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Original Article

Soft Tissue Neoplasms: Distribution and Diagnostic Strategies Including Immunohistochemical Study

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Abstract

Introduction: Tumors arising in soft tissue form a varied and complex group which may show a wide range of differentiation. In the absence of a firm histological diagnosis, it is often dangerous to attempt to predict the likely clinical course of a soft tissue neoplasm.

Materials and Methods: The surgical specimens of the patients who underwent excision of soft tissue tumors during the period March 2011-Febuary 2014 at KAPV Government Medical College, Tiruchirappalli, formed the material for this study. All the specimens are subsequently diagnosed as one of the soft tissue tumors by histopathological examination.

Results: A total of 11095 surgical specimens received in the Department of Pathology, KAPV Government Medical College, Tiruchirappalli, during the study period of which soft tissue tumor constitutes 260 (2.35%) cases. This study included those 260 soft tissue neoplasms, in which 27 were seen in pediatric patients and the remaining 233 in adults. In the 27 pediatric soft tissue neoplasms, 15 cases were seen in male children and 12 in female children. In adults, of 233 cases, 117 cases were seen in males and 116 were seen in females. Soft tissue neoplasms including both benign and malignant constituted 8.8% of total neoplasms during our study period.

Conclusion: Improving the knowledge of cytological appearance of individual tumors, through fine needle aspiration cytology as initial approach to the soft tissue neoplasms and in addition, molecular techniques could really improve the quality of diagnosis of soft tissue tumors, with which treatment modalities can be modified, and prognosis could be improved.

Key words: Histopathology, Immunohistochemistry, Soft tissue neoplasm

INTRODUCTION

Tumors arising in soft tissue form a varied and complex group which may show a wide range of differentiation. In the absence of firm histological diagnosis, it is often dangerous to attempt to predict the likely clinical course of a soft tissue neoplasm.[1-5] In this study, we analyzed the incidence and distribution of soft tissue neoplasm in relation to age, sex, and site. We also evaluated the role of immunohistochemistry (IHC) in the diagnosis and confirmation soft tissue neoplasm of critical histopathology.

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Aim

1. To study the incidence of soft tissue neoplasm in adults and pediatric patients.
2. To analyze the distribution of soft tissue neoplasm anatomically, as per the guidelines provided by association of directors of anatomic and surgical pathology (ADASP).
3. To study the usefulness of special stains.
4. To evaluate the role of IHC in soft tissue neoplasm of critical histopathology.
5. To study rare soft tissue neoplasms arising at rarer sites and confirmation by IHC.

MATERIALS AND METHODS

The surgical specimens of patients who underwent excision of soft tissue tumors during the period March 2011-Febuary 2014 at KAPV Government Medical College, Tiruchirappalli, formed the material for this study.

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All the specimens are subsequently diagnosed as one of the soft tissue tumors by histopathological examination.

A thorough clinical evaluation and gross descriptions, as per the guidelines recommended by ADASP was done in each case. A detailed history with particular attention to site, duration, depth of neoplasm and type of resection were also recorded. All lesions were placed in categories in accordance with the WHO classifications system and added to anatomical locations such as head and neck, upper extremities, trunk, lower extremities, and peritoneum.

Soft tissue neoplasms of either sex irrespective of the age group (both pediatric and adult neoplasms) were included in this study.

The specimens were received in 10% formalin and processed in the routine way small biopsy specimens (<0.5 cm) were submitted into whereas larger specimens were sampled at 1 cm intervals. Multiple bits were taken at different sites, paying particular attention to base margin, and necrotic areas.

After routine processing and paraffin embedding, 5-6 cm sections were cut. The sections were stained with hematoxylin and eosin (H and E) for evaluation of histopathologic features.

Histochemical stains - such as Masson trichrome, periodic acid Schiff, Van Gieson, and reticulin - were also performed.

IHC with S100, neuron specific enolase (NSE), CD34, and CD99 was also performed in selective cases in arriving at a final diagnosis.

IHC was performed on one representative section per case on 4 μ thick, formalin fixed, paraffin embedded sections mounted on charged slides, and baked at 60°C for 1 h. All cases were stained in parallel with appropriate positive and negative controls. Staining extent was scored as negative, focally positive, and positive or diffusively positive.

RESULTS

A total of 11095 surgical specimens received in the department of pathology, KAPV Government Medical College, Tiruchirappalli, during the study period of which soft tissue tumor constitutes 260 (2.35%) cases.

This study included those 260 soft tissue neoplasms, in which 27 were seen in pediatric patients and the remaining 233 in adults.

In the 27 pediatric soft tissue neoplasms, 15 cases were seen in male children and 12 in female children.

In adults, out of 233 cases, 117 cases were seen in males and 116 were seen in females.

Soft tissue neoplasms including both benign and malignant constituted 8.8% of total neoplasms during our study period.

The incidence of benign and malignant soft issue neoplasms in our study are given in Table 1.

Of 260 cases, benign tumors constituted 87.65% and malignant tumors accounted for 10.7% of total soft issue neoplasms.

The rest being intermediate group of neoplasms. Table 1 showed that benign tumors outnumber malignant tumors. Intermediate categories constitute only 1.9%.

Among the malignant soft issue neoplasms, malignant fibrous histiocytoma (MFH) was the most common followed by malignant peripheral nerves heath tumor. The third common malignant neoplasm was extraskeletal Ewing's sarcoma.

All soft tissue neoplasms were categorized into six groups according to their age as 1-10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years, and >50 years.

The overall incidences of soft tissue neoplasms were higher in the age group of 31-40 years (26.1%). Intermediate tumors were found in all age groups with the exception of 11-20 years.

Table 2 showed that most of the benign tumors were found in the age group of 31-40 years and malignant tumors were frequently seen in >50 years of age.

Table 3 shows the sex incidence of soft tissue neoplasms in adult and pediatric cases.

Table 1: Overall incidence of soft tissue neoplasms

Tumor types	Benign (%)	Malignant (%)	Intermediate (%)	Total
Lipomatous	149 (65)	2 (7.14)	-	151
Fibrous	18 (8.3)	3 (10.7)	4 (80)	25
Vascular	23 (10)	-	1 (20)	24
Fibrohistiocytic	2 (0.88)	6 (21.4)	-	8
Neural	36 (15.8)	4 (14.3)	-	40
Rhabdomyosarcoma	-	2 (7.1)	-	2
Synovial sarcoma	-	2 (7.1)	-	2
Extraskeletal Ewing's sarcoma	-	3 (10.7)	-	3
Leiomyosarcoma	-	2 (7.1)	-	2
Epithelioid sarcoma	-	1 (3.6)	-	1
Olfactory Neuroblastoma	-	2 (7.1)	-	2
Total	228 (87.7)	27 (10.4)	5 (1.9)	260

Benign tumors were typically found in females (51.5%), whereas malignant tumors were predilection toward males (56.5%). Most of the intermediate tumors were reported in adult males (60%). In out of 27 malignant neoplasms, 13 cases were seen in males, 11 cases in females, and 3 cases were seen in pediatric age group. Among the pediatric neoplasms, 15 cases were seen in males and 12 cases were seen in females.

A lipoma is commonly seen in females. Among the intermediate neoplasms, dermatofibrosarcoma protuberans was frequently seen in male persons. In malignant tumors sex prediction varies among different tumors.

The universal tumor lipoma was frequently encountered in trunk region followed by upper extremity, and the other histological types were usually encountered in head and neck region.

Fibrohistiocytic tumors were reported in the lower extremity.

The most frequent tumor encountered was MFH followed by malignant peripheral nerve sheath tumor (MPNST) and both the tumors were frequently encountered in the lower extremity. We encountered one case of leiomyosarcoma in labia majora and one case of epithelioid sarcoma in retroperitoneum.

In this study, 149 cases of lipoma were encountered which includes 122 conventional lipomas, 24 fibrolipomas, and 3 angiolipomas.

About 36 benign neural tumors were diagnosed which constitutes 23 neurofibromas, 11 schwannomas, 1 granular cell tumor (GCT), and 1 neurothekeoma.

Of 11 schwannomas, three cases were diagnosed as ancient schwannomas showed features of inflammatory cells, histiocytes, and increased vascularity.

We reported a rare case of neurothekeoma in medial malleolus. We encountered a case of GCT in hand.

About 18 benign fibrous tumors were observed which included 8 benign fibroma, 6 angiofibroma, 1 nodular fasciitis, 1 dermatofibroma, and 2 fibromatosis.

The malignant counterparts of fibrous tumor include 3 cases of fibrosarcomas.

One case of inflammatory myofibroblastic tumor which comes under intermediate group was found in the head and neck region (palate).

Microscopically, the tumor was composed of masses of spindle cells, inflammatory cells (mostly lymphocytes and plasma cells) against a collagenous and myxoid stroma.

The incidence of malignant tumors was shown in Table 4.

The biopsy specimens were subjected to histochemical stains in doubtful cases. For selective cases, the histochemical stains used were Masson's trichrome, Van Gieson, periodic acid Schiff, and reticulin. Masson trichrome stains were applied to five cases of MPNST, periodic acid Schiff for three cases extraskeletal Ewing's sarcoma, reticulin was applied for Kaposiform Hemangio endothelioma, and synovial sarcoma, Van Gieson was applied for desmoid tumor where diagnosis by light microscopy alone was difficult (Table 5).

In our study, of 260 cases, only six doubtful cases were subjected to IHC. The IHC markers applied were S 100, NSE, CD 34, CD 45, and CD 99 (Table 6).

Table 2: Age distribution of benign and malignant tumors

Adult	Benign (%)	Malignant (%)	Intermediate (%)	Total (%)
1-10	12 (5.2)	4 (14.3)	1 (20)	17 (6.5)
11-20	25 (11)	2 (7.1)	-	27 (10.5)
21-30	37 (16.2)	2 (7.1)	1 (20)	40 (15.5)
31-40	62 (27.2)	5 (18.5)	1 (20)	68 (26.1)
41-50	42 (18.4)	3 (10.7)	1 (20)	46 (17.6)
>50	50 (21.92)	11 (39.28)	1 (20)	62 (23.8)
Total	228	27	5	260 (100)

Table 3: Sex incidence of adult and pediatric soft tissue neoplasms

Type	Male (%)	Male (pediatric)	Female (%)	Female (pediatric)
Benign	101 (48.5)	11 (73.3%)	104 (51.5)	12 (100%)
Intermediate	3 (60)	1 (6.7%)	1 (20)	-
Malignant	13 (56.5)	3 (20%)	11 (43.5)	-
Total	117	15	116	12

Table 4: Incidence of histological types of malignant soft tissue neoplasms

Type	Total number	Percentage
MFH	6	21.42
MPNST	4	14.28
Extraskeletal Ewing's sarcoma	3	10.71
Liposarcoma	2	7.14
Rhabdomyosarcoma	2	7.14
Fibrosarcoma	3	10.71
Leiomyosarcoma	2	7.14
Epithelioid sarcoma	1	3.57
Synovial sarcoma	2	7.14
Olfactory neuroblastoma	2	7.14

Table 5: Histochemical stains

Initial diagnosis	Histochemical stain	Result	Final diagnosis
Extraskeletal Ewing's sarcoma (3 cases)	Periodic acid Schiff	(+)	Extraskeletal Ewing's sarcoma (3 cases)
MPNST (4 cases)	Masson tri chrome	(+)	MPNST (4 cases)
Desmoid tumor	Von Gieson	(+)	Desmoid
Kaposiform hemangio endothelioma	Reticulin	(+)	Kaposiform Hemangio endothelioma
Synovial sarcoma	Reticulin	(+)	Synovial sarcoma

MPNST: Malignant peripheral nerve sheath tumor

Table 6: IHC markers

Initial diagnosis in H and E	IHC marker	Final diagnosis
Extraskeletal Ewing's sarcoma/lymphoma	CD 45 (−) CD 99 (+)	Extraskeletal Ewing's sarcoma
Olfactory neuroblastoma/ rhabdomyosarcoma	NSE (+)	Olfactory neuroblastoma
Epithelioid sarcoma,/malignant mesothelioma	CD 34 (+)	Epithelioid sarcoma
MPNST/MFH	S 100 (+)	MPNST
MPNST/leiomyo sarcoma	S 100 (−)	Leiomyosarcoma
MPNST/MFH	S 100 (−)	MFH

NSE: Neuron specific enolase, IHC: Immunohistochemistry, H and E: Hematoxylin and eosin, MPNST: Malignant peripheral nerve sheath tumor, MFH: Malignant fibrous histiocytoma

DISCUSSION

The 260 soft tissue tumors analyzed in this study reveals that the proportion of soft tissue neoplasms among the total neoplasms was found to be 2.35%.

According to the National Cancer Institute's surveillance, the incidence of soft tissue sarcomas ranges from 15 to 35/1 million population.[1,2] In a study conducted by Necati Akisatal showed that 3% incidence of soft tissue sarcomas among all neoplasms, whereas Enginger *et al.*, showed that the incidence of soft tissue sarcomas was <1%. Our study correlates with the literature (1.27%).

The number of cases with soft tissue sarcomas has risen in recent years, which is in accordance with the data of soft tissue sarcoma in the USA between 1973 and 1993 analyzed by Pollock. According to the statistics of malignant tumors in Shanghai from 1963 to 1992, the incidence of soft tissue sarcomas is 0.75-1.85/1,00,000. In the USA, the annual incidence is 2/100,000.[5-11]

The incidence of soft tissue sarcomas in our institute has also increased from 0.74% to 1.78% during the study period.

In general, benign soft tissue tumors occur 10 times more frequent than malignant ones.[1,12,13] This study also shows that benign tumors constituted 87.7% as against malignant soft tissue neoplasms (10.4%).

Among the benign soft tissue tumors lipoma was found to be the most common. Ashok reported that 16% neoplasms are lipomas, and they were commonly seen on trunk and extremities. In our study, the incidence of lipoma constituted 5% among all neoplasm and 65% (n = 149) among all benign soft tissue tumors, and the common site is trunk 22.36% (n = 51).[9-11]

According to Sposto *et al.*, GCT was an uncommon benign neoplasm and it can occur between 4th and 6th decades of life, more common in women. The most GCTs are found in the head and neck region and the tongue was the most common location. In contrast with the literature, the site was hand.

The incidence of soft tissue neoplasm in trunk is a more frequent in our study (25.4% n = 66). This study also included the clinical presentation of soft tissue neoplasms in which most of the tumors presented as painless, capsulated swelling with restricted mobility. Most of the benign tumors are superficial in location, and their size is <5 cm (77%), in correlation with the literature whereas 55% of malignant tumors were >5 cm in diameter.[14-19]

The anatomic distribution of soft tissue sarcomas frequently occurred in the lower extremities (39.3% n = 11) in accordance with the literature followed by head and neck and trunk.[1-3]

Soft tissue sarcomas can be observed in any age group, while different tumor types exhibit a significant age predilection.

The incidence of malignant soft tissue tumors is slightly more in males (56.5% n = 13) and benign is more common in females (51.5% n = 104) in accordance with the literature (Figure 1).[2,4]

In this study, the gender ratio for soft tissue sarcoma was 1.02:1 MFH accounts for 20-24% of malignant soft tissue tumors, making it the most common soft tissue tumors occurring in late adult life.[2,3,19] In analysis of 200 cases of soft tissue sarcomas, Enzinger *et al.* found that 2/3 of MFH occurred in men and the majority of cases were occurring in persons between 50 and 70 years.

According to the 1240 cases of soft tissue sarcomas study recorded by the sarcoma group of French federal cancer center MFH is the most frequent tumor followed by liposarcoma. Another study conducted in Japan, in 2002, also proved.[15,16]

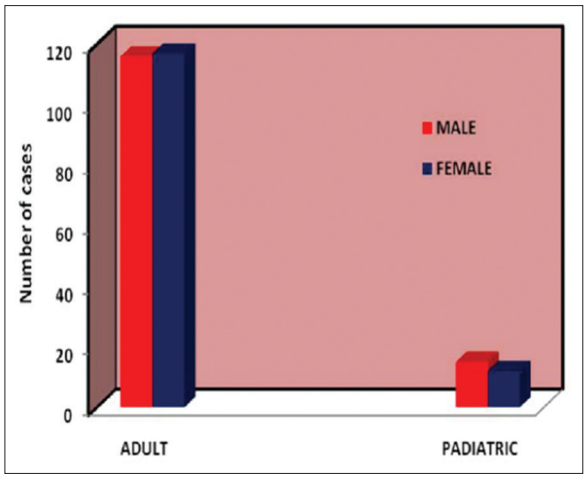

Figure 1: Sex distribution of soft tissue neoplasms

In accordance with the literature, MFH constituted the most common malignancy (21.4% *n* = 6) in this study, and the common site was lower extremity (thigh) 66.7%. The majority of them were in the sixth decade (20% *n* = 5) Most of the tumors are between 5 and 10 cm (66% *n* = 4).[4,19]

The incidence of MPNST was 5-10% of all soft tissue sarcomas. In our study, MPNST accounts for 14.3% (*n* = 4), the common site is lower extremity (39.3% *n* = 11). In contrast with the literature males are more commonly affected than females.[17]

Although liposarcoma is considered to be a frequent tumor in adults by many articles like Fang-Zhi-Wei *et al.*, in our study liposarcoma contributed only 7.14%.[3,7,8]

We reported two cases of liposarcomas, one was from thigh and another was from omentum, and the sex incidence was equal. Age group affected was >60 years.

Fibrosarcoma usually arises in the age group of 4-6th decades as per the literature.[18] However, in our study, two cases of adult FS were diagnosed in the third decade.

In AFIP series, of 345 cases of synovial sarcoma 60% of cases were found to be in lower extremity and they were commonly encountered in 15-40 years of age.[1] In accordance with the literature our study shows the common site was knee (2/2 cases) and the age group was in the second decade. In contrast to the literature females were commonly affected in our study (2/2 cases).[3,5,6]

Epithelioid sarcoma is a rare soft tissue sarcoma that occurs in the extremities, and they frequently occur in adult males.

In contrast with the literature, the incidence of epithelioid sarcoma in our study was 3.57% and the age group affected was 64 years and also the site was peritoneum.

The incidences of pediatric soft tissue neoplasms were also included in this study. In correlation with the literature, the most common benign pediatric tumor was hemangioma (54% *n* = 13) and the malignant tumor was rhabdomyosarcoma (66% *n* = 2).

Benign tumors were common in pediatric age group (88.8% *n* = 24) as against malignant tumors (11.2% *n* = 3).

Male children were more commonly affected than female children (56%). The most favorite age group in this study was <1.5 years. Males were more commonly affected (2/2 cases) and the site predilection was head and neck.[4]

CONCLUSION

In this study of 260 cases, which includes clinical findings, histopathological examination with routine H and E stains, special stain study and immunohistochemistry markers, the following conclusions are presented.

1. The incidence of soft tissue neoplasms is gradually increasing.
2. The incidence of benign tumors outnumbers malignant tumors in the both adult and pediatric age group.
3. As mentioned in the literature lipoma still appears to be there most common benign tumor.
4. In this study, in contrast to trunk appears to be the most common site for occurrence of soft tissue neoplasms.
5. The incidence of malignant soft tissue neoplasms one more in males, whereas benign tumors more in females.
6. Sarcomas of fibrohistiocytic origin outnumbered sarcomas of any other organ origin in our study.
7. In this study, in the pediatric age group, the embryonal RMS is the most common malignant tumor in correlation with the literature.
8. Most of the sarcomas presented as a mass lesion with size at least more than 5 cm.
9. Epithelioid sarcoma a rare soft tissue tumor usually occurs in extremities in adult age, but in our study, this tumor occurs in very rare site - peritoneum and the age group >2 years.
10. In doubtful case, immunohistochemical markers shall provide valuable tool in arriving at final diagnosis.

Our knowledge of the biology of the soft tissue tumors comes a long way from the time when they were classified based on gross morphology along to the present day when a combined multimodal approach using convectional histology, special histochemical stains, immune histochemistry, molecular biology, and cytogenetics are used to classify these tumors.

The time tested H and D section is still sufficient to diagnosis majority of the lesions.

In our study, we had attempted to describe the clinical and histomorphological profile of soft tissue neoplasms diagnosed in our institute.

The study of various pathological patterns of sarcomas helps in unraveling the natural history of these lesions. Without the knowledge of the tumor behavior, it would be difficult to decide treatment options. Prospective studies with adequate patient follow-up data are required for this purpose.

Improving the knowledge of cytological appearance of individual tumors, through fine needle aspiration cytology as initial approach to the soft tissue neoplasms and in addition, molecular techniques could really improve the quality of diagnosis of soft tissue tumors, with which treatment modalities can be modified and prognosis could be improved.

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