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Histopathological study of soft-tissue tumors in a medical college in South India: A two-year study

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ABSTRACT

Background: Soft tissue can be defined as non-epithelial extraskeletal tissue of the body exclusive of the reticuloendothelial system, glia, and supporting tissues of different parenchymal organs. These tumors are a highly heterogeneous group and are classified into benign, intermediate, and malignant forms according to the adult tissue they resemble. They can occur in all sites of the body. **Aims and Objectives:** The present study was undertaken to assess the histopathological pattern of various soft-tissue tumors. **Materials and Methods:** This is a prospective observational study for a period of 2 years, in which 152 soft-tissue tumors were analyzed and classified primarily as per the WHO classification. The age-wise, sex-wise, and site-wise distribution and the histopathological spectrum of soft-tissue tumors were studied. **Results:** A total of 152 soft-tissue tumors were included in the study, of which 90.79% were benign tumors, 5.92% were malignant, 2.63% were intermediate grade tumors, and 0.66% was of uncertain malignant potential. Maximum number of patients belonged to the 41–50-year age group. Males constitute 53.29% cases and females, 46.71% with a male-to-female ratio of 1.14:1. Lipoma was the most common soft-tissue tumor in the present study. **Conclusion:** Overall soft-tissue tumors are a rare category of tumors with benign tumors vastly outnumbering malignant tumors. The diagnosis of soft-tissue tumors needs a meticulous approach and team effort. Proper examination of the gross specimen and careful sampling of the tumor is required for the correct diagnosis. Hematoxylin- and Eosin-stained sections remain very important for the diagnosis of soft-tissue tumors along with immunohistochemistry and molecular markers.

Key words: Soft-tissue; Sections; Immunohistochemistry

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INTRODUCTION

Soft-tissue can be defined as non-epithelial extraskeletal tissue of the body exclusive of the reticuloendothelial system, glia, and supporting tissues of different parenchymal organs.[1] It constitutes voluntary muscles, fat, and fibrous tissue, along with the blood vessels serving these tissues. It also includes the peripheral nervous system because tumors arising from nerves present as soft-tissue masses and pose many problems in differential diagnosis and therapy. Embryologically, soft tissue is derived from the mesoderm, with some contributions from neuroectoderm.[1] These tumors are a highly heterogeneous group and are classified into benign, intermediate, and malignant forms according to the adult tissue they resemble.[2] These mesenchymal neoplasms are relatively rare and may arise anywhere in the body. These tumors exhibit a broad range of differentiation.[3] The etiology of most benign and malignant soft-tissue tumors is unknown.

In rare cases, genetic and environmental factors, irradiation, viral infections, and immune deficiency have been

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found to be associated with the development of usually malignant soft-tissue tumors.[4] Benign soft-tissue tumors usually present clinically as slow-growing masses, whereas their malignant counterparts are locally aggressive and are capable of invasive growth, recurrence, and distant metastasis.[1] Soft-tissue sarcomas occur more commonly in men but gender- and age-related incidences vary among the different histologic types. For example, embryonal rhabdomyosarcoma is almost exclusive to young individuals, whereas undifferentiated pleomorphic sarcomas predominantly occur in the elderly people.[1]

The classification of soft-tissue neoplasms is not static. New aspects once validated have to be taken into account and put into practice. Therefore, it becomes necessary to update the tumor classification from time to time.[5] In general, light microscopy supplemented by ancillary techniques wherever relevant remains the cornerstone of the classification and diagnosis of soft-tissue tumors. These ancillary techniques notably immunohistochemistry and molecular cytogenetics further facilitate the identification of previously unrecognized tumors.[6] The grading of soft-tissue sarcomas is a feature of most tumor staging systems and is increasingly one of the key factors required for the formulation of treatment strategies.[6] The present study was undertaken to assess the histopathological pattern of various soft-tissue tumors.

Aims and objectives

Aims

The aim of the study was to study the histopathological pattern of soft-tissue tumors.

Objectives

The present study was undertaken:

To assess the histopathological pattern of various soft-tissue tumors.

To assess the age-wise distribution of soft-tissue tumors.

To assess the gender-wise and site-wise distribution of soft-tissue tumors.

MATERIALS AND METHODS

The present study was conducted for a period of 2 years in the Department of Pathology, S.V. Medical College and S.V.R.R. Government General Hospital, Tirupati, Chittoor District. Ethical clearance for the study was obtained from the Institutional Ethics Committee, S.V. Medical College, Tirupati.

A total of 152 samples from patients with soft-tissue tumors, including both benign and malignant tumors were analyzed and classified primarily as per the WHO classification of soft-tissue tumors. Tumors considered to be STT but not included under the WHO classification have also been studied.

Inclusion criteria

- Those patients who are willing for the study.
- Specimens more than 6 mm in size.
- Specimens sent in proper fixative.

Exclusion criteria

- Those patients who are not willing for the study.
- Specimens <6 mm in size.
- Specimens not sent in proper fixative.

The resected surgical specimens that were sent to the department of pathology were fixed in 10% buffered neutral formalin fixative. The specimens were grossed and multiple representative bits from the tumor, and any other relevant areas were submitted for processing.

Thin sections of 3–4 microns were cut from the paraffin block. The slides prepared were routinely stained by hematoxylin and eosin stain and evaluated by light microscopy. Special histochemical stains, such as Masson Trichrome and Reticulin were used wherever necessary. Immunohistochemistry was done in few difficult cases.

Statistical analysis

Data obtained were entered into Microsoft Excel Spreadsheet and statistically analyzed using SPSS software.

RESULTS

The incidence of soft-tissue tumors were more in males (53.29%) when compared to females (46.71%). Of all the 152 soft tissue tumors that were received, 138 (90.79%) were benign and 9 (5.92%) were malignant. The age of patients ranged from 3 years to 77 years (Table 3). The mean age of patients diagnosed with benign tumors was 41.72 years and that of malignant tumors was 51.11 years. A maximum number of soft-tissue tumors were diagnosed in the 41–50 years age group. Table 1 presents the distribution of type of tumors in the study participants.

Of all 152 cases, the most common site of soft-tissue tumors in the present study was trunk (30.92%), followed by head and neck (29.61%), lower extremity (23.03%), and upper extremity (Bar 1).

Out of all 138 benign STT, the most common site was head and neck in 31.88% of cases closely followed by trunk in 31.16% of cases. 19.57% of benign STT was

located in lower extremities and the remaining 17.39% in upper extremities.

Among the 9 cases of malignant STT, 77.78% were located in lower extremities and 11.11% each in head and neck and trunk regions.

One case of GIST was located in the small intestine.

Graph 1 represents the histopathological spectrum of soft-tissue tumors. The majority of tumors are adipocytic tumors (62.5%) followed by vascular tumors (14.47%).

Table 2 shows the different histologic subtypes of soft-tissue tumors under each category in the present study.

Lipoma was the most common adipocytic tumor in the present study, i.e., 60.52% of all soft-tissue tumors. Microscopically, lipoma showed mature adipocytes arranged in sheets with few traversing delicate fibrous septae. Intramuscular lipoma shows adipocytes amidst skeletal muscle bundles (Figure 1).

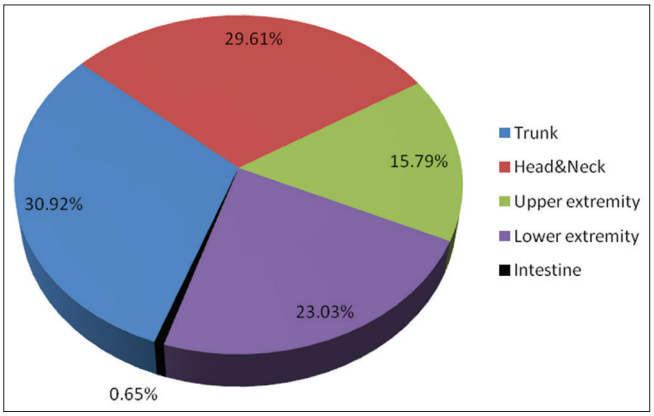
One case of pleomorphic lipoma was diagnosed. Histopathological examination showed mature adipocytic tissue, few bland spindle cells, and floret-like multinucleated giant cells and ropy collagen bundles.

Three cases of dermatofibrosarcoma protruberans were seen in this study and were characterized by a highly cellular, monomorphic appearance, composed of spindle cells arranged in storiform pattern with the cells infiltrating the subcutaneous adipose tissue (Figure 3).

Four cases of adult fibrosarcoma were diagnosed (Figure 4).

Six cases of benign fibrous histiocytoma were seen in the present study. They were composed of bland ovoid to spindle cells arranged in storiform pattern admixed with lymphocytes along with occasional multinucleated giant cells and focal stromal hyalinization.

Two cases of tenosynovial giant cell tumor were



Bar 1: Site wise distribution of soft tissue tumors. Data were presented as frequency and percentage

Table 1: Distribution of type of soft-tissue tumors

Type of tumor	Distribution (n=152)	
	Number	Percentage
Benign	138	90.79
Intermediate	4	2.63
Malignant	9	5.92
Uncertain malignant potential	1	0.66
Total	152	100.00

Data were presented as frequency and percentage

Table 2: Histologic subtypes of soft tissue tumors

S. No.	Tumor type	Distribution (n=152)	
		Number	Percentage
1	Adipocytic tumors		
	Lipoma	92	60.52
	Lipomatosis	1	0.66
	Pleomorphic Lipoma	1	0.66
	Atypical lipomatous tumor	1	0.66
	Total	95	62.50
2	Fibroblastic and myofibroblastic tumors		
	Fibroma of tendon sheath	2	1.32
	Dermatofibrosarcoma protruberans	3	1.97
	Adult Fibrosarcoma	4	2.63
	Total	9	5.92
3	So called fibrohistiocytic tumors		
	Tenosynovial giant cell tumor	2	1.32
	Deep benign fibrous histiocytoma	6	3.94
	Total	8	5.26
4	Vascular tumors		
	Hemangioma	16	10.53
	Lymphangioma	6	3.94
	Total	22	14.47
5	Neural tumors		
	Schwannoma	7	4.61
	NF	4	2.63
	Solitary circumscribed Neuroma	1	0.66
	Total	12	7.89
6	GIST		
	Gastrointestinal stromal tumor	1	0.66
	Total	1	0.66
7	Tumors of uncertain differentiation		
	Synovial sarcoma	1	0.66
	Extraskeletal Ewing sarcoma	1	0.66
	Total	2	1.32
8	Undifferentiated /unclassified sarcomas		
	Undifferentiated pleomorphic sarcoma	3	1.98
	Total	3	1.98
		152	100.00

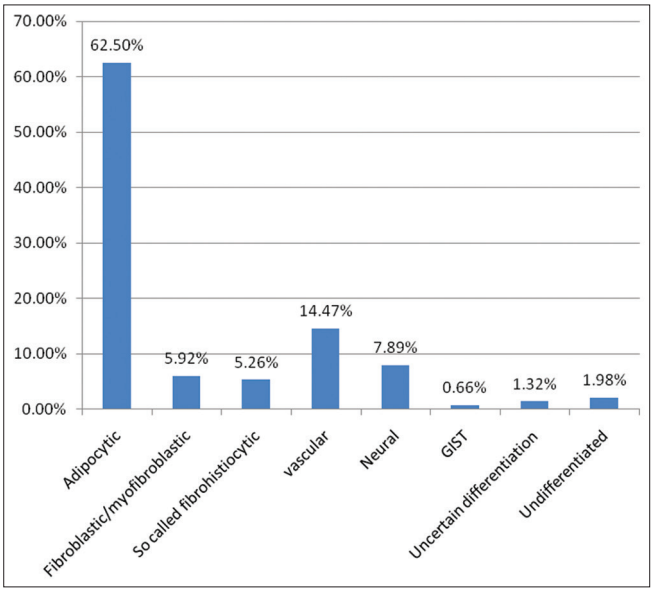
Data were presented as frequency and percentage, NF: Neurofibroma

Table 3: Age-wise distribution of different categories of soft-tissue tumors

Type of soft tissue tumor	0–10 (%)	11–20 (%)	21–30 (%)	31–40 (%)	41–50 (%)	51–60 (%)	>60 (%)	Total (%)
Adipocytic	0 (0)	3 (3.16)	19 (20)	18 (18.95%)	29 (30.53)	15 (15.79)	11 (11.57)	95 (100)
Fibroblastic/Myo-fibroblastic	1 (11.11)	1 (11.11)	1 (11.11)	1 (11.11)	3 (33.33)	2 (22.22)	0 (0)	9 (100)
So-called fibrohistiocytic	0 (0)	0 (0)	2 (25)	5 (62.5)	0 (0.00)	1 (12.5%	0 (0)	8 (100)
Vascular	4 (18.18)	4 (18.18)	3 (13.64)	4 (18.18)	1 (4.55)	6 (27.273)	0 (0)	22 (100)
Neural	0 (0)	2 (16.67)	0 (0)	1 (8.33)	3 (25)	3 (25)	3 (25)	12 (100)
Uncertain differentiation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (50.0)	2 (100)
Undifferentiated/unclassified	0 (0)	0 (0)	0	1 (33.33)	2 (66.67)	0 (0)	0	3 (100)

Table 4: Sex-wise distribution of different categories of soft tissue tumors (n=152)

Tumor types	Male (n=81)		Female (n=71)		Total	M: F
	Number	Percent	Number	Percent		
Adipocytic tumors	52	54.74	43	45.26	95	1.3:1
Fibroblastic/myofibroblastic tumor	2	22.22	7	77.78	9	0.3:1
So called fibrohistiocytic tumors	6	75.00	2	25.00	8	3:1
Vascular tumors	13	59.09	9	40.91	22	1.1:1
GIST	1	100.00	0	0.00	01	-
Neural tumors	4	33.33	8	66.67	12	0.5:1
Tumors of uncertain differentiation	2	100.00	0	0.00	02	-
Undifferentiated tumors/unclassified	1	33.33	2	66.67	03	0.5:1
Total	81	53.29	71	46.71	152	1.14:1



Graph 1: Histopathological spectrum of soft tissue tumors. Data were presented as frequency and percentage

diagnosed and histologically they showed histiocyte-like cells, few foam cells, and multinucleated giant cells in fibrocollagenous stroma.

Vascular tumors were the second largest category of soft-tissue tumors. Hemangioma was the most common diagnosis and there was a total of 16 cases (Figure 2). It was followed by lymphangiomas which were seen in 6 cases. Lymphangioma histologically showed dilated lymphatic vessels lined by one or two endothelial layers with lymphocytes beneath the endothelium.

Among the category of neural tumors, Schwannoma was the most common diagnosis, seen in 7 cases. Microscopy of schwannoma showed the characteristic features of alternating hypercellular (Antoni A) and hypocellular (Antoni B) areas. Antoni A areas showed nuclear palisading and Verocay bodies (Figure 5).

3 cases of undifferentiated pleomorphic sarcoma were seen. Histology showed variable cellularity with bizarre tumor cells with marked nuclear atypia, arranged in irregular fascicles and vague storiform pattern in a fibrocollagenous stroma. Few multinucleated giant cells and numerous mitotic figures were also seen (Figure 6).

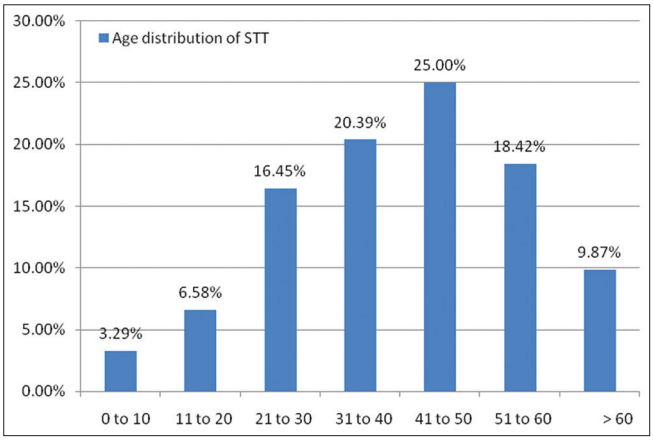
One case of GIST belonged to the age group of 31–40 years (Figure 7).

DISCUSSION

The diagnosis and classification of primary tumors of soft tissue is one of the most difficult areas of surgical pathology because of their rarity, large range of different types of tumors, and frequent overlap of their histopathological features.[7] It will not be an exaggeration to call the last two decades a revolution in the understanding of soft-tissue tumors in all aspects such as clinical, investigative, molecular, and therapeutic.[8] In the present study, benign soft-tissue tumors (90.79%) greatly outnumbered soft-tissue sarcomas (5.92%). The study by Jain et al.[9] reported the incidence of benign soft-tissue tumors as 90.60%. A similar high incidence of benign STT (93.33%) was reported in a study conducted

by Soni et al.,[7] in 2014. Malignant STT constituted 6.67% of all STT in their study. Another study on 93 soft-tissue tumors by Hassawi et al.,[10] for a period of 1 year (2007–2008) reported the incidence of benign and malignant soft-tissue tumors as 75.2% and 24.8%, respectively. Intermediate-grade tumors consisted of 2.63% of all soft-tissue tumors in the present study. In comparison, he study by Badwe and Desai[8] showed the incidence of intermediate-grade tumors to be 3.99%. The most common benign tumor was a lipoma (66.67% of all benign tumors) and the most common soft-tissue sarcoma was fibrosarcoma (44.44% of all malignant tumors). In most other studies, lipoma was the most common benign tumor. In the study by Jain et al.,[9] lipomas constituted 50.27% of all benign tumors.

In the present study, patients were aged between 3 and 77 years with an overall mean age of 41.78 years. The mean age of patients with benign tumors was 41.72 years and that of malignant tumors was 51.11 years. On the contrary, in the study by Hassawi et al.,[10] the mean age of patients with benign STT was 27.6 years, and in soft-tissue sarcomas, it was 39.1 years. In the present study, out of



Graph 2: Overall age wise distribution of soft tissue tumors

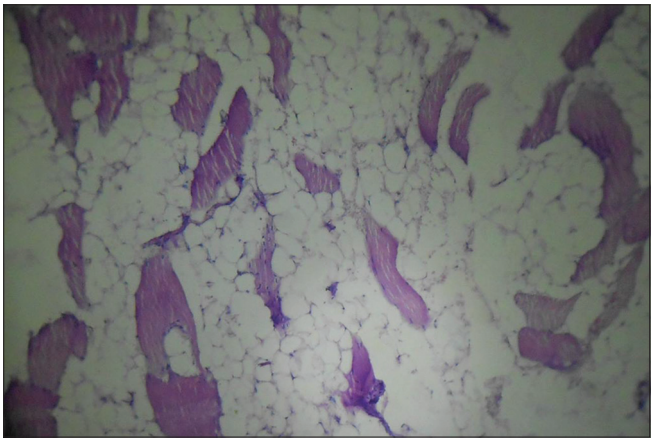


Figure 1: Intramuscular lipoma (H and E ×10)

152 cases, there were 81 males (53.29 %) and 71 females (46.71%).

In the present study, the highest incidence of benign tumors was observed in third and fourth decades of life, and the highest incidence of soft-tissue sarcomas was noted in fourth and fifth decades. Soni PB et al.[8] observed in their study that the most common age group for benign and malignant soft-tissue tumors were second and fourth decades, respectively. In the study by Roy et al.,[2] it was reported that benign tumors were relatively common above the third decade of life while soft-tissue sarcomas occurred in patients belonging to all age groups.

The overall approximate male-to-female ratio of the present study was 1.14:1 (Table 4). These observations are comparable to another study by Jain et al.,[9] in which

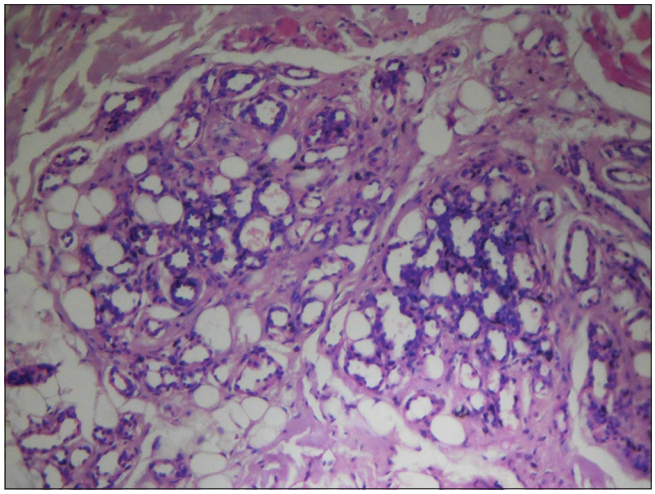


Figure 2: Capillary hemangioma showing lobules of capillaries with scanty intervening stroma (H and E ×10)

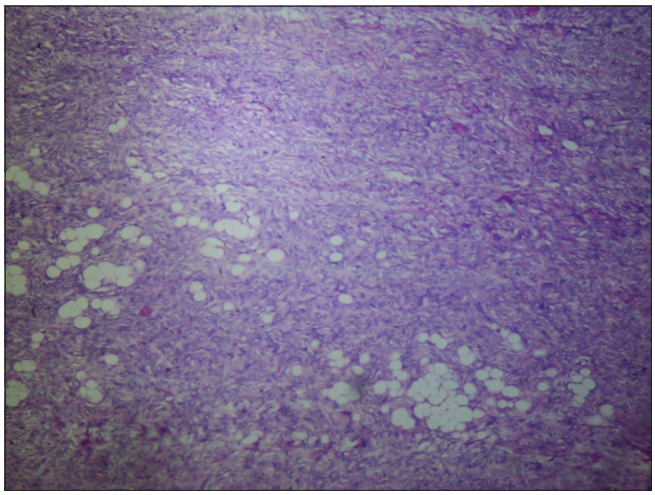


Figure 3: Dermatofibrosaroma protruberans characterised by spindle cells in vague stroriform pattern. The tumor cells seen infiltrating into subcutaneous adipose tissue (H and E ×10)

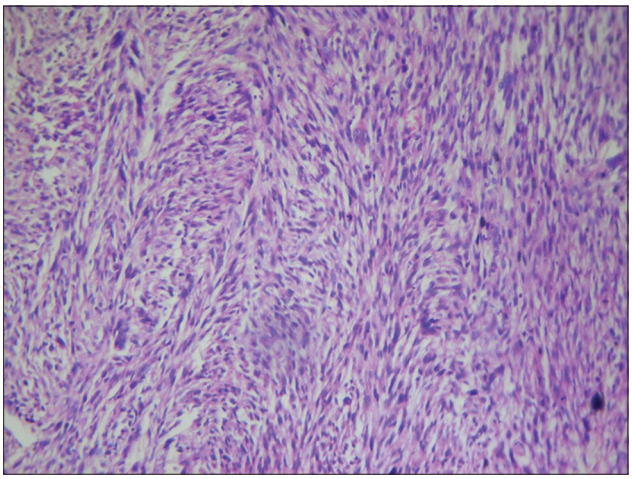


Figure 4: Fibrosarcoma with malignant spindle cells in herringbone pattern (H and E ×10)

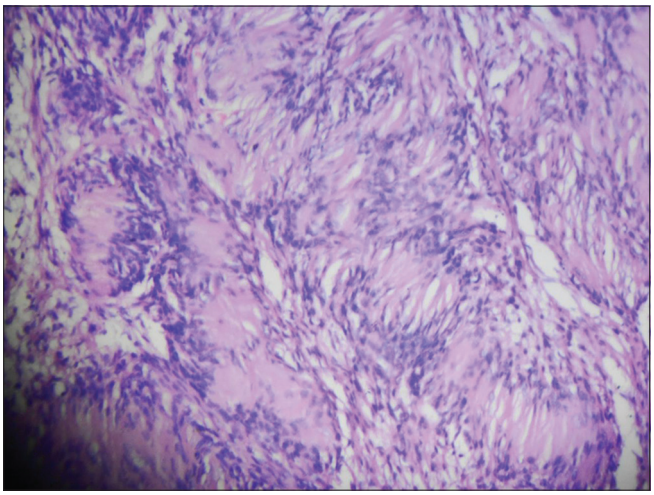


Figure 5: Schwannoma showing Antoni A (Hypercellular areas) with characteristic Verocay bodies (H and E ×10)

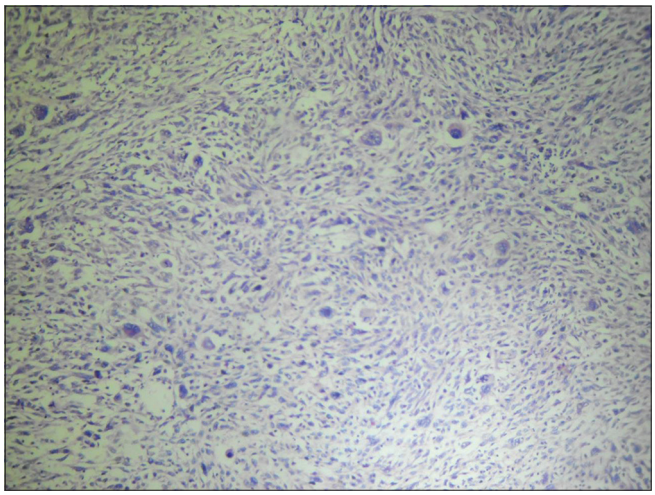


Figure 6: Undifferentiated pleomorphic sarcoma showing mostly spindled cells, many pleomorphic and bizarre-looking cells arranged in short, irregular fascicles. Multinucleated tumor giant cells and mitotic figures are also seen (H and E ×10)

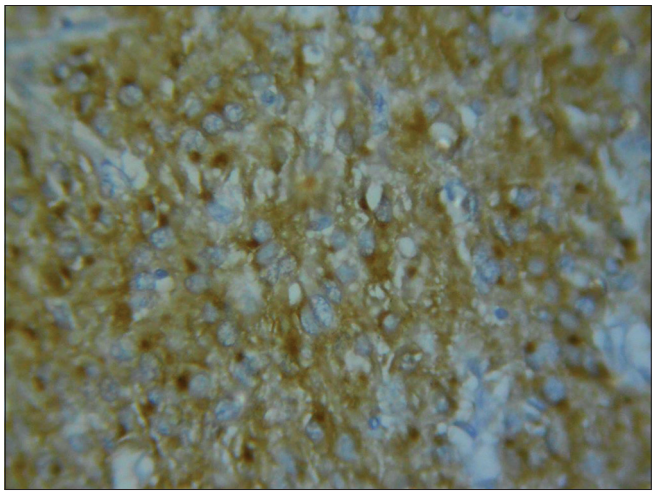


Figure 7: Tumor cells in gastrointestinal stromal tumor exhibiting CD117 immunostain positivity

out of 370 soft-tissue tumors that were studied, 206 cases (55.68%) were males and 164 (44.32%) were females, and the male-to-female ratio was 1.2:1. The present study is also in concordance to the study by Beg et al.,[11] where 64.3% of STT occurred in males and 35.7% occurred in females with approximate male-to-female ratio of 1.8:1.

Adipocytic tumors were the most common type of soft-tissue tumors to be diagnosed that constituted 62.5% of all the tumors. This finding is in concordance with the majority of other studies. In the study by Badwe and Desai[8] adipocytic tumors constituted 54.81% of all soft-tissue tumors. The study by Jain et al.[9] reported the incidence of adipocytic tumors to be 50.27%. The study by Beg et al.[11] reported slightly lower values, in which the incidence of adipocytic tumors was observed to be 40.5%. The incidence of adipocytic tumors in the study by Roy et al.[2] was much lower (25.71%). The most common adipocytic tumor in the present study was lipoma. Similarly, the studies by Beg et al.,[11] Jain et al.,[9] and Roy et al.[2] reported lipoma as the most common among adipocytic tumors. One case of lipomatosis was reported in the present study. In the study by Beg et al.,[11] out of 51 adipocytic tumors, 2 cases of lipomatosis were reported. In the present study, one case of atypical lipomatous tumor (Well-differentiated liposarcoma) was reported. It was earlier classified as a malignant adipocytic tumor but later reclassified atypical lipomatous tumor as an intermediate-grade tumor.

Incidence of vascular tumors was reported in the present study to be 14.47% and this observation is similar to the study by Soni et al.,[7] where the incidence was 16%. The studies by Jain et al. and Badwe and Desai[8] showed a slightly

higher incidence of 20% and 25.4% respectively. In a study reported in Turkey in 2011, vascular tumors accounted for the largest group among benign soft-tissue tumors, accounting to 37.5% cases.[12]

Nerve sheath tumors were included for the 1st time in the WHO classification in 2013. Nerve sheath tumors constituted 7.89% of all cases in the present study. While studies by Badwe and Desai[8] and Beg et al.[11] reported a similar incidence of 9.63% and 10.32%, respectively, Jain et al reported a slightly higher incidence of 19.72%. The most commont diagnosis among nerve sheath tumors was Schwannoma in the present study followed by neurofibroma. This finding is in concordance with the study by Beg et al.[11]

Tumors in the category Fibroblastic/myofibroblastic tumors accounted for 5.92% of all soft-tissue tumors in the present study. The studies by Badwe and Desai[8] and Jain et al.[9] reported a slightly lower incidence of 4.31%% and 2.97%, respectively.

In the present study, so-called fibrohistiocytic tumors formed 5.26% of all cases. Slightly lower number of cases were reported in the studies by Jain et al.[9] and Badwe and Desai.[8] Similar to the present study, benign Fibrous histiocytoma was the most common tumor in this category in the study by Badwe and Desai.[8]

Tumors of uncertain differentiation accounted for only 1.44% of all soft-tissue tumors. In the study by Badwe and Desai,[8] this category constituted 1.32%.

3 cases (1.98%) of undifferentiated pleomorphic sarcomas were seen in this study. In the study by Badwe and Desai,[8] their incidence was seen to be 0.33%.

Overall, benign mesenchymal tumors outnumber malignant mesenchymal tumors by a large majority.

Limitations of the study

The present study has not included molecular testing of the soft tissue tumors due to lack of the facilitites in our centre.The sample size was low.

CONCLUSION

The diagnosis of soft-tissue tumors needs a meticulous approach and team effort. Proper examination of the gross specimen and careful sampling of the tumor is required for the correct diagnosis. Hematoxylin- and eosin-stained sections remain the gold standard for the diagnosis of soft-tissue tumors along with immunohistochemistry and molecular markers. The WHO classification of soft-tissue tumors keeps evolving and offers a more logical histopathological classification and standard nomenclature of soft-tissue tumors. However, the classification leans more heavily on molecular diagnosis than morphological pattern now. For a country like India where only a few centers have all the ancillary diagnostics methods, the diagnosis of soft-tissue tumors will continue to pose a challenge.

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Authors Contribution:
JB- Design of the study, review of literature, analysis and preparing the manuscript, preparing the manuscript; **SPBV-** Review of literature; **SSKG-** Analysis and preparing the manuscript; **BS**- preparing the manuscript.

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