the tumor. Although excisional biopsies are preferred for diagnosis and treatment (especially in superficial tumors), according to the relationship of the tumor with the surrounding tissue, incisional biopsies are performed for the purpose of diagnosis in large tumors. However, considering the heterogeneity of soft tissue tumors in these small biopsies, multiple biopsies from different areas and a good clinicopathological correlation are of great importance. Before anything else, it should be decided whether the microscopic lesion is reactive or neoplastic. If neoadjuvant treatment is to be given to the patient after it has been diagnosed as neoplastic, the histological grade and subtype of the tumor can be given as possible. However, it should be kept in mind that the histological grade given to soft tissue tumors in small biopsies may not reflect the histological grade of the entire tumor (8-11). Significant changes have emerged in the WHO 2014 classification with the contribution of molecular pathology. Soft tissue tumors are divided into two subgroups according to their classification in terms of genetic changes: (i) sarcomas containing specific genetic changes and (ii) non-specific multiple complex karyotype anomalies. Specific genetic changes include oncogenic translocations, oncogenic mutations and deletions, and gene amplifications. For example, translocations of the EWSR1 gene in PNET/Ewing's sarcomas, the SSX gene in synovial sarcomas, and PAX3 and PAX7 genes in alveolar rhabdomyosarcomas with different genes have been detected (1,12). The main method of treatment is surgery. Radiotherapy and chemotherapy are included as well (13-15).

In this study, childhood soft tissue tumors were more common in men than in women, which is similar to other studies (16-18). In a study evaluating all age groups in the Black Sea region, a higher rate was found in women (54.4%) (19). The size was bigger than 5 cm in malignant tumors, but it was smaller than 5 cm in benign tumors. As malignant tumors are expected to be larger, this ratio was found to be compatible with the literature (20). In the current study, the most common localization was the head–neck, which was followed by the extremities and trunk. In different studies conducted in Turkey, the most

common localization was the wrist. In these studies, localization was grouped differently; all age groups and ganglion cysts were included in the study (19,21). In the current study, the cases were grouped as the head–neck, trunk, and extremities in accordance with the WHO 2020 soft tissue tumor classification. In another study, although it was proportionally lower, the most frequent localization was the head–neck, with a rate of 37% (17), which is similar to the current study. In our series, vascular, nerve sheath, and adipocytic tumors were the most common. In another study, vascular tumors were most frequently seen, followed by nerve sheath tumors. However, vascular tumors were observed with a lower rate (30%) in that study (16). In a different study including all age groups, lipomatous tumors were most frequently seen, with a rate of 28.5%, whereas vascular tumors were determined to be the fourth, with a rate of 17.1% (17). The majority of the cases in the current study constituted benign tumors, followed by malignant and intermediate tumors. Although the rates are different, benign tumors are more common in series including the pediatric age group (17,19,20). In this study, benign tumors were most common in the head–neck, and malignant tumors were more common in the trunk. Benign tumors were more frequently found in the hand and wrist, whereas malignant tumors were more commonly seen in the thigh. However, all age groups were included in these studies, and soft tissue tumors were divided into more than ten regions (19,21).

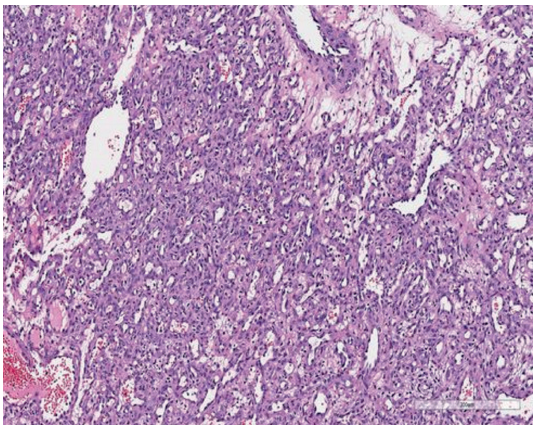

Figure 1. Partially anastomosed vascular proliferation lined by single row of endothelial cells without atypia. (Hematoxylin & Eosin stain x100)

Hemangiomas are the most common childhood soft tissue tumors, and 55% of them are present at birth. The tumor can range in size from a few millimeters to 5 cm or more. Sixty percent are located in the head–neck and 15% in the extremities. The female/male ratio is 3 (22). It is histologically characterized by the proliferation of small and large vascular structures lined with a single row of endothelial cells (Figure 1). Vascular markers such as CD34, CD31, and factor 8 are stained immunohistochemically. Although it was seen less frequently in the current study, in accordance with the literature, the most common soft tissue tumor was hemangioma, and the most frequent location was the head–neck (22,23). In this study, malignant cases were not found in the second most common nerve sheath tumors, and similar to the studies in the literature, neurofibroma was most frequently seen (16,23). Adipocytic tumors constitute less than 10% of all childhood soft tissue tumors, and most of them are benign. It was the third most common soft tissue tumor in our series, and the rates were consistent with the literature (24). In this study, there was one malignant case among adipocytic tumors, and the histological subtype was myxoid liposarcoma.

Rhabdomyosarcomas are the most common malignant soft tissue tumors in childhood, and they constitute more than 50% of all soft tissue malignancies. Approximately 65%–75% of them are embryonal and 25%–32% alveolar (25-27). Rhabdomyosarcomas are characterized by the proliferation of primitive mesenchymal cells with varying degrees of skeletal muscle differentiation. Different morphological appearances can be seen according to different subtypes, such as embryonal, alveolar, pleomorphic, and spindle cell/sclerosing rhabdomyosarcoma. In embryonal rhabdomyosarcoma, neoplastic cells are round or spindle-shaped, and rich and poor areas of cells are observed in collagenized/myxoid stroma (Figure 2). Round, hyperchromatic nucleus, narrow cytoplasm cells, and multinuclear, neoplastic giant cells are seen in the alveolar type. These cells give an alveolar appearance by showing loss of cohesion within the fibrovascular septal structures. Immunohistochemically, they react positively with muscle markers such as desmin, myogenin, and myoD1 (28).

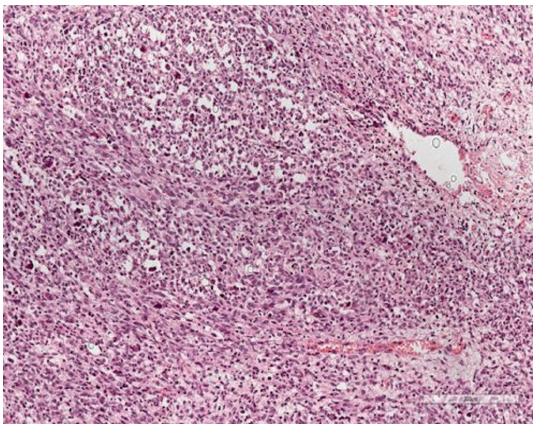

Figure 2. Cells with eosinophilic cytoplasm with small, primitive, round, spindle hyperchromatic nuclei in the fibrovascular stroma. (Hematoxylin & Eosin stain x300)

Similar to the literature, rhabdomyosarcoma was found to be the most common malignant soft tissue tumor in this study. The most common subtype was embryonal rhabdomyosarcoma. The second most common malignant tumor was extra-osseousbone PNET/Ewing's sarcoma, followed by synovial sarcoma. Our findings were consistent with similar studies in the literature (25-27).

CONCLUSION

In conclusion, hemangioma was the most frequently seen benign soft tissue tumor in childhood, and rhabdomyosarcoma was found to be a malignant soft

tumor. All the skeletal muscle tumors were malignant, and all the peripheral nerve sheath tumors were benign. One of the cases of adipocytic tumors in this study was malignant, and its subtype was myxoid liposarcoma. It is hoped that this study will contribute to the literature as it is the first study to cover all childhood soft tissue tumors at national and regional scale.

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Competing Interests: The authors declare that they have no competing interest.

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