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Evaluation of soft tissue tumors with immunohistochemistry correlation

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Abstract: *Background:* Soft tissue tumors (STTs) are heterogeneous group of tumor and Immunohistochemistry (IHC) has assumed an increasingly important role in their diagnosis. *Objectives:* To estimate the relative frequency of various STTs with age, gender and site wise distribution, study their histomorphological spectrum, grade the soft tissue sarcomas and evaluate the role of IHC. *Materials and Methods:* This observational study was conducted in tertiary care hospital and cases diagnosed as STTs from January 2018 to December 2020 were included in the study. Clinical findings were obtained from patients' case files. Histological findings were evaluated and grading was done in soft tissue sarcomas. IHC was performed wherever required. Descriptive and comparative statistical analysis was performed. *Results:* STTs were encountered more in female than male. Benign STTs were more common than malignant. Incidence of malignancy increased with age, malignant tumors being most common in fifth decade. Adipocytic tumors (n=162, 63.8 %) formed major bulk of benign tumors. Most common malignant STTs were smooth muscle tumors (n=6, 23.1 %). IHC was very important in diagnosis of STTs because of frequent difficulty of diagnosis on morphological basis alone. *Conclusions:* Adipocytic tumors were most common benign STTs and most common malignant STTs were smooth muscle tumors.

Keywords: Soft tissue tumors, Benign, Malignant, Intermediate, Histopathology, Immunohistochemistry.

Introduction

Soft tissue tumors (STTs) are a highly heterogeneous group of tumors that are classified by their line of differentiation, according to the adult tissue they resemble. They are usually divided into benign, intermediate (borderline or low malignant potential) and malignant forms [1].

With the exception of skeletal muscle neoplasms, benign soft tissue tumors are 100-fold more frequent than their malignant counterparts, the sarcomas. In the United States, the incidence of soft tissue sarcomas is approximately 12,000 per year, which is less than 1% of all cancers. Sarcomas, however, cause 2% of all cancer mortality, reflecting their aggressive behavior and resistance to chemotherapy. Most soft tissue tumors arise in the extremities, particularly the thigh. Approximately 15% arise in children; the incidence increases with age [2]. In India, the projected incidence of soft tissue sarcomas in 2020 is 14,637 cases with crude rate of 1.0 and cumulative risk of 1 in 936 persons [3]. Immunohistochemistry (IHC) has assumed an increasingly important role in diagnosis of majority of soft issue tumors [4]. This study was focused to estimate the relative frequency of various benign, intermediate and malignant STTs. Aim of the study was to study the histomorphological spectrum of different STTs, evaluate the role of IHC and to grade the soft tissue sarcomas.

Material and Methods

General study details: An observational three years study was conducted (two years retrospective and one year prospective) in the Department of Pathology of tertiary care hospital of Ahmedabad city as per the ethical guidelines outlined in the Declaration of Helsinki (2013), Good Clinical Practice guidelines and the Indian Council of Medical Research guidelines. The study was approved by the Institutional ethics committee for

biomedical and health research on 8th Feb 2020 (approval number 139/2020). Informed consent from the participants was not required as it was an observational study.

Participants:

- All type of biopsies- incisional, excisional, tru-cut, ultrasonography guided and computed tomography guided, received in histopathology lab during the period from January 2018 to December 2020 and diagnosed as STTs were included in the study irrespective of age and gender.
- All the non-mesenchymal tumors and bone tumors were excluded from study.

Variables: The primary aim of the study was to estimate the relative frequency of various benign, intermediate and malignant STTs along with age, gender and site wise distribution. The secondary aim was to study the histomorphologic spectrum of various STTs, to evaluate the role of IHC in diagnosis of STTs along with grading of soft tissue sarcomas.

Study methodology: All biopsies and resected specimens of the STTs were fixed in 10% formal saline. Gross characteristics were noted and representative sections were taken from resected specimens and small biopsies were processed entirely. Staining of sections was done with routine hematoxylin and eosin (H & E) stain. Microscopic pathological findings were evaluated on these slides and histological sub typing was done into benign, intermediate and malignant categories. IHC was performed wherever required for final diagnosis and significance of the same was also analyzed. Grading was done in soft tissue sarcomas. Clinical findings were obtained from patients' case files retrieved from the Medical Record Department.

Definitions: STTs were categorized according to World Health Organization (WHO) classification of Soft tissue and bone tumour. Sarcomas were graded into grades 1, 2 and 3 according to French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading system (Supplementary Appendix 1: Table 1) [5-6]. Risk stratification for Gastrointestinal Stromal Tumors (GISTs) was done according to algorithm by Miettinen and Lasota [7].

Supplementary Appendix 1- Table-1: FNCLCC grading system for sarcoma

Histologic Grade	Tumor differentiation + mitotic count + tumor necrosis
Tumor differentiation	
Score 1	Sarcomas that closely resemble normal adult mesenchymal tissue
Score 2	Sarcomas for which histologic typing is certain
Score 3	Embryonal and undifferentiated sarcomas, synovial sarcoma and sarcomas of uncertain differentaition
Mitotic count	
Score 1	0-9/10 hpf
Score 2	10-19/10 hpf
Score 3	20 or more/ 10 hpf
Tumor necrosis	
Score 1	No necrosis
Score 2	< 50% tumor necrosis
Score 3	50% or more tumor necrosis
Histologic Grade	
Grade 1	Total score 2, 3
Grade 2	Total score 4, 5
Grade 3	Total score 6, 7, 8

Statistics: All the collected data was analyzed and descriptive as well as comparative statistical analysis like calculation of percentage value, ratios, mean, median, standard deviation, p value, Tukey's test and coefficient of correlation(r) were performed using the Statistical Package for the Social Sciences (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA: IBM Corp.).

Results

General: Over the period of three years out of the total 15,554 surgical specimens received in the histopathology section, 290 (1.86 %) specimens were STTs after considering all the inclusion and exclusion criteria.

Table 1 shows gender wise distribution of total STTs according to tumor differentiation. STTs across all the categories were more common in females than males, though not significant statistically significant (p=0.774, >0.05). The ratio of benign to malignant STTs

was 9.8:1. Maximum numbers of benign STTs were seen in the third decade whereas malignant STTs were most numerous in the fifth decade (Supplementary appendix 1: Table 2). The mean age of patients with benign, intermediate and malignant STTs was 37.38 ± 14.51 years, 44.10 ± 18.11 years and 54.62 ± 12.29 years respectively. The Tukey's test showed a significant difference between mean age and different tumor categories (benign, intermediate and malignant) (F value 1.73, p = 0.002). Correlation between age and different categories of tumors showed that the frequency of malignant tumors increases with age (r= 0.318, p =0.0001).

Table-1: Distribution of soft-tissue tumors according to tumour differentiation, category and gender

Tumor differentiation with total cases (n, %)	Category of Soft tissue tumors						Total no. of cases (n)	
	Benign (n)		Intermediate(n)		Malignant (n)			
	M	F	M	F	M	F	M	F
Adipocytic (166, 57.2%)	84	78	2	1	1	0	87	79
PNST (36, 12.4%)	14	20	0	0	0	2	14	22
Vascular (35, 12.1 %)	19	15	0	0	0	1	19	16
Fibroblastic/ Myofibroblastic (12, 4.1%)	3	3	1	4	0	1	4	8
Fibrohistiocytic (9, 3.1%)	2	7	0	0	0	0	2	7
Unclassified (9, 3.1%)	1	3	0	1	1	3	2	7
Smooth muscle (8, 2.7%)	0	2	0	0	3	3	3	5
GIST (7, 2.4%)	0	2	1	0	3	1	4	3
Uncertain origin (3, 1%)	0	0	0	0	1	2	1	2
Undifferentiated (3, 1%)	0	0	0	0	1	2	1	2
Pericytic (1, 0.3%)	1	0	0	0	0	0	1	0
Chondro-osseous (1, 0.3%)	0	0	0	0	1	0	1	0
Gender distribution category wise	124 (48.8%)	130 (51.2%)	04 (40%)	06 (60%)	11 (42.3%)	15 (57.7%)	138 (47.6%)	152 (52.4%)
Total n (%)	**254 (87.6%)**		**10 (3.4%)**		**26 (9.0%)**		**290(100%)**	

Supplementary Appendix 1- Table-2: Age wise distribution of soft tissue tumors

Age group	Benign (n, %)	Intermediate (n, %)	Malignant (n, %)
0-10 years	8(3.1 %)	0	0
11-20 years	20(7.9 %)	1(10 %)	1(3.8 %)
21-30 years	57(22.4 %)	2(20 %)	0
31-40 years	73(28.7 %)	1(10 %)	3(11.5 %)
41-50 years	54(21.3 %)	1(10 %)	4(15.4 %)
51-60 years	28(11.0 %)	3(30 %)	10(38.5 %)
61-70 years	12(4.7 %)	2(20 %)	7(26.9 %)
> 70 years	2(0.8 %)	0	1(3.8 %)

n : number of cases

Among the total STTs, adipocytic tumors formed the largest group of tumors (n=166, 57.2%), followed by peripheral nerve sheath tumors (PNST) (n=36, 12.4%) and vascular tumors (n=35, 12.1%). Adipocytic tumors (n=162, 63.8 %) formed the major bulk of benign tumors and the most common malignant STTs were smooth muscle tumors (n=6, 23.1 %) (Table1). Individually benign and malignant STTs showed maximum predilection for upper limb (n=60, 23.6%) and head and neck region (n=7, 26.9%) respectively. 38 tumors (13.1%) were deep-seated and 252 tumors (86.9 %) were superficial. Tumor (T) size varied from 0.4 to 50 cm with mean size 4.7 $\pm$ 4.6 cm and median was 3.5 cm. T-size was $\geq$ 5 cm seen in 105 (36.2 %) cases. Table 2 shows the histomorphological spectrum of various STTs.

Table-2: Histomorphological spectrum of various soft tissue tumors

Tumor differentiation	Benign	Intermediate	Malignant
Adipocytic (n=166)	Classical Lipoma (n=156) Fibrolipoma (n=5) Angiolipoma (n=1)	Atypical lipomatous tumour (n=1) Well differentiated liposarcoma (n=2)	Pleomorphic liposarcoma (n=1)
PNST (n=36)	Neurofibroma (n=17) Schwannoma (n=13) Dermal nerve sheath myxoma (n=1) Granular cell tumor (n=1)	nil	Malignant PNST (n=2)
Vascular (n=35)	Capillary type hemangioma (n=13) Arteriovenous malformation (n=9) Mixed type hemangioma (n=7) Lobular capillary hemangioma (n=2) Epithelioid hemangioma (n=1) Cherry hemangioma (n=1) Lymphangioma (n=1)	nil	Angiosarcoma of soft tissue (n=1)
Fibroblastic/ Myofibroblastic (n=12)	Fibroma of tendon sheath (n=3) Myositis ossificans (n=2) Calcifying aponeurotic fibroma (n=1)	Desmoid type fibromatosis (n=3) Dermatofibrosarcoma protrubens (n=2)	Low grade fibromyxoid sarcoma (n=1)
Fibrohistiocytic (n=9)	Tenosynovial giant cell tumor-localized type (n=7) Deep BFH (n=2)	nil	Nil
Unclassified (n=9)	Spindle cell morphology (n=4)	Spindle cell tumor with hemangiopericytoma like areas (n=1)	Spindle cell morphology (n=4)
Smooth muscle (n=8)	Disseminated peritoneal leiomyomatosis (n=1) Leiomyoma of prostate (n=1)	nil	Leiomyosarcoma (n=6)
GIST (n=7)	Very low risk (n=1) Low risk (n=1)	Moderate risk (n=1)	High risk (n=4)
Uncertain origin (n=3)	nil	nil	Synovial sarcoma (n=2) Clear cell sarcoma of soft tissue(n=1)
Undifferentiated (n=3)	nil	nil	Spindle cell morphology (n=2) Pleomorphic morphology (n=1)
Pericytic (n=1)	Glomus tumor (n=1)	nil	Nil
Chondro-osseous (n=1)	nil	nil	Extraskeletal Osteosarcoma (n=1)

n: number of cases, PNST: Peripheral nerve sheath tumor; GIST: Gastrointestinal stromal tumor, BFH : Benign Fibrous Histiocytoma

Adipocytic tumors: Majority of the adipocytic tumors were benign lipomas (*n* = 162, 97.6%) which were located predominantly superficially in the limbs followed by head and neck region. Two of the patients had recurrent lipoma. Benign tumors were seen two decades earlier compared to intermediate and malignant tumors which included atypical lipomatous tumor located in nape of neck, well differentiated liposarcoma located in retro peritoneum and pelvis and pleomorphic liposarcoma located in axillary region. Well differentiated liposarcoma were graded as Grade 1 whereas pleomorphic liposarcoma was graded as Grade 3 on the FNCLCC grading.

Peripheral nerve sheath tumors: Most of the PNSTs were benign (n=34, 94.4%) and mostly located superficially in the limbs followed by head and neck region. Two patients with neurofibroma were known case of neurofibromatosis with one of them having plexiform neurofibroma. IHC for S-100 was performed to differentiate between Neurofibroma and Schwannoma and to differentiate between cellular Schwannoma/ ancient Schwannoma from low grade malignant PNST (MPNST) wherever required. Cases with strong and diffuse positivity for S-100 were reported as Schwannoma.

Patient with dermal nerve sheath myxoma had history of recurrent tumor on wrist. Grossly it presented as a well demarcated nodule. Cut surface was well capsulated, multiloculated and lobules filled with jelly like material. Microscopic examination revealed lobules of variable sizes composed of relatively uniform spindle cells embedded in abundant myxoid stroma. No mitoses were seen. Alcian blue stain highlighted the presence of abundant mucin in the background.

Granular cell tumour presented as an axillary mass in a female patient and IHC was performed for confirmation as it was an unusual site for this tumor. Tumor was positive for S-100 and CD 68.

Out of the two cases of MPNST one was recurrent and located on the thigh. The other was large in size (14 cm) and located in the retro peritoneum. IHC for S-100 was positive in patchy fashion while Smooth Muscle Actin (SMA), Desmin, Pan Cytokeratin (CK), Epithelial Membrane Antigen (EMA), CD 117 and Neuron Specific Enolase (NSE) were negative; which confirmed the neural origin. FNCLCC grading of MPNST is not recommended.

Vascular tumors: Majority of the vascular tumors were benign hemangioma (*n* =24, 68.6%). Most of them were seen in the limbs followed by head and neck region, in younger patients (mean age 30.6 $\pm$ 15.5 years) and presented as small swellings (<5 cm). Six of them were infantile hemangioma. Epithelioid hemangioma presented as a big paraspinal mass (15 cm). Lymphangioma presented as a large swelling (13 cm) on the chest wall.

Angiosarcoma (*n* =1, 2.8%) was seen in a 52 years female, presented as a fungating axillary mass and microscopically showed epithelioid morphology. IHC was done to differentiate it from primary breast carcinoma or metastatic carcinoma. Tumor was positive for vimentin and vascular markers like CD 31 and Factor VIII whereas it was negative for Estrogen receptors (ER), CK 7 and CK 20. FNCLCC grading of angiosarcoma is not recommended.

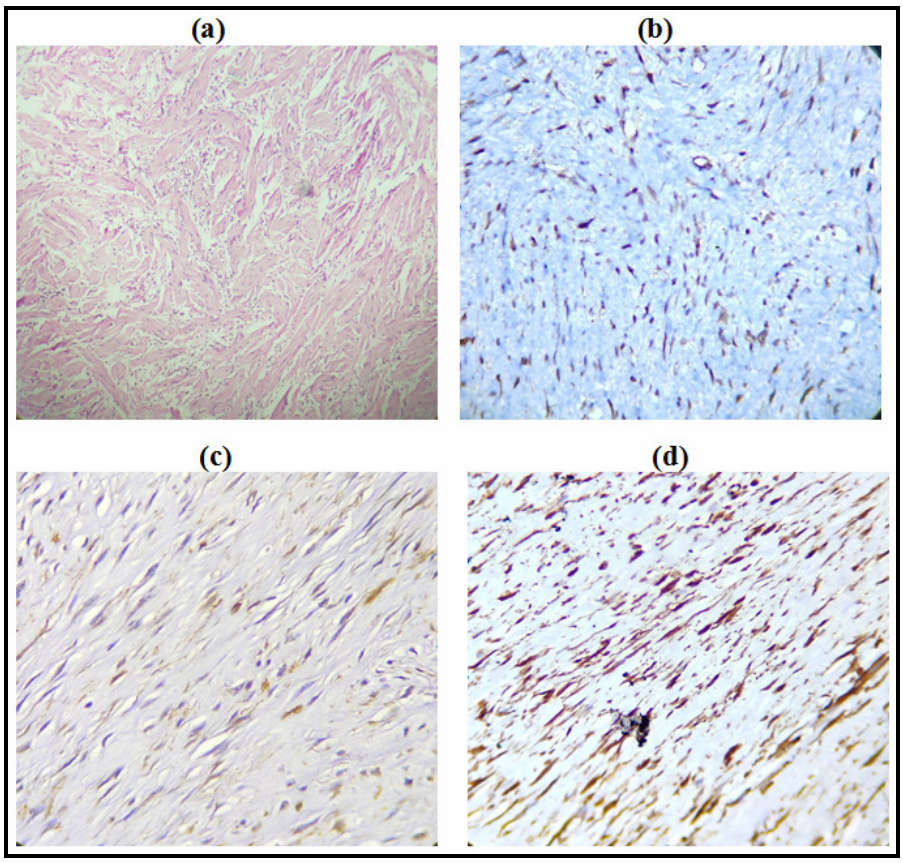
Fibroblastic/ myofibroblastic tumors: Benign cases were more common (n=6, 50%) and had size up to 6 cm and showed a propensity for the limbs, while intermediate tumors having size up to 7 cm were seen commonly in the head and neck region. In all the three cases of desmoid type fibromatosis IHC was performed to differentiate it from other spindle cell lesions. They were positive for beta-catenin (nuclear), vimentin and SMA whereas negative for CD 34, Discovered on GIST 1(DOG-1), cyclin D1, Pan CK and S-100 (Fig. 1(a-d)).

Out of the two cases of dermatofibrosarcoma protuberans (DFSP) one was incisional biopsy whereas other was excisional biopsy. In case of incisional biopsy IHC for CD 34 was performed to differentiate it from deep Benign Fibrous Histiocytoma (BFH). CD 34 was diffusely positive and hence reported as DFSP.

Low grade fibromyxoid sarcoma presented as an 8 cm mass in the retroperitoneal region.

The tumor had low cellularity with bland spindled cells with diffuse whirling in heavily collagenized stroma with abrupt transition to myxoid areas and was graded as FNCLCC Grade 1. IHC markers were positive for CD 99, BCL 2, Vimentin and EMA whereas were negative for Pan CK, SMA, Desmin, S-100 and CD 34; which confirmed the diagnosis.

Fig-1: Desmoid type fibromatosis- (a) H & E stain, 10x (b) beta catenin-2, 10x (c) Smooth muscle actin, 10x (d) Vimentin, 10x



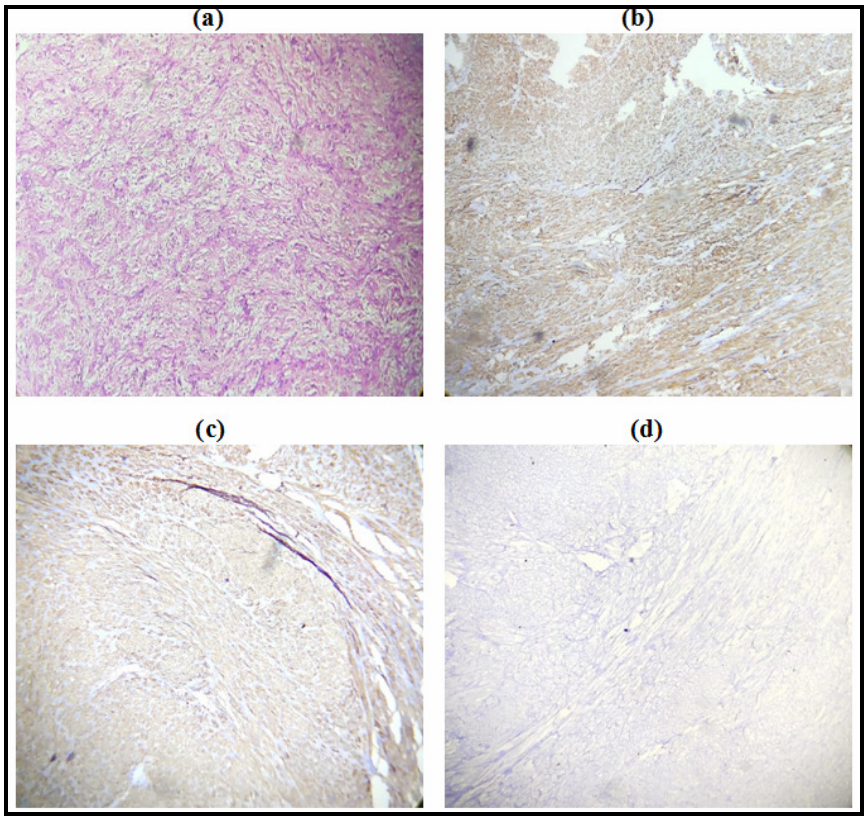
Fibrohistiocytic tumors: All these tumors were benign and showed propensity for upper limb. IHC was performed in cases of deep BFH. IHC markers were positive for Vimentin and SMA whereas were negative for Pan CK, S-100 and CD 34 which ruled out Dermatofibrosarcoma protrubens.

Smooth muscle tumors: Disseminated peritoneal leiomyomatosis was seen in a 48 years female patient. She presented with multiple intraabdominal (pelvic and serosal) masses and had a past history of hysterectomy before six years for multiple uterine leiomyomata. Now on CT scan it was suspected as a case of lymphoma with largest lesion measuring 8 cm in diameter. Initial trucut biopsy was reported as benign spindle cell lesion. Follow up excision biopsy was performed. IHC markers were positive for Vimentin, SMA and desmin whereas were negative for S-100, CD 117, Pan CK, Calretinin and Leucocyte common antigen (LCA), confirming the smooth muscle cell histogenesis. Majority of the smooth muscle tumors were malignant (n=6, 75%) and presented at various sites like lower limb, abdomen, upper esophagus, gall bladder and retro peritoneum. The retroperitoneal mass presented as a recurrent tumour. IHC was performed in all the cases and was positive for vimentin, SMA and desmin. Ki-67 was also done to see for proliferative index. On FNCLCC grading, one tumour was Grade 1, two were Grade 2 and three were Grade 3.

Gastrointestinal stromal tumors (GISTs): There were total seven cases of GISTs, one in stomach and the rest in small intestine - four

in jejunum, one in ileum and one in duodenum. Six cases had spindle cell morphology whereas one case had epithelioid morphology. IHC markers were positive for Vimentin, SMA, CD 117, DOG 1 and negative for S-100, Pan CK, CD 34 and Desmin. SMA was negative in GIST of stomach. Ki-67 was also done to see for proliferative index. All the four cases of jejunum were high risk tumors, ileal GIST was moderate risk, duodenal GIST was a low risk and the one in stomach was very low risk tumor (Fig. 2(a-d)).

Fig-2: Gastrointestinal stroma tumor, very low risk tumor- (a) H & E stain, 10x (b) DOG -1, 10x (c) CD 117, 10x (d) Ki-67< 1%, 10x



Tumors of pericytic differentiation: This included a glomus tumor of 0.5 cm which presented as a tiny mass on the index finger of the patient. There was no evidence of cytological atypia.

Tumors of chondro-osseous differentiation: This included a case of extra skeletal osteosarcoma located in the inguinal region.

Tumors of uncertain origin: Both the cases of synovial sarcoma had biphasic morphology and IHC was carried out to differentiate from other tumors with similar morphology. They were positive for Pan CK, Vimentin, CD 99 and negative for CD 34, Desmin, S-100, DOG 1, SMA and CD 117. One was Grade 2 tumor (Ki-67 labeling index-<2%) and the other was Grade 3 (Ki-67 labeling index-40%) on FNCLCC grading. Clear cell sarcoma of soft tissue on IHC was found to be positive for Vimentin, S-100 and HMB 45 and negative for desmin, myogenin and high molecular weight keratin (HMWK). FNCLCC grading of Clear cell sarcoma is not recommended.

Undifferentiated sarcomas: Amongst undifferentiated sarcomas of spindle cell morphology IHC markers were positive for vimentin only whereas they were negative for CK 7, p53, EMA, CD 68, CD 34, Desmin, S-100 and SMA. One case had pleomorphic morphology; IHC was positive for Vimentin and CD 68 but was negative for Pan CK, Desmin, S-100, SMA and CD 57. Ki-67 labeling index was performed and on FNCLCC grading all the three tumors belonged to Grade 3.

Unclassified: These tumors were categorized as unclassified as they didn't have any specific histomorphologic features. IHC could not be performed in these cases due to various reasons like scanty tissue, financial constraints of patients or lost to follow up.

Discussion

This was the first study undertaken in this tertiary care institute on evaluation of STTs with IHC correlation. Benign STTs were more common than malignant tumors in the present study similar to other studies (Supplementary Appendix 1: Table 3) [8-15]. There was female predominance in both the categories however there was no statistical significance of the same. Majority of benign STTs were seen in the third decade whereas malignant STTs were most numerous in the fifth decade. These findings were in concordance with study conducted by Jain et al [15].

Supplementary Appendix 1- Table-3: Comparative analysis of benign and malignant soft tissue tumors

Studies	No. of cases (%)		Ratio
	Benign	Malignant	
Gogoi et al.,2017 [8]	733(92.8%)	61(7.6%)	12
Ivan et al.,2015 [9]	139(89.7%)	16(10.3%)	8.6
Deepak et al.,2016 [10]	213(85.2%)	30(12%)	7.1
Baste et al.,2017 [11]	65(95.6%)	03(4.4%)	21.6
Janaki et al.,2015 [12]	193(92%)	09(4.2%)	21.4
Soni et al.,2016 [13]	140(93.3%)	10(6.7%)	14
Jain et al.,2017 [14]	280(89.7%)	28(9.2%)	9.7
Jain et al.,2014 [15]	335(90.6%)	35(9.4%)	9.5
Present study	254(87.6%)	26(9.0%)	9.8

Table-3: Comparative analysis of soft tissue tumors according to tumor differentiation

Tumor differentiation	Ivan et al. 2015 [9]	Baste et al. 2017 [11]	Soni et al. 2016 [13]	Jain et al. 2014 [15]	Singh et al. 2017 [16]	Present study
Adipocytic	76 (49%)	46 (67.6%)	70 (46.7%)	186 (50.3%)	92 (34.1%)	166 (57.2%)
PNST	28 (18.1%)	8 (11.8%)	24 (16%)	73 (19.7%)	30 (11.1%)	36 (12.4%)
Vascular	33 (21.3%)	6 (8.8%)	24 (16%)	74 (20%)	50 (18.5%)	35 (12.1%)
Fibroblastic/ Myofibroblastic	12 (7.7%)	3 (4.4%)	11 (7.3%)	11 (3.0%)	19 (7.0%)	12 (4.1%)
Fibrohistiocytic	0	2 (2.9%)	13 (8.7%)	12 (3.2%)	16 (5.9%)	9 (3.1%)
Unclassified	0	0	0	0	32 (11.9%)	9 (3.1%)
Smooth muscle	4 (2.6%)	0	2 (1.3%)	6 (1.6%)	13 (4.8%)	8 (2.7%)
Striated muscle	1 (0.6%)	0	0	5 (1.3%)	3 (1.1%)	0
GIST	0	0	0	0	0	7 (2.4%)
Uncertain origin	1 (0.6%)	2 (2.9%)	3 (2%)	3 (0.81%)	12 (4.5%)	03 (1%)
Undifferentiated	0	1 (1.5%)	1 (0.7%)	0	0	3 (1%)
Pericytic	0	0	1 (0.7%)	0	3 (1.1%)	1 (0.3%)
Chondro-osseous	0	0	1 (0.7%)	0	0	1 (0.3%)
Total	**155**	**68**	**150**	**370**	**270**	**290**

PNST: Peripheral nerve sheath tumour; GIST: Gastrointestinal stromal tumour

The most common site involved by benign STTs was upper limb followed by head and neck region whereas sarcomas most commonly occurred in head and neck region followed by upper and lower limbs. In study by Soni et al.,[13] the commonest site for benign and malignant STTs was upper limbs followed by trunk and the lower limbs followed by trunk region respectively. On evaluating histological subtypes in this study, adipocytic tumors were the most common followed by PNSTs and vascular tumors. This finding was comparable with other studies as shown in Table 3.

Benign lipoma was the most common amongst adipocytic tumors (n=162, 97.6 %). This finding was similar to studies by Ivan et al.,[9] Jain et al. [14] and Jain et al. [15] who reported 92.3%, 99.3% and 94% of lipoma respectively. Only malignant lipomatous tumor in present study was pleomorphic liposarcoma reported in axillary region in 63 years male similar to study by Jain et al. [14] which also had a single case of round cell liposarcoma. The study of Jain et al. [15] reported 11 cases of malignant lipomatous tumors.

PNSTs were second most common tumors and accounted for 12.4% *(n=36)* of the total STTs which is similar to studies done by Baste et al. (11.8%) [11] and Singh et al. (11.1%) [16]. There was female preponderance which was similar to study done by Deepak et al [10] There were two cases of MPNST in the present study, one in lower limb and other in retro peritoneum. Findings were similar to study done by Singh et al [16].

Among the vascular tumors, hemangioma was the most common (n = 32, 91.4%). This observation is in concordance with the studies conducted by Soni et al, [13] Jain et al. [14] and Singh et al. [16] Only one case of angiosarcoma was seen in the present study. Soni et al [13] and Jain et al. [14] did not report any case of angiosarcoma whereas Singh et al. [16] reported two cases of angiosarcoma in the extremities.

Benign, intermediate and malignant fibroblastic/ myofibroblastic tumors were 50%, 41.7% and 8.3 % respectively which are comparable to findings by Singh et al. **[**16**]**. Fibrohistiocytic tumors comprised 3.1% (n=9) of the total STTs which is comparable to the findings in studies done by Baste et al. [11] and Jain et al. [15]

Benign and malignant smooth muscle tumors were 25% (n=2) and 75% (n=6) respectively compared to Jain et al. [15] which had 33.3% and 66.6% of them respectively. There was one case of leiomyomatosis peritonealis disseminata which is a rare condition in which multiple smooth muscle or smooth muscle–like nodules develop in a sub peritoneal location throughout the abdominal cavity [1].

There were seven (2.4%) cases of GISTs in the present study whereas none of the similar studies has reported even a single case (Table 3). In the present study, 86% cases (n=6) were of spindle cell morphology whereas the remaining 14% (n=1) were of epithelioid morphology. Depending on the tumour location and morphology tumors such as fibromatosis (desmoids tumour), schwannoma, leiomyoma, leiomyosarcoma, solitary fibrous tumors, glomus tumors, inflammatory fibroid polyps, carcinomas and malignant lymphoma are subject to the differential diagnoses [17].

Risk stratification of GISTs was done according to guidelines by Miettinen and Lasota which includes anatomic site as a factor according to which small bowel GISTs carry a higher risk of progression than gastric GISTs of similar size and mitotic activity [7]. Similar findings were seen in the present study in which majority of the cases of small bowel were high risk tumors. There was one case of glomus tumor located subungally in the index finger which is similar to the study done by Gogoi et al. [8] in which there were two cases of glomus tumor and both of them were located in the upper extremity.

There was one case of tumor with chondro-osseous differentiation which is similar to study done by Soni et al. [13]. This patient was a 48 years male; was a known case of renal cell carcinoma and given radiotherapy for the same. Tumor developed post radiotherapy in the radiation damaged tissue. Both the cases of synovial sarcoma presented with multiple metastasis. Clear cell sarcoma commonly arises from large tendinous sheaths

and aponeuroses of extremities. In the present study the tumor was present on hand. There were three cases of undifferentiated sarcomas, out of which one developed post radiotherapy in a known case of malignant lymphoma. 3.1% of the cases (n=9) could not be classified due to various reasons which is comparable to study done by Jain *et al.* (2%) [14].

Role of IHC in soft tissue tumors [1, 18]: Initially a differential diagnosis is reached by correlating clinical, radiologic and histomorphologic features of the tumor. H & E stained sections represent the mainstay of diagnosis but occasionally must be supported by ancillary techniques like histochemistry and IHC. A definitive diagnosis to establish a potential line of histogenesis in difficult cases is done by IHC. IHC is rarely decisive for distinguishing a benign lesion from a malignant one, but it can contribute to identify some benign pseudo malignant lesions and for confirmation of STTs at unusual site.

It is mostly required in diagnosis of malignant soft tissue tumors as an adjunct to histology and is very important in the field of STTs because of their variety and the frequent difficulty of diagnosis on morphological basis alone. Four common histologic scenarios of STTs in which IHC can provide valuable clues to the correct diagnosis are undifferentiated round cell tumor, monomorphic spindle cell tumor, and poorly differentiated epithelioid tumor, as well as "orphan sarcomas." Orphan sarcomas includes tumors with no known normal cell counterpart (e.g., undifferentiated pleomorphic sarcoma) as well as those with a known cell counterpart (e.g., liposarcoma, osteogenic sarcoma, chondrosarcoma) but with no reliable, useful specific markers at present. Whereas markers for osteosarcoma have been developed, such as SATB2, osteocalcin, and osteonectin, these appear to be markers of osteoblastic differentiation and osteoid production, rather than lineage-specific markers of osteosarcoma.

Though IHC is a simple technique, outcome depends on technical expertise and experienced eyes of the histopathologist. Ki-67 labeling index is performed to look for proliferative index. Significant associations have been shown between a Ki-67 labeling index of more than 20% with high-grade, shortened overall survival and the development of metastatic disease.

Limitations of the study: Benign STTs greatly outnumber malignant tumors, and because many benign tumors like lipomas and hemangiomas, do not undergo biopsy, direct application of data from most hospital series is invalid for general population. The diagnostic process of STTs relies upon a combination of conventional microscopy, IHC and molecular genetics. STTs like well differentiated liposarcoma, GIST, synovial sarcoma, undifferentiated round cell sarcomas, clear cell sarcoma and few more require molecular genetics testing for diagnostic, prognostic and therapeutic purposes. Further evaluation by molecular genetics and new IHC markers was not possible in the present study due to unavailability of the same and financial constraints.

Future perspective: The ultimate goal for a pathologist is to render a specific diagnosis that provides diagnostic, prognostic and therapeutic information to guide patient care. A multidisciplinary approach by pathologists, clinicians and geneticists can translate novel findings into more rationale as well as effective treatments in case of STTs.

Conclusion

Benign STTs were more common than malignant STTs with incidence of malignancy increasing with age, malignant tumors being most common in the fifth decade. Adipocytic tumors were the most common benign STTs and most common malignant STTs were smooth muscle tumors. IHC plays an important role in the diagnosis of STTs however selection of an appropriate IHC panel is crucial to reach a correct diagnosis. Tumor grading remains one of the most powerful and inexpensive ways of assessing prognosis, progression and treatment response in a soft tissue sarcoma.

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