Clinicopathological Study of Malignant Soft Tissue Neoplasms: Experience at Rural based Tertiary Teaching Hospital

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ABSTRACT

Introduction: Malignant mesenchymal neoplasms amount to less than 1% of the overall human burden of malignant tumors but they are life threatening and may pose a significant diagnostic and therapeutic challenge since there are more than 50 histological subtypes of soft tissue sarcoma, which are often associated with unique clinical, prognostic and therapeutic features. Objectives is to study the frequency of malignant soft tissue neoplasms among all other neoplasms and all soft tissue neoplasms and to note any variation regarding age, sex and histopathological features

Materials and Methods: This is descriptive study conducted in the department of pathology over the period of Jan 2010 – July 2012. In this study we collected clinical profile of the 154 patients and correlated with gross and histopathological features. For histopathological study samples were collected, processed to prepare paraffin embedded sections and stained by H and E stains.

Results: Malignant soft tissue neoplasms contributed 1.63 % of all types of neoplasms. Among all soft tissue neoplasms, malignant soft tissue neoplasms accounted only 10.38 %. Commonest encountered histological group was the fibrohistiocytic tumors. Malignant soft tissue neoplasms showed equal predilection for sex and the mean age was 50.8 years.

Conclusion: Malignant soft tissue neoplasms accounts very small percentage among all neoplastic lesions reported. The majority of soft tissue neoplasms were from fibrohistiocytic tumor group. The mean age of malignant soft tissue neoplasms is 50.8 years with equal sex predilection. Commonest involved site is upper extremity. Immunohistochemistry is useful in difficult cases.

Keywords: Malignant soft tissue neoplasms, Histopathological

INTRODUCTION

Malignant soft tissue neoplasms contribute less than 1% of the overall human burden of malignant tumors but they are life threatening and having significant diagnostic, therapeutic challenge since there are more than 50 histological subtypes of soft tissue neoplasms, which are often associated with unique clinical, morphological, prognostic and therapeutic features.[1,2]

Malignant lesions were more commonly noted in elderly patients except embryonal rhabdomyosacroma that was observed in a younger age group patients.[3] Soft tissue sarcomas occur more commonly at the deep soft tissues of the extremities and the retroperitoneum, but certain types of sarcomas have site-specific incidence rates.[4]

Histopathology is the most reliable and definitive guide for accurate diagnosis and predicting the clinical behavior of these neoplasms. Recently these neoplasms offer a better clinicopathological correlation due to availability of modern histogenetic classification and standard nomenclature.[5] The pathogenesis of most soft tissue neoplasms is still unknown. The recognized possible causes may be various physical factors, chemical factors, ionizing radiations, and inherited or acquired immunologic, genetic disorders.[1]

The definitive and accurate diagnosis of soft tissue neoplasms is dependent on detailed history, clinical examination, advanced radiology support with subsequent core needle biopsy under organ imaging control. Portions of the biopsy should be submitted for histopathology, immunohistochemistry, genetics, electron microscopy, and any other ancillary techniques.[6]

Data regarding clinicopathological study of malignant soft tissue neoplasms in rural set up are lacking in literature. Here an attempt has been made to collect and evaluate same in institution and compare available data is exercised.

Objectives of the study were to study the frequency of malignant soft tissue neoplasms (STN) among all other neoplasms in population attending rural based hospital, to find out the relative frequency of malignant STN among all STN in hospital population over period of two and half years and to note any variation regarding age, sex and detailed histopathological features of these neoplasms.

MATERIALS AND METHODS

This is descriptive study conducted in the department of pathology over the period of Jan 2010 – July 2012.Cases of malignant soft tissue neoplasms diagnosed on the basis of history and clinical examination and subjected to biopsy or surgery and subsequent histopathological examination were included in this study.Patients who were treated conservatively or patients referred to other hospitals were excluded from this study. Soft tissue neoplasms of systemic organs (like leiomyoma of uterus) were excluded from this study.

In this study, we collected clinical profile of the patients according to the age, sex, anatomical location, clinical diagnosis, relevant investigations, histopathological features and immunohistochemistry wherever necessary. Anatomical sites were categorised as - upper extremity (including shoulder, arm, forearm, wrist and hand), lower extremity (including buttock, thigh, leg and foot), trunk (including abdomen,

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How to cite this article: Vikas V. Narhire, Arvind N. Bagate, Grace F. D'Costa. Clinicopathological study of malignant soft tissue neoplasms: experience at rural based tertiary teaching hospital. International Journal of Contemporary Medical Research 2016;3(3):793-796.

back and chest wall), head and neck.
The specimens were received in 10% formalin as a fixative. After fixation gross findings like size, shape, colour and consistency were recorded. Then sections of size 1 X 1.5 cm and 4 mm thick were taken from representative areas. Very tiny specimens received in the form of biopsy were wrapped in the filter paper. In selected cases, photographs of the specimen were taken.
Tissue processing was done to prepare paraffin embedded sections and there after stained by H and E stains. Slides were studied under light microscopy. Correlation of gross and histopathological examination will be carried out. Special staining like immunohistochemistry was done wherever necessary.
All soft tissue neoplasms were classified according to WHO classification of soft tissue tumors (2002)[2] and histologic classification of soft tissue tumors[1] (in cases of PNST related lesion group).
Here, an attempt was made to correlate clinical presentation and histopathological diagnosis.
Statistical analysis was done with basic statistical tests like mean, range, percentage, standard deviation. (As study design was descriptive type)

RESULTS

The present study includes 154 cases of soft tissue neoplasms. Total number of malignant soft tissue neoplasms was 16. Total number of all types of neoplasms was 979 during two and half year study period from January 2010 to July 2012. Malignant soft tissue neoplasms contribute 1.63% of all types of neoplasms in the present study. The present study includes 16 cases of malignant soft tissue neoplasms out of 154 soft tissue neoplasms. Malignant soft tissue neoplasms contributed 10.38% amongst all soft tissue neoplasms.
The majority of malignant soft tissue neoplasms were from fibrohistiocytic tumor group (5.2%) followed by neoplasms of uncertain differentiation (3.3%). (Table No. 1). In this study we reported 8 cases each of male and female. Malignant soft tissue neoplasms showed equal sex wise distribution with M: F ratio of 1:1.
Malignant soft tissue neoplasms encountered in adults with peak distribution in fifth and sixth decades and mean age 50.8 years (SD: ± 13.87). The age range was 25 to 70 years. Fibrohistiocytic tumors were more common in 41-60 years age group and tumors of uncertain differentiation were common in 21-40 years age group.
The largest number of malignant soft tissue neoplasms were accounted in extremities [Upper (37.5%) > Lower(31.25)], followed by trunk (25%) and head neck region (6.25%).

Fibroblastic tumors

A case of sclerosing epithelioid fibrosarcoma accounted in a 65 years old man over neck region. Grossly, tumor was 4 cm, nodular, hard in consistency grey white on cut surface. Microscopy revealed tumor tissue arranged in cords, strands and nests. Tumor cells were round epithelioid with prominent nucleoli in densely sclerotic collagenous background with areas of necrosis and haemorrhage.
Single case of fibromyxoid sarcoma accounted in a 35 years old female over thigh region. Microscopy revealed tumor tissue arranged in fascicular pattern in alternating hypercellular fibrous and hypocellular myxoid area.

Malignant fibrohistiocytic neoplasms

Malignant fibrohistiocytic neoplasms [8 cases (50%)] were the most common malignant soft tissue neoplasms. They found in adult age group from 35-70 years, peak in sixth decade of life with equal predilection for sex with M: F ratio 1:1. They showed striking predilection for extremities.
Five cases (31.2%) of undifferentiated pleomorphic sarcoma (UPS) were found in older age group ranging from 35-70 years with predilection for lower extremity. Grossly, tumor varied from 7–10 cm, irregular and grey white to black on cut surface with areas of haemorrhage and necrosis. Microscopy revealed tumor tissue composed of plump bizarre spindle cells and giant cells arranged predominantly in storiform and fascicular pattern. Individual tumor cells are highly pleomorphic with round to oval nuclei and prominent nucleoli with abundant eosinophilic cytoplasm and high mitotic activity.
In two cases (out of 5 cases) of UPS histopathological diagnosis of pleomorphic sarcoma was kept later on advised immunohistochemistry. Immunohistochemistry showed positivity for vimentin only and remaining most of panels were negative. Immunohistochemistry confirmed diagnosis of undifferentiated pleomorphic sarcoma. (Table No. 2)
Three cases (18.8%) of Dermatofibrosarcoma protuberans (DFSP) were found in old age group ranging from 45-65 years with predilection for upper extremity.

Uncertain differentiation tumors

Neoplasms of uncertain differentiation [5 cases (31.25%)] were second most common malignant soft tissue neoplasms observed. They were found in age group of range from 25-65 years with slight female predominance and predilection for extremities.
Immunohistochemistry (IHC) diagnosis of synovial sarcoma (SS) was done in two cases. On histopathology, diagnosis of malignant mesenchymal tumor was kept and IHC was advised for further typing. IHC showed immunoreactivity towards synovial sarcoma. (Table No. 2)
Single case of extra skeletal myxoid chondrosarcoma was observed in 40 year female over right buttock. Microscopy revealed tumor tissue composed of round uniform cells arranged in lobules and cords separated by myxoid material.

Sr. No.	Group of neoplasms	Malignant soft tissue neoplasms	Frequency %
1.	Adipocytic	0	0
2.	Fibroblastic	2	1.4
3.	Fibrohistiocytic	8	5.2
4.	Smooth and skeletal muscle	0	0
5.	Vascular	0	0
6.	Chondro-osseous	0	0
7.	Uncertain differentiation	5	3.3
8.	PNST and related lesion	0	0
9.	Paraganglioma	1	0.6
	Total	16	10.4

Table-1: Group wise distribution of various malignant soft tissue neoplasms

Only one case of alveolar soft part sarcoma was encountered in 60 year female over trunk region. Single case of extraskeletal Ewing's sarcoma was observed in 40 year female at right scapular region. Microscopy revealed tumor tissue composed of uniform small round cells arranged in lobules separated by thick fibrous septa. At places cells were arranged around central fibrillary material forming rosettes.

Paraganglioma neoplasm

Single case of malignant Paraganglioma was accounted in 45 year old male at retroperitonium, which later on confirmed on immunohistochemistry. Grossly, tumor was fungating, smooth in consistency brown on cut surface. Microscopically tumor cells were arranged in trabecular, zellbalen and nest pattern separated by vascular septa. Areas of necrosis and vascular invasion were evident. Immunohistochemistry showed positivity for synaptophysin and chromogranin. The Ki 67 index was < 1%. (Table No. 2)

DISCUSSION

In the present study, soft tissue neoplasms comprised 154 of all types of neoplasms received over a period of two and half years in the department of pathology. Out of which, malignant soft tissue neoplasms contributed 1.63 % of all neoplasms.

IHC Markers	Histopathological Diagnosis				
	PS	PS	MMT	MMT	MP
Vimentin	+	+		+	
BCL 2				+	
CK7			+		
EMA			+		-
Synaptophysin					+
Chromogranin					+
Ki67					< 1 %
Pancytokeratin	-	-			-
CD34				-	
CD99				-	
S – 100	-	-		-	
SMA	-	-		-	
Desmin	-	-		-	
MSA	-	-			
Myogenin	-	-			
MDM 2	-	-			
CDK 4	-	-			
h-caldesmon	-	-			
IHC Diagnosis	UPS	UPS	SS	SS	MP

IHC - Immunohistochemistry, MMT – Malignant mesenchymal tumor, MP – Malignant paraganglioma, PS – Pleomorphic sarcoma, SS – Synovial sarcoma, UPS - Undifferentiated pleomorphic sarcoma

Table-2: Histologic type and its Immunoreactive markers

A total of 154 soft tissue neoplasms were studied in the present study. Benign soft tissue neoplasms contributed [138 cases (89.6%)] and malignant tumors contributed [16 cases (10.38%)].

Malignant soft tissue neoplasms accounted small percentage amongst all soft tissue neoplasms, which is comparable with all the studies. The percentage of malignant neoplasms (10.4%) was relatively more than the study of Myhre-Jensen O 1981[9] (5.4%) and Agravat AH et al 2010[3] (6.5%) which can be explained by the inherent bias in a referral population. Relatively increased percentage of malignant neoplasms in the study of Kransdorf 1995[7,8] (39.8%) from AFIP records and Bashar AH et al 2010[10] (24.8%) may be due to the case material referred to a highly specialized centre. (Table No. 3)

In this study, the commonest malignant soft tissue neoplasm was undifferentiated pleomorphic sarcoma (31.2%) followed by DFSP (18.8%), Fibrosarcoma (12.5%) and SS (12.5%). The percentage of undifferentiated pleomorphic sarcoma (31.2%) was comparable with study of Kransdorf MJ 1995[8] (24.1%). The percentage of firosarcoma (12.5%) was comparable with Agravat AH et al 2010[3] (16.7%). Malignant fibrohistiocytic tumors (50%) were most common malignant soft tissue neoplasms. In fibrosarcoma group, Sclerosing epitheliod fibrosarcoma (SEFS) and fibromyxoid sarcoma were noticed as variants of fibrosarcoma. (Table No. 4)

Fibrosarcoma was categorised under malignant fibroblastic group, undifferentiated pleomorphic sarcoma and dermatofibrosarcoma protuberans were categorised under malignant fibrohistiocytic group. Synovial sarcoma, extraskeletal myxoid chondrosarcoma, alveolar soft part sarcoma, extraskeletal Ewing's sarcoma were categorised under malignant uncertain differentiation tumor group whereas malignant paraganglioma included under separate group.

In present study, malignant neoplasms presented with a male to female ratio of 1:1 while in the study of Myhre-Jensen O 1981[9], it was 2: 1. This difference may be due to inherent bias in a referral population.

The mean age in malignant soft tissue neoplasm was 50.8 years comparable with studies of Myhre-Jensen O 1981[9] (49.5) and more than Kransdorf MJ 1995[8] (42) and Bashar AH et al 2010[10] (39.1) may be due to inherent bias in a referral population. Malignant soft tissue neoplasms encountered in adults with peak distribution in fifth and sixth decade. The age range was 25 years to 70 years.

In the present study, malignant neoplasms showed predilection for the upper extremity (37.5%) followed by lower extremity, trunk and head and neck. Kransdorf MJ 1995[8] found predilection for lower extremity (37.1%) fallowed by upper extremity (18%).

Sr. No.	Authors	No. of cases	Benign (B)	Frequency (%)	Malignant (M)	Frequency (%)	B:M Ratio
1.	Myhre-Jensen O (1981)[9]	1403	1331	94.6%	72	5.4%	18.5:1
2.	Kransdorf MJ (1995) [7,8]	31047	18677	60.2%	12370	39.8%	1.5:1
3.	Agravat AH et al (2010)[3]	92	86	93.5%	6	6.5%	14.4:1
4.	Bashar AH et al (2010)[10]	93	70	75.2%	23	24.8%	3:1
5.	Present study (2012)	154	138	89.6%	16	10.4%	8.6:1

Table-3: Comparative frequency of benign and malignant soft tissue neoplasms

Tumor Type	Study			
	Kransdorf MJ (1995)[8]	Agravat AH et al (2010)[3]	Bashar AH et al (2010)[10]	Present study (2012)
Fibrosarcoma	5.3%	16.7%	-	12.5%
Undifferentiated pleomorphic sarcoma (UPS)	24.1%	-	8.7%	31.2%
Dermatofibrosarcoma protuberans (DFSP)	6.2%	-	-	18.8%
Synovial sarcoma (SS)	5.4%	-	4.4%	12.5%
Extraskeletal myxoid chondrosarcoma (ESMC)	2.1%	-	-	6.25%
Alveolar soft part sarcoma (ASPS)	0.5%	-	-	6.25%
Extraskeletal Ewing's sarcoma	1.1%	-	21.7%	6.25%
Paraganglioma	0.1%	-	-	6.25%

Table-4: Comparative analysis of distribution of various malignant soft tissue neoplasms

CONCLUSION

Malignant soft tissue neoplasms accounts very small percentage among all neoplastic lesions reported. Benign soft tissue neoplasms outnumber the malignant neoplasm by a marginal difference. The majority of malignant soft tissue neoplasms were from fibrohistiocytic tumor group followed by neoplasms of uncertain differentiation. The commonest accounted tumor is undifferentiated pleomorphic sarcoma. The mean age of malignant soft tissue neoplasms is 50.8 years with equal sex predilection. Commonest involved site is upper extremity. Haematoxylin and Eosin (H and E) stained sections remain the best method for establishing the primary diagnosis. Immunohistochemistry is very helpful in accurate categorization of soft tissue neoplasms when there is dilemma in histopathological diagnosis.

ABBREVIATIONS

ASPS – Alveolar soft part sarcoma, B – Benign, Cm - Centimetre, DFSP – Dermatofibrosarcoma protuberans,
H and E – Haematoxyline and eosin, IHC - Immunohistochemistry, M – Malignant, M:F – Male: Female, MFH – Malignant fibrous histiocytoma, MMT – Malignant mesenchymal tumor, Mm - Millimetre, MP – Malignant paraganglioma, PNST – Peripheral nerve sheath tumor and related tumor, PS – Pleomorphic sarcoma, SS – Synovial sarcoma, STN – Soft tissue neoplasms, STS – Soft tissue sarcoma, STT – Soft tissue tumor, UPS – Undifferentiated pleomorphic sarcoma, WHO – World Health Organisation, % - Percentage, + : Positive, - : Negative

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 27-01-2016; **Published online**: 17-02-2016