Original Article

Histopathological Spectrum of Soft-tissue Tumors in a Rural Teaching Hospital

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ABSTRACT

Background: Soft-tissue tumors represent a major diagnostic challenge to pathologist. Tumors vary in incidence, clinical presentation, and exhibit a wide range of histomorphological features. Histopathological examination is a gold standard for diagnosis of soft-tissue tumors. **Aims and Objectives:** The objectives of the study were as follows: (1) To find out frequency of benign and malignant soft-tissue tumors in relation to age, sex, and anatomical site of soft-tissue tumors, (2) to study gross and histological features of benign and malignant tumors, and (3) to analyze various types of soft-tissue tumors. **Materials and Methods:** All the cases of soft-tissue tumor specimens received in the form of biopsy or resected specimen in the department of pathology from October 2017 to August 2019. **Results:** A total of 141 cases of soft-tissue tumors were received during a period of October 2017–August 2019. Soft-tissue tumors constituted 9.3% of all tumors. Benign soft-tissue tumors accounted for 8.5% and malignant 0.4%. Male-to-female ratio for all soft-tissue tumors was 1.31:1. Majority of soft-tissue tumors were encountered in the 3rd to 6th decades. Majority of soft-tissue tumors showed predilection for trunk followed by upper extremity. Lipoma was the most common benign tumor and small round cell tumor was most common malignant neoplasm. **Conclusion:** A good clinical acumen, thorough description and grossing of specimen, and microscopic evaluation of hematoxylin and eosin (H and E) stained sections are fundamental aspects in diagnosis of soft-tissue tumors. H and E stained sections represented the mainstay of diagnosis of soft-tissue tumors in majority of cases. However, diagnostic accuracy can be increased by performing ancillary technique such as special stains and immunohistochemistry.

Key words: Immunohistochemistry, Histopathology, Soft tissue tumor

INTRODUCTION

Soft tissue can be defined as non-epithelial extraskeletal tissue of the body exclusive of the reticuloendothelial system, glia, and supporting tissue of the various parenchymal organs. It is represented by the voluntary muscles, fat, and fibrous tissue, along with the vessels serving these tissues.[1]

Embryologically, soft tissue is derived principally from mesoderm, with some contribution from neuroectoderm.[2]

Soft-tissue tumors can occur at any age. Both benign and malignant soft-tissue tumors usually present as painless mass. They arise nearly everywhere in the body.[3]

The large majority of soft-tissue tumors are benign, with a very high cure rate after surgical excision. Malignant mesenchymal neoplasms amount to <1% of the overall human burden of malignant tumors.[4]

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The annual incidence of soft-tissue tumor is 1.4 per 100,000 populations. Soft-tissue tumors are the fourth most common malignancy in children, after hematopoietic neoplasm, neural tumor, and Wilms tumor. Soft-tissue sarcomas account for 15% of all childhood cancers. Benign tumors outnumber malignant ones by margin of 100:1.[5]

The etiology of most benign and malignant soft tissue tumors is unknown.

Soft-tissue tumor and tumor-like lesions have fascinated pathologist for many years because of their remarkably wide variety and the close histopathological similarities between certain tumors with only subtle difference detectable on careful microscopic examination, thus posing a diagnostic challenge to histopathologist.[6]

Correct histopathological diagnosis is, therefore, crucial. Immunohistochemistry (IHC) is used to detect tumor-specific alterations which add significantly to histological interpretation, but several groups of tumors still lack reliable immunohistochemical markers. A core biopsy, an excisional biopsy, and incisional biopsy are the appropriate technique used for diagnosing most soft-tissue tumors. Open biopsy has long been considered the gold standard for diagnosis of soft-tissue mass.[7]

Different special techniques such as special stains, IHC, electron microscopy and cytogenetic, and molecular methods are applied to increase diagnostic accuracy of soft-tissue tumors. Accurate diagnosis of soft-tissue tumors by clinical history such as age, duration, location, size, and pathological examination is helpful to make differential diagnosis of the tumor.[8] Therefore, grade of malignant tumors is the single most established criteria in predicting the biological behavior of these tumors, which is vital for the institution of proper therapy. The various parameters used are cellularity, mitotic count, tumor differentiation, and necrosis.[9,10] Hematoxylin and eosin (H and E) sections on light microscopy examination remain the standard technique for the diagnosis of soft-tissue tumors.

Aims and Objectives

The objectives of the study were as follows:

1. To find out frequency of occurrence of benign and malignant soft-tissue tumors
2. To study frequency of soft- tissue tumors in relation to age, sex, and anatomical site
3. To study gross and histological features of benign and malignant soft-tissue tumors
4. To analyze various types of soft-tissue tumors.

MATERIALS AND METHODS

The present study comprises all the soft-tissue tumors received in the department of pathology in a rural teaching hospital satisfying the inclusion and exclusion criteria. This prospective study was carried out from October 2017 to August 2019. The specimens included in the study were received in the form of biopsy or resected specimens in the department of pathology.

The record of brief history with age, registration number, biopsy number, and presenting signs and symptoms along with relevant findings was taken. A detailed clinical data including history and examination were carried out.

Gross findings such as size, shape, color, and consistency were noted. All the specimens were fixed in 10% formalin solution for 24 h and then sections from representative areas were submitted for routine processing. Then after processing, paraffin blocks were prepared which were cut at 4–5 microns thickness. They were subsequently stained with H and E. Special stains such as Periodic acid–Schiff, reticulin stain, and IHC were employed wherever necessary.

The classification adopted for the present study is based on the WHO classification of soft-tissue tumors (2013).

Inclusion Criteria

All soft-tissue tumor specimens received in the form of excision biopsy or surgical resection were included in this study.

Exclusion Criteria

All the non-mesenchymal tumors and bone tumors were excluded from the study.

OBSERVATIONS AND RESULTS

During the period of October 2017 to August 2019, total numbers of 141 soft tissue specimens were received in Pathology department of our medical college which were fulfilling inclusion criteria of this study. Soft tissue tumors constituted 9.3 % of all tumors that were received in Pathology department of our hospital [Table 1].

Benign tumors constituted 80.4 % of all tumors and the malignant counterparts formed 19.6 % of all tumors. Benign to malignant ratio for all tumors was 4.1:1.

Benign soft tissue tumors accounted for 8.5 % of all benign tumors. Malignant soft tissue tumors formed only 0.4 % of all malignant tumors.

Benign soft tissue tumors out number malignant ones by vast difference by ratio of 21.5:1. [Table 2].

Benign soft tissue tumors constituted 91.5%, intermediate and malignant tumors formed 4.25% each, of all soft tissue tumors. [Table 3].

According to Table 4, Out of 141 soft tissue tumors, adipocytic tumors accounted for the majority of soft tissue tumors (52.5%) followed by nerve sheath tumor (14.9%). Majority of benign soft tissue tumors were adipocytic tumors (51.1%) followed by nerve sheath tumor (14.9 %) & vascular tumors (12.1%). Majority of intermediate soft tissue tumors were fibroblastic / myofibroblastic tumours (2.8%) followed by gastrointestinal stromal tumors (0.7%) & adipocytic tumors (0.7%). Majority of malignant soft tissue tumors were tumours of uncertain differentiation (2.1%).

Majority of the benign tumors (70.7% out of 91.5%) occurred in the 3rd to 6th decade with a peak incidence in the 4th to 5th decade. Majority of intermediate category of tumor were found in the 2th to 4th decade. Majority of malignant tumors (3.55% out of 4.25%) occurred after 5th decade [Table 5].

According to above Table 6, males (56.7%) preponderance was seen in the present study. Male to female ratio for all soft tissue tumors was 1.31:1.

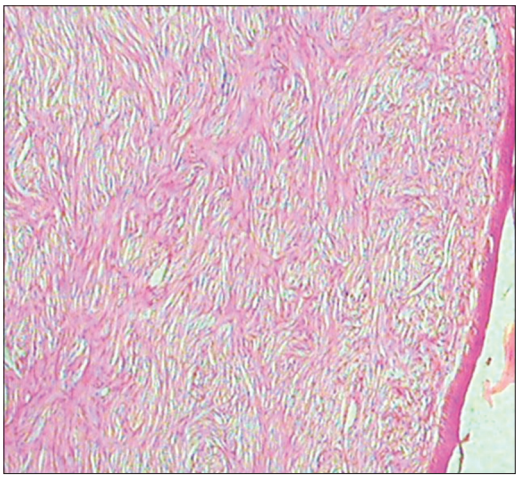

Figure 1 : Photomicrograph of DFSP showing tumor mass with overlying epidermis. (H and E, 5×)

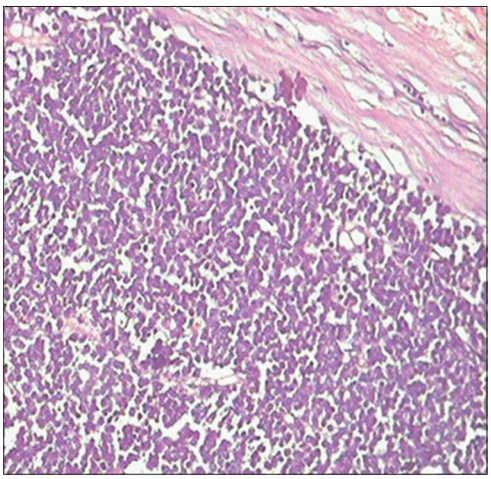

Figure 3: Photomicrograph of extraskeletal Ewing's sarcoma showing capsule on one side and below is seen tumor mass. (H and E, 5×)

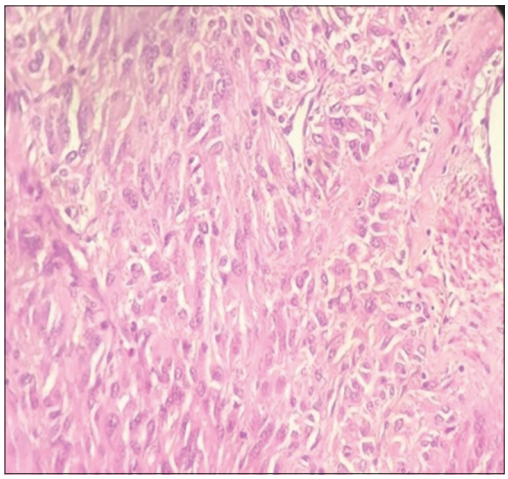

Figure 2: Photomicrograph of gastrointestinal stromal tumor showing mixture of epithelioid and spindle-shaped tumor cells. (H and E, 10×)

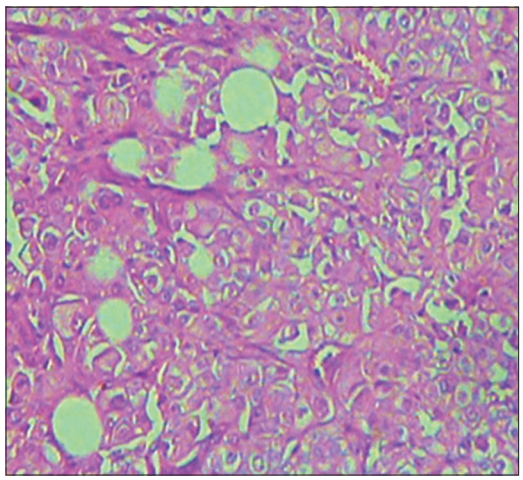

Figure 4: Photomicrograph of alveolar soft part sarcoma showing nests of large polygonal cells. (H and E, 10×)

Table 1: Percentage of soft-tissue tumors

Total number of tumors	1516
Total number of soft-tissue tumors	141
Percentage incidence of soft-tissue tumors out of all tumors	9.3

Table 2: Occurrence of benign and malignant tumors

Type	Total		Benign (B)		Malignant (M)		B:M ratio
	No	%	No	%	No	%	
All tumors	1516	100	1219	80.4	297	19.6	4.1:1
Soft-tissue tumors	141	9.3	129	8.5	6	0.4	21.5:1

Table 3: Relative occurrence of soft-tissue tumors

Soft-tissue tumor	No	Percentage
Benign (B)	129	91.5
Intermediate (I)	6	4.25
Malignant (M)	6	4.25
Total	141	100

Table 4: Occurrence of soft-tissue tumors according to histological classification

Tumors	Benign (%)	Intermediate (%)	Malignant (%)	Total (%)
Adipocytic tumors	72 (51.1)	1 (0.7)	1 (0.7)	74 (52.5)
Fibroblastic/ myofibroblastic tumors	3 (2.1)	4 (2.8)	0	7 (4.9)
So-called fibrohistiocytic tumors	9 (6.4)	0	0	9 (6.4)
Smooth muscle tumors	3 (2.1)	0	0	3 (2.1)
Pericytic (perivascular) tumors	3 (2.1)	0	0	3 (2.1)
Vascular tumors	17 (12.1)	0	1 (0.7)	18 (12.8)
Gastrointestinal stromal tumors	1 (0.7)	1 (0.7)	0	2 (1.4)
Nerve sheath tumors	21 (14.9)	0	0	21 (14.9)
Tumors of uncertain differentiation	0	0	3 (2.1)	3 (2.1)
Undifferentiated/ unclassified sarcoma	0	0	1 (0.7)	1 (0.7)
Total	129 (91.5)	6 (4.25)	6 (4.25)	141 (100)

According to above Table 7, Soft tissue tumors occurred predominantly in trunk (31.2%) followed by upper extremity (27.7%) and Head Neck region (25.5%).

Out of total 129 cases of benign soft tissue tumors most commonly found benign tumor in this study was Lipoma (50.4%) followed by haemangioma (12.5%). Intermediate soft tissue tumors found were one case each of atypical lipomatous tumor (16.66%), dermatofibrosarcoma protuberans (16.66%) [Figure 1] and Gastrointestinal stromal tumor (GIST) (16.66%) [Figure 2]. Malignant tumors were each cases of Extraskeletal Ewing's sarcoma [Figure 3], Epitheloid haemangioendothelioma, Alveolar soft part sarcoma [Figure 4] and Undifferentiated pleomorphic sarcoma [Table 8].

IHC was done in 9 cases of soft tissue tumors out of which 1 case was of benign category, 5 cases was of intermediate category and 3 cases were of malignant category [Table 9].

DISCUSSION

Of all the neoplastic specimens, soft-tissue tumor constituted 9.3% of all tumors of which 8.5% were benign soft-tissue tumors and 0.4% was malignant soft-tissue tumors.

In the present study, out of 141 cases, the frequency of benign tumors was 91.5%, intermediate tumors formed 4.25%, and malignant tumors formed 4.25% which was comparable with studies done by Janaki *et al*.[11]

Frequency of malignant tumors was far less than benign tumors which are comparable with the studies done by Janaki *et al*.,[12] Jobanputra *et al*.,[2] and Solanki *et al*.[13]

Benign soft-tissue tumors outnumber malignant counterparts by a considerable margin. In the present study, the age ranged from 6 years to 90 years. Benign tumors occurred in middle-aged group patients whereas malignant tumors were found in older age group patients.

The average age in the case of benign tumors was 40.9 years and 65.2 years in the case of malignant tumors, which is comparable to the studies of Jobanputra *et al*.[2] and Myhre-Jenson.[14]

There were 80 males and 61 females with male-to-female ratio of 1.31:1, which is comparable with the studies done by Ducimetiere *et al*.,[15] Susruthan *et al*.[16] and Vani *et al*.,[17] and Rao *et al*.[8]

In the case of benign tumor group, there were 72 males and 57 females with a male-to-female ratio of 1.26:1, which is comparable to the study of Janaki *et al*.[12] where the male-to-female ratio was 1.38:1 as outlined above. A study done by Swagata *et al*.[4] and Rao *et al*.[8] found that male-to-female ratio in their

Table 5: Age-wise distribution of soft-tissue tumors

Soft-tissue tumors	Age (years)								
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	80–90
Benign	2	11	23	30	34	14	7	8	0
Intermediate	0	2	1	1	0	1	1	0	0
Malignant	0	0	1	0	0	1	1	2	1
Total	2	13	25	31	34	16	9	10	1
%	1.4	9.2	17.8	22	24.1	11.3	6.4	7.1	0.7

study was 1.53:1 and 2.56:1. A study done by Chouhan *et al*.[7] found that male-to-female ratio in their study was 0.95:1 showing slight female preponderance.

In case of intermediate tumor group, there were four males and two females with a male-to-female ratio of 2:1. In a study done by Swagata *et al*.,[4] male-to-female ratio was 1:1, whereas Janaki *et al*.[12] found only three male patients in intermediate category of soft-tissue tumors.

In case of malignant tumor group, there were four males and two females with a male-to-female ratio of 2:1, which is comparable to the study of Janaki *et al*.[11] where the male-to-female ratio was 2:1 as outlined above. A study done by Janaki *et al*. (2015),[12] Rao *et al*.,[8] and Chouhan *et al*.,[7] male-to-female ratio was 1.42:1, 1.6:1, and 1.8:1, respectively.

In the present study, the most common site for soft-tissue tumor was trunk (31.3%) which is comparable with the study done by above-mentioned authors such as Batra *et al*.,[18] Janaki *et al*.,[12] Anitha and Kumari,[19] and Chouhan *et al*.[7]

In benign soft-tissue tumors of the present study, the most common site was the upper extremity (26.9%) followed by trunk (26.2%), which is comparable to the studies of Janaki *et al*.[12] whereas a study done by Swagata *et al*.[4] who shows that benign group of tumors has more predilection for head and neck region followed by upper extremity. A study done by Baig[5] and Chouhan *et al*.[7] who shows that benign group of tumors has more predilections for trunk region.

In intermediate category of soft-tissue tumors of the present study, the most common site was trunk (1.4%) and lower extremity (1.4%) which is comparable to the studies of Swagata *et al*.[4] and Janaki *et al*.[12]

The malignant soft-tissue tumors were having a strong predilection for trunk forming 3.5% which is comparable with a study done by Batra *et al*.[18] and Janaki *et al*.[12] A study done by Baig[5] and Chouhan *et al*.[7] found lower extremity to be more commonly affected.

Most common benign soft-tissue tumor encountered was lipoma (50.4%) followed by hemangioma (12.5%). Authors such as Umarani *et al*.,[3] Navya *et al*.,[20] Goyal *et al*.,[21] and Chouhan *et al*. (2018)[7] also had similar findings.

Table 6: Sex-wise distribution of soft-tissue tumors

Gender	Soft-tissue tumors	Percentage	Male:female ratio
Male	80	56.7	
Female	61	43.3	
Total	141	100	1.31:1

Table 7: Anatomical site wise distribution of soft-tissue tumors

Anatomical sites	Total	%
Upper extremity	39	27.7
Lower extremity	22	15.6
Trunk	44	31.2
Head and neck	36	25.5
Total	141	100

Commonly encountered malignant tumors in the present study were extraskeletal Ewing sarcoma (33.33%). Umarani *et al*.[3] found liposarcoma to be more common, Navya *et al*.[20] found leiomyosarcoma to be more common, Goyal *et al*.[21] found gastrointestinal stromal tumors to be more common, and Chouhan *et al*.[7] found fibrosarcoma to be more common.

SUMMARY

In the present study, the soft-tissue tumors (141 cases) accounted for 9.3% of all tumors. Benign soft-tissue tumors constituted 8.5% of all benign tumors and malignant soft- tissue tumor accounted for 0.4% of all malignant tumors diagnosed during the study period. Soft-tissue tumors were observed between 6 and 90 years of age group. Benign soft-tissue tumors showed a peak age incidence in the fifth decade. Intermediate soft-tissue tumor showed a peak age incidence in the second decade. Malignant soft-tissue tumors showed a peak age incidence in the eighth decade. Soft-tissue tumors in general showed slightly male preponderance with a male–to-female ratio of 1.31:1. Overall soft-tissue tumors were most commonly seen in trunk. The benign soft-tissue tumors were most commonly seen in upper extremity followed by trunk. The intermediate soft-tissue tumors were most commonly seen in lower extremity and trunk. The

Table 8: Histological types of common soft-tissue tumors

Histological type	Category	Tumors	No.	Percentage
Adipocytic	Benign	Lipoma	65	50.4
		Angiolipoma	3	2.3
	Intermediate	Atypical lipomatous tumor	1	16.66
	Malignant	Myxoid liposarcoma	1	16.66
Fibroblastic	Benign	Angiomyofibroblastoma	2	1.5
		Fibroma of tendon sheath	1	0.8
	Intermediate	Dermatofibrosarcoma protuberances	1	16.66
		Fibromatosis – desmoid type	1	16.66
		Plantar fibromatosis	1	16.66
		Low-grade myofibroblastic sarcoma	1	16.66
Fibrohistiocytic	Benign	Benign fibrous histiocytoma	4	3.1
		Tenosynovial giant cell tumor	5	3.9
GIST	Benign	Gastrointestinal stromal tumor (GIST)	1	0.8
	Intermediate	Gastrointestinal stromal tumor (GIST)	1	16.66
Nerve sheath	Benign	Schwannoma	8	6.2
		Neurofibroma	13	10
Perivascular	Benign	Glomus tumor	1	0.8
		Angioleiomyoma	2	1.5
Smooth muscle	Benign	Leiomyoma	3	2.3
Vascular	Benign	Hemangioma	16	12.5
		Lymphangioma	1	0.8
Tumors of uncertain differentiation	Malignant	Extraskeletal Ewing's sarcoma	2	33.33
		Epithelioid hemangioendothelioma	1	16.66
		Alveolar soft part sarcoma	1	16.66
Undifferentiated/unclassified sarcoma	Malignant	Undifferentiated pleomorphic sarcoma	1	16.66

Table 9: IHC done in soft-tissue tumors

Initial diagnosis on H and E	IHC marker	Final diagnosis
Malignant small round cell tumor	Positive – MIC2 and CK.	Extraskeletal Ewing sarcoma
Malignant spindle cell tumor	Negative – S100, SMA, Desmin.	Undifferentiated pleomorphic sarcoma
Dermatofibrosarcoma protuberans	Positive – CD34	Dermatofibrosarcoma protuberans
Low-grade spindle cell tumor	Positive – C-kit and CD34	Gastrointestinal stromal tumor, mixed epithelioid and spindle cell type
Low-grade spindle cell and neoplasm	Positive – SMA, desmin, and beta-catenin	Fibromatosis – desmoid type
Low-grade spindle cell sarcoma	Positive – desmin, SMA, and CD34	Low-grade cd34-positive spindle cell sarcoma of fibroblastic/ myofibroblastic origin

malignant soft-tissue tumors were most commonly seen in trunk. On histopathological examination, the single most common histological group was the adipocytic tumors which accounted for 51.1% of all soft-tissue tumors. The most common benign tumor was lipoma (46.1%) of all benign tumors of soft tissue followed by hemangioma (11.3%) and neurofibroma (9.2%). Various tumors found in intermediate category of soft-tissue tumors were atypical lipomatous tumor (0.7%), dermatofibrosarcoma protuberances (0.7%), and gastrointestinal stromal cell tumors (0.7%). Various tumors found in malignant category of soft-tissue tumors were extraskeletal Ewing sarcoma (1.4%), epithelioid hemangioendothelioma (0.7%), alveolar soft part sarcoma (0.7%), myxoid liposarcoma (0.7%), and undifferentiated pleomorphic sarcoma (0.7%). Special stains such as PAS, PTAH and reticulin, and IHC were used wherever required. IHC proved to be of great value and was very useful to accurately classify soft-tissue tumors.

CONCLUSION

Soft-tissue tumors form a significant specimen load of histopathology laboratory. Even though benign soft-tissue tumors outnumber malignant ones by vast margin, the diagnosis and management of soft-tissue tumors require a team perspective.

Even though soft-tissue sarcomas are rare and usually present just as painless masses, it must be diagnosed early for better management and improvement of prognosis. A good clinical acumen, thorough description and grossing of specimen, and microscopic evaluation of H and E stained sections are fundamental aspects in diagnosis of soft-tissue tumors. A careful gross examination of the specimen and

adequate sampling of the tumor is essential. H and E stained sections represented the mainstay of diagnosis of soft -tissue tumors in majority of cases. However, diagnostic accuracy can be increased by performing ancillary technique such as special stains and IHC.

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