Section: Pathology

Original Research Article

INCIDENCE OF SOFT TISSUE TUMORS AND THE ROLE OF KI67 IN GRADING MALIGNANT SOFT TISSUE TUMORS- EXPERIENCE IN A TERTIARY CARE HOSPITAL OVER A PERIOD OF TWO YEARS

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ABSTRACT

Background: Soft tissue tumors are a highly heterogenous group of tumors. The grading of soft tissue sarcomas is essential for selection of treatment. **Aims and objectives:** The main aim of this study is to categorize the soft tissue tumors as benign and malignant and to compare ki67 grading with FNCLCC grading. **Materials and Methods:** The present study is a retrospective study conducted in the department of Pathology, Tirunelveli medical college. A total number of 373 cases of soft tissue tumors were received during this period. The nature of soft tissue tumor was determined. For all the cases diagnosed as malignant, Ki67 IHC was done. Grading of soft tissue sarcomas was done according to FNCLCC grading and KI67 index. **Result:** Of the 373 cases 93.3% (348) were benign and 6.7% (25 cases) were malignant. The most common benign tumor diagnosed was lipoma 69.5% (242 cases). The most common malignant tumor diagnosed was fibrosarcoma 32% (8 cases). HPE grading was done according to FNCLCC grading system which includes tumor differentiation, necrosis and number of mitosis as criteria. From the result it was observed that there was significant disagreement between FNCLCC grading and Ki67 grading system. Immunohistochemistry by ki 67 can be used as an additional tool in grading soft tissue sarcomas as Ki67 is expressed in all stages of cell cycle and is a better measure of dividing cell than counting the number of mitosis by H&E staining.

INTRODUCTION

Soft tissue can be defined as a nonepithelial extra-skeletal tissue of the body excluding the viscera covering the brain and lymphoreticular system.[1] Soft tissue tumors are a highly heterogenous group of tumors that are classified on a histogenetic basis according to the adult tissue that resemble. Soft tissue tumors are classified as benign and malignant.[2]

The benign tumors are more common than the malignant ones by 100:1.[1] They can occur in any age group but the distribution of soft tissue tumors is definite for particular age and site.[3] Soft tissue sarcomas can occur with increasing age with median age of presentation at 65 years. They have a slight male preponderance.[4] They mostly occur in extremities. Other sites being trunk and retroperitoneum.[1] Soft tissue tumors are diagnosed with the help of incision, excision and core biopsy. Open biopsy is the gold standard investigation for diagnosing soft tissue tumors occurring in extremity.[5] The staging of soft tissue sarcomas is essential for selection of treatment.[6] Staging depends on the stage of tumor. Three criterias including tumor differentiation, mitotic count and pattern of necrosis were necessary in attributing a tumor grade.[7] The soft tissue sarcomas are graded using FNCLCC system (Federation Nationale des Centres de Lutte Contre le Cancer) and NCI system. Among these FNCLCC is easy and commonly used. According to this, tumor is graded according to tumor differentiation, mitosis and necrosis.[1,2] Proliferation can be assessed by counting the number of mitosis per 10 HPF, labelling of radioactive thymidine, determining S phase fraction using flow cytometry and IHC using Ki67.[1] The S factor of flow cytometry is hampered by 30-40% non-informative histogram. Labelling of proliferating cells by radioactive thymidine is an intense procedure, so it is not currently used.[1] IHC for Ki67 is easy to perform and is suitable for routine use.[1,9] Instead of mitotic count Ki67 is easy to perform and is suitable for routine use. So, in this study we have planned to report our two-year experience in the incidence of soft tissue tumors and we have compared the FNCLCC grading with Ki67 in grading the soft tissue sarcomas.

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MATERIALS AND METHODS

The present study is a retrospective study conducted in the department of Pathology, Tirunelveli medical college for a period of two years from January 2016-December 2017. A total number of 373 cases of soft tissue tumors were received during this period. The clinical data including age, sex, site of lesion, clinical features, gross and microscopic appearance were taken from the records. Tissues received were fixed in 10% formalin. Blocks were cut and stained by routine hematoxylin and eosin staining. The nature of soft tissue tumor was determined. For all the cases diagnosed as malignant, Ki67 IHC was done. Grading of soft tissue sarcomas was done according to FNCLCC grading and KI67 index.

Inclusion Criteria

All the benign and malignant soft tissue tumors received during the study period were included.ki 67 was done for malignant cases.

Exclusion Criteria

Uterine tumors were not included in the study

Malignant tumors diagnosed by incisional biopsy were excluded from ki67 IHC due to insufficiency of material.

RESULTS

The total number of biopsy specimens received during this period was 8553. Out of which 373 cases were reported as soft tissue tumors. This constitutes 4.36% of total biopsy specimen. Of the 373 cases 93.3% (348) were benign and 6.7% were malignant (Table 1). Of the 373 cases 47.2% (176) were diagnosed in males and 52.3 % (197) were diagnosed in females.

Table 1: Incidence of Soft Tissue Tumors

TOTAL NUMBER OF SOFT TISSUE TUMORS	BENIGN	MALIGNANT
373	348(93.3%)	25(6.7%)

The common age incidence of benign tumor was between 30-40 years 23.9% (83 cases), followed by 40-50 years 23.6% (82 cases). [Table 2]

The common age incidence of malignant tumor was above 60 years, 36% followed by 40-50 years, 20%. [Table 2]

Table 2: Age wise distribution of bengn and malignant soft tissue tumors

AGE GROUP (in years)	BENIGN	MALIGNANT
0-10	10	0
20-Nov	21	1
21-30	50	4
31-40	83	1
41-50	82	5
51-60	69	5
>60 years	33	9
TOTAL	348	25

Table 3: Age and sex wise distribution of benign and malignant tumors

S.NO	AGE	MALE		%	FEMALE		%
		BENIGN	MALIGNANT		BENIGN	MALIGNANT	
1	0-10	5	0	2.8	5	0	2.8
2	20-Nov	13	1	8	8	0	4
3	21-30	27	1	15.9	23	3	13.1
4	31-40	36	0	20.5	47	1	24.2
5	41-50	30	1	17.6	52	4	28.8
6	51-60	34	4	21.6	35	1	18.2
7	>60	16	8	13.6	17	1	9.1

In case of benign tumors, the most common site involved was trunk 29.8% (111cases) followed by head and neck 27.3% (102 cases), upper limb 26.5% (99 cases) and lower limb 16.4% (61 cases)

In case of malignant tumors, the most common site involved was trunk 36% (9cases) followed by extremities 48% (12 cases) and head and neck 16% (4 cases)

The most common benign tumor diagnosed was lipoma 69.5% (242 cases) followed by vascular tumors 13.8% (48 cases), schwannoma 4.6% (16 cases), neurofibroma 4.3% (15 cases) and other tumors 7.8%(27 cases). [Table 4]

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Table 4: Distribution of benign soft tissue tumors

S.NO	TUMORS	TOTAL
1	LIPOMA	242
2	VASCULAR TUMORS	48
3	SCHWANNOMA	16
4	NEUROFIBROMA	15
5	OTHERS	27
	TOTAL	348

The most common malignant tumor diagnosed was fibrosarcoma 32% (8 cases) followed by dermatofibrosarcoma protuberans 24% (6 cases). (15.56%), respectively, and Pseudomonas in 13 (12.5%) and 24 (14.37%), while all other organisms appeared only in small numbers. [Table 5]

Liposarcoma 20% (5 cases) and MPNST 16% (4 cases). This is followed by GIST constituting 8% (2cases). [Table 5]

Table 5: Distribution of malignant soft tissue tumors

S. No	Tumors	Total
1	FIBROSARCOMA	8
2	LIPOSARCOMA	5
3	DERMATOFIBROSARCOMA	6
4	MPNST	4
5	GIST	2
	TOTAL	25

Among the 25 malignant soft tissue tumors, ki67 immunohistochemistry was done in 16 cases. In 9 cases, immunohistochemistry was not done due to insufficient tissue material.

Histological grade is a means of quantitating the differentiation by applying a set of histological criteria. According to FNCLCC grading, three criteria were taken into account.

1. tumor differentiation
2. number of mitoses per 10 HPF
3. presence or absence of necrosis

Tumor differentiation
Score 1 -sarcomas closely resembling normal tissues
Score 2- sarcomas for which histological type is certain
Score 3- embryonal and undifferentiated sarcomas: sarcomas of uncertain type
MITOTIC COUNT
Score 1 – 0-9 mitosis per 10 HPF
Score 2 – 10-19 mitosis per 10 HPF
Score 3 - >20 mitosis per HPF
TUMOR NECROSIS
Score 0- no necrosis
Score 1 -<50% necrosis
Score 2 - >50%necrosis
HISTOLOGICAL GRADE
GRADE 1- total score 2,3
GRADE 2 -total score 4,5
GRADE 3 – total score 6,7,8
Ki67 scoring system
Score 1 - 0-9% of tumor cells showing positivity
Score 2 – 10-29% of tumor cells showing positivity
Score 3 - > 30% of tumor cells showing positivity

HPE grading was done according to FNCLCC grading system which includes tumor differentiation, necrosis and number of mitosis as criteria. Among the 16 cases, 14 cases were reported as grade 1 and 2 cases were reported as grade 2. [Table 6,7]

Table 6: Grading of soft tissue sarcomas by FNCLCC grading

FNCLCC GRADING	NUMBER OF CASES
GRADE 1	14
GRADE 2	2
GRADE 3	0
TOTAL	16

Table 7: Grading of sarcomas by FNCLCC grading

S.NO	DIAGNOSIS	GRADE 1	GRADE 2	GRADE 3	TOTAL
1	MPNST	4	-	-	4
2	FIBROSARCOMA	6	2	-	8
3	LIPOSARCOMA	5	-	-	5
4	DFSP	6	-	-	6
5	GIST	-	2	-	2
		20	4	0	24

Among the 16 cases for which IHC was done, 9 tumors were assigned score 1, 5 tumors were assigned score 2 and 2 tumors were assigned score 3. [Table 8]

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Table 8: Grading of Soft Tissue Sarcomas Using KI67

GRADING	NUMBER OF CASES
GRADE 1	9
GRADE 2	5
GRADE 3	2
TOTAL	16

FNCLCC and ki67 score were same in nine cases. Discrepancy was noted in 7 cases.

Table 9: Comparison of grading by FNCLCC grading system and KI67

GRADE	GRADING BY FNCLCC	GRADING BY KI67	KI 67 NOT DONE
GRADE 1	14	9	9
GRADE 2	2	5	
GRADE 3	0	2	
TOTAL	16	16	

Table 10: Comparison of grading by FNCLCC and ki67 in cases with discrepancy

S.NO	DIAGNOSIS	FNCLCC	KI67
1	DERMATO FIBROSARCOMA PROTUBERANS	1	2
2	DERMATO FIBROSARCOMA PROTUBERANS	1	2
3	DERMATO FIBROSARCOMA PROTUBERANS	1	2
4	DERMATO FIBROSARCOMA PROTUBERANS	1	3
5	MYXO FIBROSARCOMA	1	3
6	MYXO FIBROSARCOMA	2	1
7	MYXO FIBROSARCOMA	1	2

Four tumors reported as grade 1 using FNCLCC were given a score of 2 using ki67. Two tumors reported as grade 1 using FNCLCC were given a score of 3 using ki67. One tumor reported as grade 2 by FNCLCC was given a score of 1 using Ki67, which was a case of low grade myxofibro sarcoma by H&E.

Table 11: Individual tumor grading by FNCLCC and ki67

S.NO	DIAGNOSIS	TUMOR GRADE	BY FNCLCC	BY KI67
1	LIPOSARCOMA	1	4	3
		2		1
		3		
2	FIBROSARCOMA	1	3	3
		2	1	
		3		1
3	MPNST	1	2	2
		2		
		3		
4	DFSP	1	5	1
		2		3
		3		1
5	GIST	1		
		2	2	2
		3		

DISCUSSION

Among the 8553-biopsy material, 373 cases were reported as soft tissue tumors. Out of them, 348 (93.3%) were benign and 25 cases (6.7%) were malignant. This was similar to that observed by Reily Ann Ivan et al and Dr.B.Syam sundar et al.[10,3] Benign to malignant ratio is 14:1.

Of the 376 cases, 176 (47.2%) were reported in males and 197 cases (52.8%) were reported in females. Male to female ratio is 0.9:1.

Benign soft tissue tumors were common in females than males. This was similar to that observed by Reily Ann Ivan et al,[10] but contrast to study done by Dr.B.Syam sundar et al,[3] Myhre Jenson et al,[11] Angervall et al.[12]

Malignant tumors were common in males (19 cases) than females (6 cases) with a ratio of 3.2:1. This was similar to that observed by Reily Ann Ivan et al.[10]

The common age incidence of benign tumor was between 30-40 years (23.9%). This was similar to that observed by Reily Ann Ivan et al.[10]

The common age incidence of malignant tumor was above 60 years (36%). This was in contrast to that observed by Reily Ann Ivan et al,[10] in whom the malignant tumors were common in 41-50 years.

In case of benign tumors, the most common site involved was trunk 29.8% (111 cases) followed by head and neck 27.3% (102 cases). This was in contrast to that observed by Dr.B.Syam sundar et al,[3] in which the common site involved was head and neck.

In case of malignant tumors, the most common site involved was trunk 36% (99 cases) followed by extremities 24% (6 cases). This was in contrast to that observed by Dr.B.Syam sundar et al,[3] in whom the common site involved was lower extremity.

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The most common benign tumor diagnosed was lipoma 69.5% (242 cases) followed by vascular tumors 13.8% (48 cases), schwannoma 4.6% (16 cases) and neurofibroma 4.3% (15 cases). This was similar to that observed by by Reily Ann Ivan et al, Dr.B.Syam sundar et al,[10,3] and Bharathi G Ramana et al.[13]

The most common malignant tumor diagnosed was fibrosarcoma 32% (8 cases) followed by dermato fibrosarcoma protuberans 24% (6 cases). Liposarcoma and MPNST each constituting 20 % (5 cases). This was similar to that observed by Dr.B.Syam sundar et al.[3]

Grading by FNCLCC and Ki67 scoring were different in 7 cases. In the remaining 9 cases grading by both systems were the same.

The diagnosis and classification of soft tissue tumors is one of the most difficult areas in surgical pathology. WHO has classified soft tissue tumors based on clinical, histological and genetic information. Usually, soft tissue tumors are divided into benign and malignant tumors. Important features for predicting the survival rate and metastasis in malignant soft tissue tumor is the type and grade of tumor.

From the result it was observed that there was significant disagreement between FNCLCC grading and Ki67 grading system. This was similar to that observed by Kazuhiro et al.[6] Ki 67 grading system might exhibit better reproducibility in the assessment of histological grading of soft tissue sarcomas than mitotic score. Among the 16 cases, 9 cases show discordance between FNCLCC and grading by ki67. This was not negligible. Ki67 is expressed in all stages of cell cycle except G0 and is a better measure of dividing cells than H&E staining.[19]

CONCLUSION

The diagnosis and classification of soft tissue tumors is one of the most difficult area in surgical pathology. Important feature for predicting the survival rate and metastasis in malignant soft tissue tumors is the type and grade of tumor. Though mitotic count is often cited to diagnose and classify mesenchymal tumors, there are many other histological features which aid in diagnosis. An accurate mitotic count is always a subject of interobserver variability. Hence ki 67 index in a soft tissue sarcoma specifically gives the amount of all tumor cells which are not in G0 phase, there by conveying the tumor aggressiveness. Immunohistochemistry by ki 67 can be used as an additional tool in grading soft tissue sarcomas as Ki67 is expressed in all stages of cell cycle and is a better measure of dividing cell than counting the number of mitosis by H&E staining.

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