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Histopathological study of soft tissue tumors: A three year experience in tertiary care centre

Preeti Rihal Chakrabarti[1,*], Suvadip Chakrabarti[2], Ajita Pandit[3], Purti Agrawal[4], Shilpi Dosi[5], Mukul Raj Jain[6]

[1,4,5,6]Assistant Professor, Dept. of Pathology, [2]Senior Resident Dept. of Surgical Oncology, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh
[3]Ex Professor Pathology, D Y Patil School of Medicine, Navi Mumbai

***Corresponding Author:**
Email: preetirihal@yahoo.co.in

ABSTRACT

Background: *Soft tissue sarcomas compared with carcinomas and other neoplasms are relatively rare and constitute less than 1% of all the cancer. Soft tissue sarcomas may occur anywhere in the body but most arise from large muscle of extremeties, the chest wall, the mediastinum and the retroperitoneum.*

Aims and objectives: *To study the macroscopic and microscopic pathology of benign and malignant soft tissue tumour and there clinicopathological correlation.*

Materials and methods: *The study was conducted in Dr .D .Y Patil School of Medicine, Navi Mumbai, from 1st of January 2008 to December 2010. A Cross sectional study of 150 cases of soft tissue tumors were carried out in details. A pretested proforma was used to classify each tumor and details like age, sex, clinical features, gross and microscopic findings were noted.*

Results: *The most common soft tissue tumor in the study were benign tumors (140 cases), followed by malignant (9 cases) and one case was reported as borderline. Lipomas were the most common benign tumors accounting for 49 out of 140 cases. Benign smooth muscle tumors were the next most common tumor accounting for 44 cases.Benign vascular and benign peripheral nerve sheath tumor accounted for 19 cases in each category. Of 19 cases of benign vascular tumor, 16 cases were of haemangioma, 3 cases were of angiofibroma. Of 19 benign peripheral nerve sheethtumor, 12 cases were reported as neurofibroma and 7 schwannomas. Of 5 cases of fibrohistiocytictumor, 3 cases were benign, 1 case of borderline (Dermatofibrosarcoma protuberance) and 1 case of malignant fibrous histiocytoma (MFH). Of 7 cases of Fibrous tumor, 6 cases were of Benign and 1 cases of malignant variant (Fibrosarcoma). Out of 6 cases which were reported as benign, comprised of 2 cases each of fibroma, fibromxyoma, and palmar fibromatosis. 9 out of 150 cases were malignant tumors,3 cases were malignant peripheral nerve sheath tumor(MPNST) ,whearas Gastrointestinal stromal tumor(GIST),leiomyosarcoma, MFH, atypical lipomatoustumor, Fibrosarcoma, Embryonal rhabdomyosarcoma accounted for one case each.*

Conclusion: *Benign soft tissue tumors outnumbered malignant tumors by a ratio of 14:1. Lipomas and leiomyomas of gynaec origin were the most common benign tumors and MPNST were the most common malignant tumor in the present study. Most patients with soft tissue neoplasm presented with painless mass. Sarcomas, for the most part develop as deeply located mass. Hematoxylin and eosin stained sections represented the mainstay of diagnosis, however ancilliary techinque like immunohistochemistry (IHC) plays a important role in diagnosis.*

Keywords: *Soft tissue neoplasm, Benign, Malignant*

INTRODUCTION

Soft tissue sarcomas compared with carcinomas and other neoplasms are relatively rare and constitute less than 1%of all the cancer.[1] Soft tissue sarcomas may occur anywhere in the body but most arise from large muscle of extremities, the chest wall, the mediastinum and the retroperitoneum. They occur at any age and like carcinomas are more common in older patients, about 15% affect persons younger than 15 years, and 40 % affect persons 55 years or older.[1]

Genetic factors, environmental factors, irradiation, viral infections and immune deficiency have been found to be associated with development of unusually malignant soft tissue tumors. There has also been reports of sarcoma arising from surgical procedures or thermal or acid burns, a fracture site and vicinity of plastic or metal implant usually after latent period of several years.[2] Environmental carcinogens have also been reported to development of sarcomas eg-asbestos, phenocyacetic acid, chlorophenols and their contaminants. Radiation induced soft tissue sarcomas are quite uncommon. The incidence of post radiation sarcomas is difficult to estimate but reports generally range from 0.03%to 0.80%. Most incidence estimates are based on breast cancer patients treated with radiation as adjuvant therapy. The risk increases with dose. Most patients have received total dose of 5000 cGY or more. [3]

Several benign soft tissue tumors have been attributed to occur in familial or inherited basis.The most common examples are probably hereditary multiple lipomas (often angiolipomas). Desmoid tumors occur in patients with familial gardner syndrome. Neurofibromatosis (type 1 and 2) is associated with multiple benign nerve tumors. Near around 2% of the patients with neurofibromatosis type 1 developin malignant peripheral nerve sheath.[4]

AIMS AND OBJECTIVES

1. To analyse the various types and subtypes of soft tissue tumors.
2. To find out the incidence of benign and malignant soft tissue tumours.
3. To estimate the age, sex and location of benign and malignant soft tissue tumour.
4. To study the macroscopic and microscopic pathology of benign and malignant soft tissue tumor

MATERIALS AND METHODS

The study was conducted in Dr. D. Y Patil School of Medicine, Navi Mumbai, from 1st of January 2008 to December 2010. Total 150 cases of soft tissue tumors were analysed in the study period. Formalin fixed paraffin embedded sections were stained with Haematoxylin and Eosin and studied (H & E). The histopathological diagnosis was given and thus results obtained were analysed. The cases were further divided into following catogories:1) lipomatous tumor 2) Smooth muscle tumor 3)Skeletal muscle tumor 4)Fibrous tumor 5) Fibrohistiocytic tumor 6) Peripheral nerve sheath tumor 7) Blood vessel tumor. In each case, tumor were futher subclassified and details like age, sex, clinical features, gross and microscopic findings were noted. The results of IHC were noted wherever possible.

RESULTS

Out of total 150 cases in our study, 140 cases were benign in nature, 1 case was borderline and 9 were malignant [Table 1]. Of 50 lipomatous tumors, 49 cases were lipomas and one case was of liposarcoma. 41/49 cases(83.7%) of lipomas were classical type and 8/49 cases(16.3%) were fibrolipoma. The highest number of cases, 15/49(30.61%) were reported in the 4thand 5th decade of life with trunk being the commonest site with 20/49 cases (40.08%) and 34/ 49cases(69%) were seen in female[Table 2,3,4]. Benign smooth muscle tumors were the next most common tumor accounting for 44 cases with maximum no of cases in 4th and 5th decade. 42/44 cases were reported in uterine cavity including one each in broad ligament and cervix.

Benign vascular and peripheral nerve sheath tumor account for 19 cases in each category. Out of the 19 cases of benign blood vessel tumors,16 cases(84.2%) were reported as Haemangioma and 3 cases(15.7%) as angiofibroma. 7/19 cases (36.8%) were reported in the 2nd decade of life, with male predominance11/ 19 cases (56%) and Head and neck region was the commonest location 14/19 cases (73.6%) [Table 2,3,4]. Malignant tumor in this category was not observed in the present study. Of 19 benign peripheral nerve sheath tumor, 12 cases were reported as neurofibroma and 7 schwannomas. 5/12 cases (41.7%) of neurofibromas were seen in 2nd decade, with male predominance 8/12 cases (66.6%) and head and neck was the commonest location accounting for 5/12 cases (41.7%). All neurofibromas in present study had solitary presentation. Of 7 schwannomas, maximum no of cases 5/7 cases (71.4%) were seen in 4th decade, upper extremity being commonest location accounting for 4/7 cases (71.4%), with female predominance 5/7 cases (71.4%).[Table 2,3,4]

All 3 cases of MPNST were reported in male patients in the 2nd decade measuring more than 10 cm. Two cases were of classical type and one case of epithelioid type. Two cases were on back and one on scapula. 5 cases of fibrohistiocytic tumor, 3/5 cases (60%) were benign and 1 each were borderline and malignant. Out of the 3 cases of Fibrous histiocytoma, 2/3 cases (66.6%) were reported in 5th decade. 2/3 cases (66.6%) were seen in back, male to female ratio was 2:1[Table2,3,4]. 7 cases of Fibrous tumor were reported, 6/7 cases (85.7%) were benign and 1 case of fibrosarcoma. Fibroma, fibromyxoma, palmar fibromatosis were 2 cases(33.33%) each in benign fibrous group. 3/ 6 cases (50%) were seen in 3rd decade and were located in head and neck region, male to female ratio was 2:1 [Table 2,3,4]. Benign tumors under the category of skeletal muscle tumor were not seen in the present study. However one case of embryonal rhabdomyosarcoma was reported in 8 year male patient who presented with mass over a left thigh since 2 years.

Table 1: Total 150 cases were divided under following category

Type of tumor	Benign	Malignant
Lipomatous tumor	49	1
Smooth muscle tumor	44	2
Blood vessel tumor	19	0
Fibrohistiocytic tumor *	3	1
Fibrous tumor	6	1
Peripheral nerve sheet tumor	19	3
Skeletal muscle tumor	0	1

*One borderline tumor (DFSP) was reported under fibrohistiocytic category.

Table 2: Age wise distribution of benign soft tissue tumors

Age group (Yrs)	Lipomatous Tumor	Vascular tumors	Nerve sheath tumors		Smooth muscle tumor	Fibrous tumor	Histiocytic tumors
			Neurofibroma	Schwanoma			
0-10	1	1	0	1	0	1	0
11-20	3	7	1	5	0	0	1
21-30	11	4	0	2	3	3	0
31-40	14	5	5	2	19	0	0
41-50	15	2	0	1	19	0	0
51-60	6	0	1	0	2	0	2
61-70	2	0	0	1	1	1	0
>71	0	0	0	0	0	1	0

Table 3: Site wise distribution of benign soft tissue neoplasm

Distribution of tumors	Head and neck face	Trunk	Upper extremity	Lower extremity
Lipomatous tumors	6	20	12	11
Vascular tumors	14	1	4	0
Nerve sheeth tumor-Schwannoma	2	1	4	0
Nerve sheeth tumor-Nurofibroma	5	2	4	1
Fibrous tumor	3	0	2	1
Fibrohistocytic tumor	1	2	0	0
Smooth muscle tumor	0	44	0	0

Table 4: Histopathological subtype division of benign soft tissue neoplasm

Type	cases
Lipomatous tumor	
Fibrolipoma	8
Lipoma classical	41
Blood vessel tumor	
Haemangioma	16
Angiofibroma	3
Peripheral nerve sheath tumor	
Neurofibroma	12
Schwannoma	7
Smooth muscle tumor	
Angioleiomyoma	1
Leiomyoma- classical type	39
Leiomyoma- hyaline type	3
Cellular leiomyoma	1
Fibrous tumor	
Fibroma	2
Fibromyxoma	2
Palmar fibromatosis	2
Fibrohistocytic tumor	
Benign fibrous histiocytoma	3

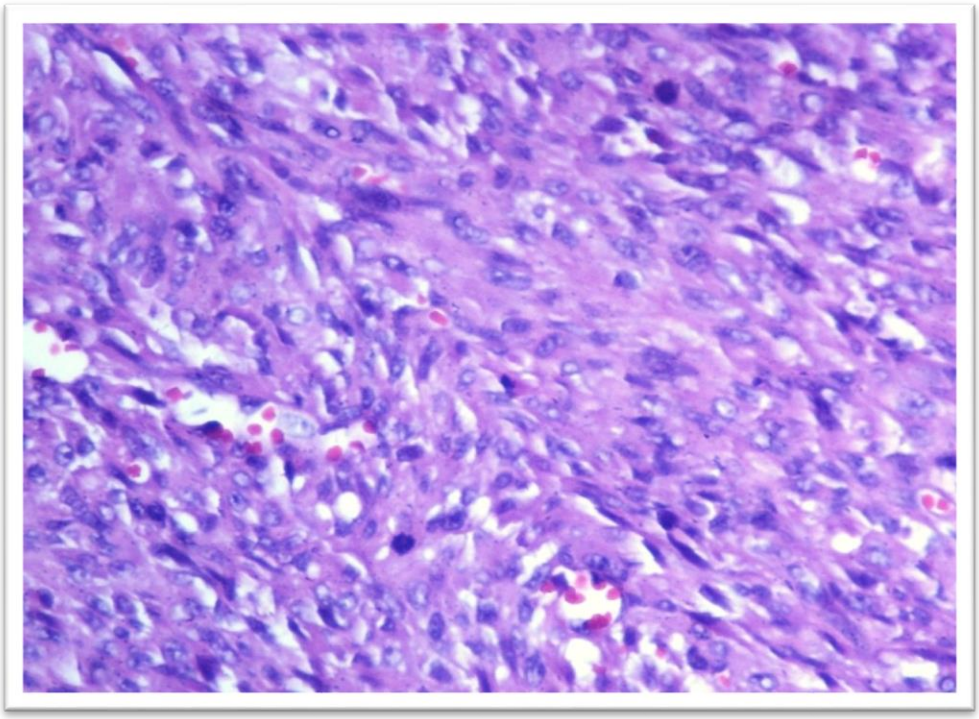

Figure 1: MPNST: photomicrograph showing irregular buckle shaped nuclei characteristic of schwann cell with mitotic figures. (H & E:400x)

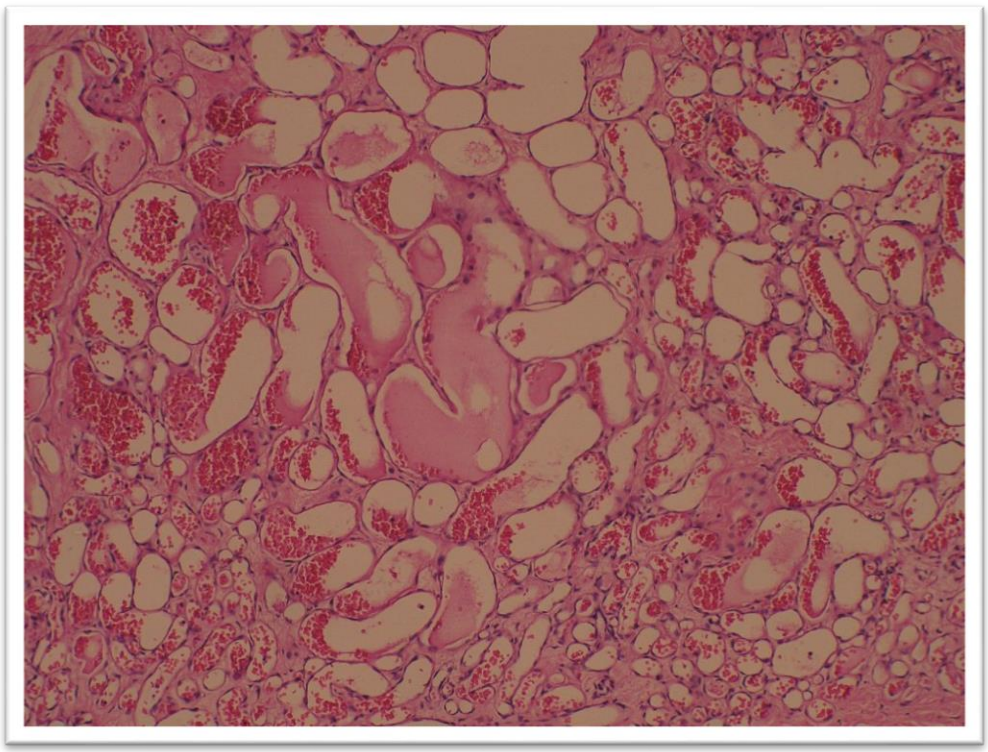

Figure 2: Cavernous Haemangioma: photomicrograph showing large vascular spaces filled with RBCs.(H & E : 100x)

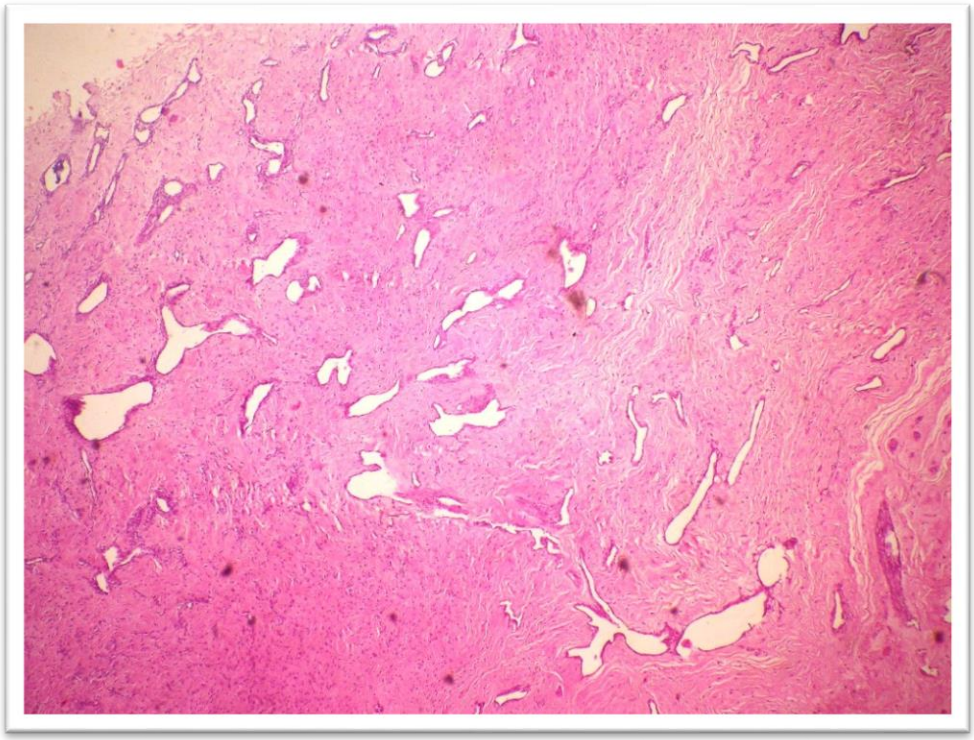

Figure 3: Angiofibroma: photomicrograph showing ectatic blood vessels surrounded by collagenised stroma. (H&E: 40x)

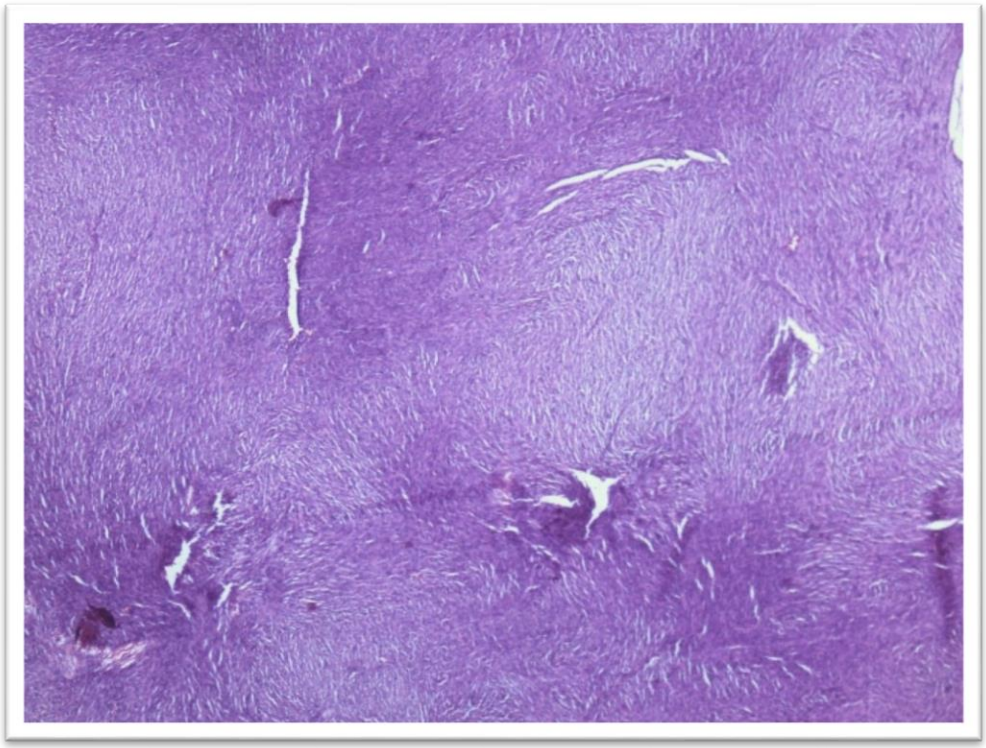

Figure 4: DFSP: photomicrograph showing tumor cell arranged in storiform pattern (H & E: 100x)

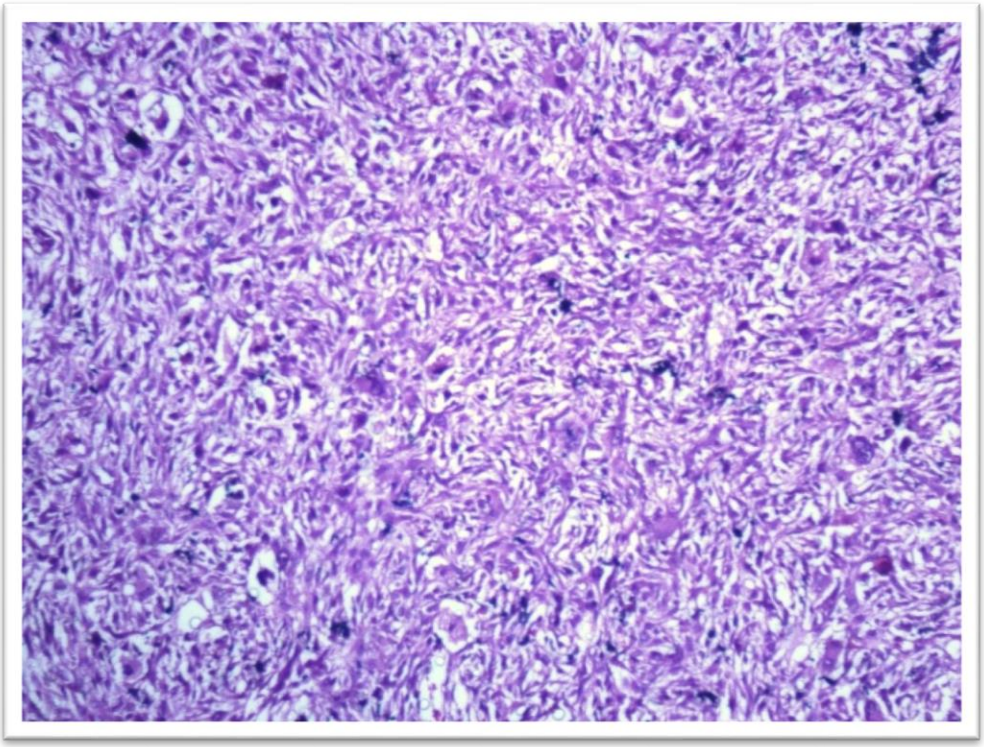

Figure 5: MFH: photomicrograph showing tumor cells with greater degree of nuclear atypia with giant cells.(H & E : 100 x)

DISCUSSION

Soft tissue tumors are relatively rare and constitute less than 1% of all the cancers. Benign mesenchymal tumors outnumbered sarcomas by the factor of at least 100.The annual clinical incidence of benign soft tissue tumors has been estimated up to 3000/million population i.e.-less than 1% of all the malignant tumors.[5] Lipomas are the most common neoplasm of mesenchymal origin arising in any location where fat is present. At least one third of benign tumors are lipomas, one third are fibrohistiocytic tumors and fibrous tumors, 10% are vascular and 5 % are nerve sheath tumors.

In present study, there were 140 benign soft tissue tumours, out of which 49 cases were reported as lipomas which formed largest group among all benign soft tissue tumors, with peak incidence in 5th decade and commonest location being trunk. Two commonest variants in the study by Ndukweet al[6] and Lin et al[7] were conventional and fibrolipomas which coordinated with our study also. On gross examination, lipomas presented as encapsulated, yellow, glistening mass, size ranging from 5-10 cm. Microscopy examination revealed sheets of adipocytes admixed with dilated congested blood vessels and fibrous tissue in few cases. Of the 9 malignant soft tissue tumors in the present study, one case was reported as atypical lipomatous tumor on the anterior aspect of thigh of 50 year male patient. Gross examination showed well circumscribed yellow, greasy soft tissue, mass with attached muscle with focal haemorrhagic areas on cut surface. On microscopic examination tumor composed of sheets of adipocytes with eccentric placed irregular hyperchromatic nuclei with indentation and vacuolated cytoplasm separated by fibrous septae with focal areas of myxoid change and chronic inflammatory cell infiltrate.

In a study by Sharon and Weiss[8] of 92 cases of well differentiated liposarcomas, tumor occurred most frequently in extremity (46 cases), followed by retroperitoneum (23 cases). Our findings were in concordance with their study. Second most common benign soft tissue tumor in our study were smooth muscle tumor accounting for 44 cases, in which 42 cases were seen in uterine cavity including one in broad ligament and one in cervix. However, 2 cases of smooth muscle tumors were reported in males in which one was in scrotum and other was in hand. Uterine leiomyomas are extremely common neoplasm of uterus with estimated rate of 20-40% of women over 30 years of age.[9] Siegel and Gaffey demonstrated rarity of scrotal leiomyoma as only they reported 11 cases in a review of 11000 cases of scrotal tumors.[10]Grossly, leiomyomas presented as greyish white firm masses with whorled appearance on cut surface. Microscopy showed benign spindle shape cells arranged in interlacing fascicles. One case showed blood vessels lined by plump endothelial cells blending with additional smooth muscle, hence

diagnosed as angioleiomyoma in male patient who presented with painful swelling in the hand. In a series reported by Hachisuga et al[11], 66.6%of angioleiomyoma were reported in lower extremity with tumor measuring less than 2 cm and with pain as the presenting complaint.In our study patient gave the history of painful swelling and size of tumor was 2x1x0.5 cm. Malignant tumor reported under smooth muscle cateogory was leiomyosarcoma of uterus in 54 year patient. Grossly, it presented as single pedunculated sub mucosal greyish yellow mass 10x8x8 cm with stalk protruding through endocervical canal. Microscopy showed spindle shaped cells showing plump nuclei and moderate cytoplasm arranged in interlacing fascicles. Intracytoplasmic vacuoles along with abnormal mitosis were also seen.In this study we reported one case of GIST in 56 y female patient who presented with history of pain and mass per abdomen since 3-4 months. Grossly, tumor presented as ulcer proliferative growth 4x3x3 cm surrounded by numerous fibrous adhesions and necrotic areas. Microscopy showed a malignant tumor arranged in fascicles, with tumor cells showing pleomorphism, round to spindly with hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm. Hypo and hypercellular area admixed with giant cells and area of necrosis were also noted.In a study by Lakshmi et al[12] of 176 cases of mesenchymal origin, GIST (52.8%) were studied, with smooth muscle tumor comprising 38.1% forming second largest group and stomach and small intestine was the commonest site.95 % of GISTwere in 4th and 5th decade and male to female ratio 3:1. Most tumor had spindle cell morphology,with 4 cases had a pure epithelioid cell in their study.However in this study, GIST was reported in female patient but age incidence was in concordance with Lakshmi et alstudy and it also showed spindle cell morphology. However immunohistochemistry was not done in this case.

Following benign smooth muscle tumor, next most common tumor under benign category were vascular and peripheral nerve sheath tumours, 19 cases were reported in each category.In benign peripheral nerve sheath tumor, neurofibroma were12/19 cases(63.2%), and schwannoma 7 /19(36.8%) cases.Donner et al[13] over a period of 22 years revealed 288 benign tumors of major peripheral nerve reported neurofibromaas the most common followed by schwannoma which correlated with our study.Gross examination revealed a characteristic gelatinous appearance. Microscopy revealed interlacing bundles of elongated cells with wavy nuclei. Neurofibromas were commonly seen in 2nd decade, with male predominance with head and neck as commonest site which was in accordance with a study by Lin et al[14].In present study, Schwannomas were commonly seen in 3rd decade with female predominance and the commonest location was upper extremity.This was in accordance with Enzinger findings.[15]Grossly, schwannoma were encapsulated, yellow white in appearance. Microscopy revealed Antony A and Antony B areas.

MPNST account for approximately 5-10 % of all soft tissue tumor, about one fourth to half occur in setting of neurofibromatosis. We reported 3 cases of MPNST with 1 case of epithelioid MPNST and 2 classical MPNST. All the 3 cases were seen in males, with 2 cases reported on the back and 1 on the scapula. One case reported recurrence within one year. All the 3 cases reported in 2nd decade and were more than 10cm in dimension. Grossly, they presented as grey white, fleshy, firm to hard with focal necrotic and haemorrhagic areas. Microscopy showed malignant tumor composed of slender shaped cells with wavy nuclei arranged in interlacing fascicles.Tumor cells showed pleomorphism, hyperchromatism with scant amount of eosinophilic cytoplasm. Few hypocellular and hypercellular areas were also seen with intervening stroma showing mononuclear cell infiltrate with focal areas of necrosis [Fig 1]. However 1 case of MPNST also showed plump epithelioid cells. In a study by Ducatman et al[16] of 120 cases of MPNST, 52 were male and 68 were female. In our study, male preponderance was observed, which was in accordance with their study[16].

In our study 19 cases of benign vascular tumor were reported, 16/19 cases were of haemangiomas and 3/19 cases of angiofbroma. Head and neck region was commonest location with peak incidence in 2nd decade with male predominance. Gross examination of all showed grey white, soft, polypoidal bits ranging from 0.5 to 1cm. Microscopy examination showed vaguely lobular pattern displaying numerous blood vessels lined by plump endothelial cells. In few cases large dilated vascular channels were seen.[Fig 2] Malami et al,[17] study showed vascular tumor as the commonest soft tissue tumor of childhood with majority hemangiomas (27.3%), with male predominance and head and neck as common site which correlated with our findings. We reported 3 cases of angiofibromas in males in the 2nd decade of life located in the nasal cavity. Gross examination revealed soft to firm, polypoidalmas ranging from 2-5cm.Microscopic examination revealed a tumor composed of numerous ectactic blood vessels surrounded by pauci cellularstroma. [Fig 3] Our study was in accordance with the findings of Enzinger.[18]

In our study 5 cases of fibrohistiocytictumor were reported, 3/5 cases were benign fibrohistiocytic tumor, 1 boderline(DFSP) and 1 MFH. 2/3 cases of fibrous histocytoma were noted in males. 2/3 cases were noted in back and 1 noted in the nasal

cavity.Fletcheret al[19]in their study of benign fibrous histiocytoma, noted male predominance with lower limb being the most common site. In ourstudy, majority were reported in male although the commonest location was the back.One case of intermediate malignancy i.e, DFSP was reported in 45 year old male patient over the abdomen. Grossly, tumor was grey white, firm, appear well circumscribed and showed a characteristic storiform pattern on microscopy[Fig 4]. Patients had been operated for the same lesion 1 year back and presented to us with recurrence.Our studyfindings were in accordance with observations of Taylor et al[20]. 1 case of MFHwas reported in 50 year female with history of mass on lateral aspect of thigh. Histology revealed, well circumscribed, grey white, fleshy mass measuring -7x7x5 cm and microscopy revealed a tumor composed of spindle cells arranged in fascicles and bundles with spindly, hyperchromatic nuclei and moderate amount of eosinophilic cytoplasm. At places herring bone pattern was also seen with large areas of necrosis and giant cell [Fig 5]. IHC of same was done which showed tumor was vimentin+,desmin-, S100-, SM Actin-and our diagnosis of MFH was confirmed. Weiss and Enzinger[21] analysed 200 cases of MFH and tumor occurred mainly as a mass on extremities (lower followed by upper) with peak incidence between 61 to 70 years with male predominance. The rate of local recurrences of tumor was 44 % and of metastasis 42 % with commonest site being lung and lymph node. In this study, mass was in lower extremity but we could not comment on local recurrences as there was no follow up.

Under category of fibrous tumors, 6 cases were benign and comprised of 2 cases each of fibroma, fibromyxoma, and palmar fibromatosis. Palmar fibromatosis were reported in female in the 3rd decade of life presenting with history of swelling over the wrist of more than 6 months duration without history of antecedent trauma. Gross examination revealed grey white, firm masses ranging from 1-2 cm with whorled cut surface.Histologically, it showed elongated spindle cells arranged in patternless pattern separated by collagen and muscle fibres. Lisset al[22]in metaanalysis of 10 previously published studies and found association between trauma in the form vibration and development of palmar fibromatosis. Under malignant category of fibrous tumors, we reported a case of fibrosracoma in 64 year female patient who presented with swelling in lumbar region since 1 year.Grossly, it was grey white, fleshy, well circumscribed mass measuring-14 x8 x7 cm with area of necrosis and haemorrhage. Microscopy showed an infiltrative tumor composed of cells arranged in fascicles and herring bone pattern.In a study by Prichard et al[23] on fibrosarcoma, 60%, 30% and10% of the study population were noted in lower extremity, upper extremity and trunk respectively with male predominance. However in this study we reported a female patient with mass in trunk.

Rhabdomyosarcoma is not only the most common soft tissue sarcoma in children under 15 years of age but also one of the most common soft tissue sarcoma of adolescents and young adults[24]. We reported a case of embryonal rhabdomyosarcoma in 8 year male patient who presented with mass over a left thigh since 2 years. Grossly mass was lobulated, grey white and cut surface of growth showed a gelatinous area with hamorrhage and necrosis. Microscopy, tumor showed hypocellular and hypercellular areas. Hypercellular area showed round strap like cells, typical cross striations and classical rhabdomyoblast were not seen.

CONCLUSION

Painless mass was the most common presenting symptom in our study. Benign soft tissue tumor outnumbered malignant tumor by a ratio of 14:1. Lipomas and leiomyomas of gynaecological origin were the common tumour to be reported. Vascular tumor were commonly noted in adolescence male. MPNST were the most common malignant tumor in the present study.Location provides an ancillary help in differential diagnosis. Sarcomas, for the most part develop as deeply located mass. H&E stained sections represented the mainstay of diagnosis,however ancilliary techinque like IHC play a important role in diagnosis.

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