

Role of fine needle aspiration cytology in the diagnosis of soft tissue tumors - a prospective study

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Background: Soft tissue can be defined as non- epithelial, extraskelatal tissues of the body exclusive of reticulo-endothelial system, glia and supporting tissues of various parenchymal organs. The annual incidence of soft tissue tumor is 1.4 per 1,00,000 population. FNAC is almost painless, easy to perform, safe and cost effective procedure without any anaesthesia and acts as a useful diagnostic technique in the initial diagnosis of tumors. **Aims:** To study the utility of fine needle aspiration cytology (FNAC) in the diagnosis of soft tissue tumours and in distinguishing benign or malignant tumors. **Material and Methods:** 105 cases of soft tissue tumors were included in this study for cytologic and histologic correlation. FNAC air dried smears were stained with Leishman stain and 95% ethanol fixed smears were stained with H&E. Smears were categorised as benign, malignant, inconclusive or undetermined along with specific subtyping of the lesion. All diagnostic FNAC results were compared for diagnostic concordance using histology results as the gold standard. **Results:** The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 82.6%, 100%, 100%, 93.3% and 95% respectively. **Conclusion:** FNAC is an important preliminary diagnostic tool in palpable soft tissue tumors with high degree of correlation with histopathology report.

Keywords: Benign, FNAC, Histopathology, Malignant, Soft tissue tumors

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Introduction

Soft tissue tumors are defined as mesenchymal proliferations which occur in the extra-skeletal non epithelial tissues of the body, excluding the viscera, coverings of brain and lymphoreticular system [1]. Soft tissue tumours constitute a heterogeneous group of neoplasms in terms of clinical presentation, morphologic features and clinical behaviour [1]. The annual incidence of soft tissue tumor is 1.4 per 1,00,000 population[2]. Benign tumours outnumber malignant ones by 100:1[1]. Because of the rarity of primary tumors of soft tissue and large range of different types of tumours, the diagnosis and classification of soft tissue tumors becomes most difficult areas in surgical pathology and absence of recognisable tissue architectural patterns in cytological preparation makes diagnosis by fine needle aspiration cytology even more difficult [3].

However, FNAC is useful in distinguishing accurately between benign and malignant soft tissue tumours and also sub classify them into general, clinically relevant categories that permit initiation of therapy in many of the patients. In benign neoplasms, surgery can be avoided in the patients who are of poor surgical risk, and in malignant tumors, FNAC allows administration of a palliative treatment.

The main advantage of FNAC is its simplicity. It is a safe, cheap, relatively painless procedure, easy to perform without anaesthesia and is acceptable to the patient [2]. It produces a speedy result and it acts as useful diagnostic technique in the initial diagnosis of tumours.

The present study was done to find out the efficacy of FNAC in the diagnosis of soft tissue tumors and in classifying benign and malignant tumours.

Materials and Methods

Type of study: This is a prospective cytohistological correlation study done at two tertiary care hospitals in the Department of Pathology, Andhra Medical College and King George Hospital, Vishakhapatnam and Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar.

Period of study: The present study was conducted over a period of one year between July 2018 and June 2019. A total number of 105 cases, 65 cases from King George Hospital and 40 cases from Chalmeda Anand Rao Institute of Medical Sciences were studied.

Complete clinical details, examination findings and radiological investigations were studied.

FNAC was done after taking consent with 23/24 G needle attached to 10 ml disposable plastic syringe and air dried smears were stained with Leishman stain and 95% ethanol fixed smears were stained with H & E stain. The cytosmears were studied and categorized into benign, malignant and inconclusive cases. The excised tissue specimens of all above cases were processed routinely and stained with H & E. Special stains were done as and when required. All diagnostic FNAC

Results from patients who underwent a subsequent surgical excision were compared for diagnostic concordance using histology results as the gold standard. In addition FNAC results were analysed for ability to recognize malignancy using statistical parameters of sensitivity, specificity, positive predictive value and negative predictive value.

Histopathological diagnosis of soft tissue tumors were done based on degree of cellularity, cellular pleomorphism, mitotic activity, degree of necrosis, invasive growth, haemorrhage and inflammatory infiltrate. Grading of soft tissue sarcomas was done by Federation Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) system.

Ethical clearance was taken from the Andhra medical college and Chalmeda Anand Rao Medical College.

Inclusion criteria: Palpable soft tissue tumors of size more than 1 cm.

Exclusion criteria: Inflammatory swellings, autolysed biopsy specimens

Results

A total number of 105 cases clinically suspected as soft tissue tumors were subjected to FNAC and compared with histopathology. The observations of the study were as follows:

Table-1: Age and sex distribution of soft tissue tumors

Age (Years)	Male	Female	Total
0 – 10	3	1	4
11 – 20	6	6	12
21 – 30	6	14	20
31 – 40	10	13	23
41 – 50	6	18	24
51 – 60	6	8	14

61 – 70	3	4	7
71 – 80	1	-	1
Total	41	64	105

Most of tumors were observed between the age group of 21-50 years. Male: female ratio was 1:1.5 (Table-1).

Table-2: Anatomical distribution of various soft tissue tumors.

Head & neck	Upper extremity	Lower extremity	Trunk	Retroperitoneum
20	25	30	21	9

Majority of the tumors were observed in the lower extremity, followed by upper extremity (Table -2)

Table-3: Tumor size of various soft tissue lesions

Tumor size (cm)	Benign	Intermediate	Malignant	Total
<5	36	5	7	48
6-10	24	4	8	36
11-15	7	2	11	20
>15	-	-	1	1

Tumor size was highly variable irrespective of the grade of the lesion. Majority of benign tumors were <5 cm and malignant tumors were >10 cm in size (Table-3).

Table-4: Categorisation of soft tissue tumors on FNAC

Diagnosis on FNAC	Number of cases (%)
Benign	60 (63%)
Malignant	19 (20%)
Inconclusive diagnosis	16 (17%)
Scanty material / only blood	10 (10%)
Total	105(100%)

Inadequate material was obtained in 10 (9.5%) cases. FNAC smears have been reported under three basic categories as benign, malignant and inconclusive or undetermined in this study. In 16/95 (17%) cases, the material yielded on FNAC was adequate but not sufficient to classify them as benign or malignant (Table-4).

Table-5: List of cases with inconclusive diagnosis

Diagnosis on FNAC	Histopathological diagnosis	No. of cases
Myxoid mesenchymal tumour	Myxoid liposarcoma	1
Myxoid / chondroid lesion	Extra skeletal chondroma	1
Granular cell tumor/ Alveolar soft part sarcoma	Granular cell tumour	1

Spindle cell neoplasm	Fibromatosis	6
Spindle cell neoplasm	Dermatofibrosarcoma protuberance	2
Spindle cell neoplasm	Hemangioendothelioma	2
Spindle cell neoplasm	Nodular fasciitis	1
Spindle cell neoplasm	Fibrosarcoma	1
Spindle cell neoplasm	Infantile fibrosarcoma	1
Total		16

Most of the cases with inconclusive diagnosis on FNAC turned out to be intermediate grade lesions on histopathology (Table-5).

Table-6: Correlation between FNAC and histopathology-79 cases:

	Correlated	Not Correlated	Total
Benign	53 (94.64%)	3(5.3%)	56
Intermediate	2	-	2
Malignant	16 (76.19%)	5 (23.8%)	21
Total	71(90%)	8(10%)	79(100%)

Majority of benign tumors (94.64%) showed positive correlation on histopathology compared to malignant tumors (76.19%).

Table-7: List of cases with discordant results.

FNAC Diagnosis	HPE Diagnosis	Number of Cases
Lipoma	Neurofibroma	1
Pleomorphic adenoma / Myoepithelioma	Schwannoma	1
Benign vascular lesion	Schwannoma	1
Lipoma	Well differentiated liposarcoma	2
Benign nerve sheath tumour	Malignant peripheral nerve sheath tumour	2
Round cell sarcoma	Synovial sarcoma	1
Total		8

True positive cases (TP) = 19

True negative cases (TN) = 56

False positive cases (FP) = 0

False negative cases (FN) = 4

Sensitivity= 82.6%

Specificity= 100%

Predictive value of positive test= 100%

Predictive value of negative test= 93.3%

Accuracy = 95%

Discussion

Soft tissue can be defined as non- epithelial, extraskeletal tissues of the body exclusive of reticulo-endothelial system, glia and supporting tissues of various parenchymal organs. It is represented by voluntary muscles, fat and fibrous tissue along with the vessels serving these tissues.

By convention, it also includes peripheral nervous system [3]. The annual incidence of soft tissue tumor is 1.4 per 1,00,000 population[4].

Because of the rarity of primary tumors of soft tissue and large range of different types of tumors, the diagnosis and classification of soft tissue tumors become most difficult areas in surgical pathology and absence of recognizable tissue architectural patterns in cytological preparation makes diagnosis by fine needle aspiration cytology even more difficult[5]. Benign tumors are more common than malignant counterparts with a ratio of at least 100: 1[6].

FNAC is painless, easy to perform, safe and cost effective without any anaesthesia and acts as a useful diagnostic technique in the initial diagnosis of tumors [7].

For distinguishing benign tumors from malignant tumors, FNAC was very useful except for exact categorization of tumors [8].

However FNAC as a preliminary diagnostic tool offers several advantages as it can provide a predictive diagnosis of a benign or malignant neoplasm. In benign neoplasm, surgery can be avoided in the patients who are of poor surgical risk, and in malignant or recurrent cancers, FNAC allows the administration of a palliative treatment [9,10].

In the present study adequate material was obtained in 95/105(90%) cases. The possible causes for inadequacy of material in the 10 cases were either due to aspiration of blood (in vascular lesions), collagen (desmoid type fibromatosis) or due to pain (in neural lesions). Collagen rich intercellular stroma, areas of hyalinization, fibrosis and prominent vascularity are known to influence the yield[11].

Gonzalez – Campora R stated that the final cytology report should place the soft tissue tumors in one of the three basic categories – benign, malignant and inconclusive or undetermined [12].

Table-8: Comparison of results on FNAC with other studies

Maitra A et al [13]	Benign on FNAC		Malignant on FNAC		Inconclusive on FNAC	
	42 (58%)		18 (25%)		12 (16%)	
	Benign on HPE	Malignant on HPE	Benign on HPE	Malignant on HPE	Benign on HPE	Malignant on HPE
	39(93%)	3 (7%)	1 (6%)	17(94%)	5(42%)	7(58%)

Present study	Benign on FNAC		Malignant on FNAC		Inconclusive on FNAC	
	60 (63%)		19 (20%)		16 (17%)	
	Benign on HPE	Malignant on HPE	Benign on HPE	Malignant on HPE	Benign on HPE	Malignant on HPE
	56(93%)	4 (7%)	0	19(100%)	3 (28%)	13 (72%)

Correlation between cytological diagnosis on FNAC with histopathological diagnosis in the present study was comparable with other studies.

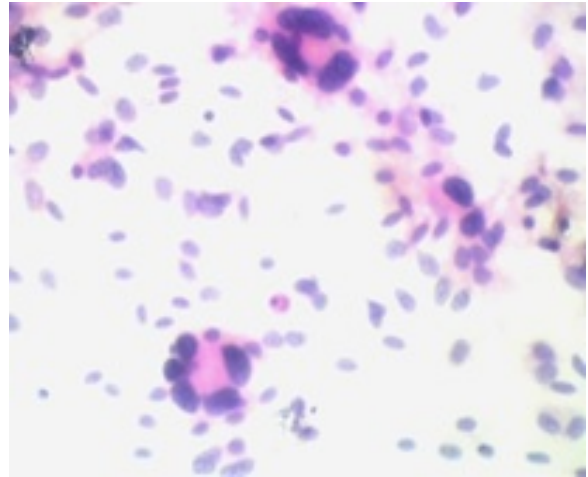


Figure-1: Pleomorphic Lipoma- FNAC smears show floret like giant cells and spindle cells (H&E, x400)

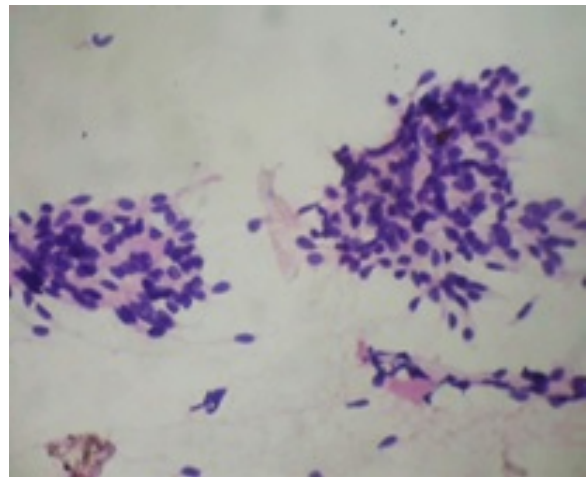


Figure-2: Cytosmears show bland looking round to spindle cells in synovial sarcoma (H&E, x400)

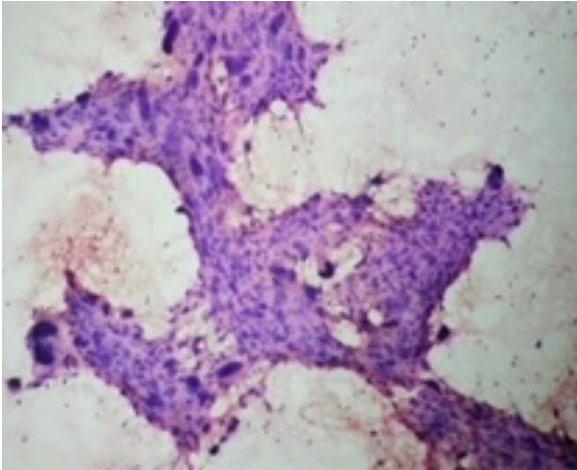


Figure-3: Smears show syncytial sheet of pleomorphic spindle cells in MFH (H & E, x 100).

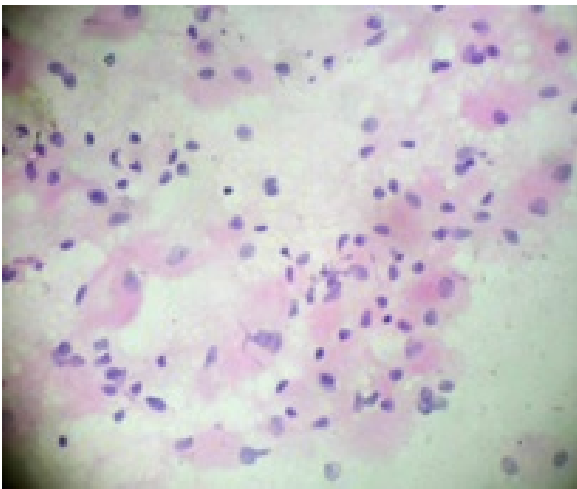


Figure-4: FNAC smears show loose sheets of large polygonal cells with abundant granular eosinophilic cytoplasm in granular cell tumor (H&E,x400).

In the present study 16 of 95 (17%) cases were labeled under the group of inconclusive diagnosis—that is even though the material was adequate for interpretation, it was difficult to classify them as benign or malignant (Table-4). 3 of 16 (72%) were subsequently diagnosed as benign and 13 of 16 (72%) malignant on histopathology. Neoplasms arising from fibrous tissue have varied patterns on morphology.

It is essentially a diagnosis by exclusion. Fibromatosis, dermatofibrosarcoma protuberance, nodular fasciitis and low-grade sarcomas have almost similar morphology on cytology.

It is only histopathology which can differentiate them, basing on infiltrative growth pattern, long fascicles, herringbone pattern, collagenous stroma and inflammatory cells at the border of infiltration [14]. Hence, 11/16 (68.75%) cases of fibrous tumors were given the diagnosis of spindle cell neoplasm on cytology.

Gonzalez – Compura et al, in their FNAB study of 16 myxoid soft tissue tumours opined that the only cells of diagnostic value in smears of lipomatoustumours were lipoblasts [14]. In the present study, a case of myxoidliposarcoma yielded only myxoid matrix with paucity of lipoblasts and hence the diagnosis was inconclusive (Table-5). Chondroid lesions are difficult to aspirate and usually they are hypocellular, as in our case of extraskeletalchondroma which yielded only amphophilic matrix with scattered round to oval cells showing minimal pleomorphism. Vascular lesions usually yield blood and endothelial cells, which resemble spindle cells. Hence, 2 cases of hemangioendothelioma were given the diagnosis as spindle cell neoplasm. Granular cell tumour and alveolar soft part sarcoma show similar cytological features; hence the diagnosis was inconclusive in one of our case (Table-5).

Maximum correlation was seen in benign lesions (Table-6). A case of neurofibroma reported as lipoma on FNAC due to sampling error. A case of schwannoma in the parotid region was reported as pleomorphic adenoma / myoepithelioma due to similar morphology. Another case of schwannoma with high vascularity yielded blood and spindle cells on FNAC (Table-7).

5/21 (23.8%) malignant lesions were not correlated. Two cases of liposarcoma were under diagnosed as lipoma due to lack of typical lipoblasts on FNAC smears (Table-6). Two cases of low-grade malignant peripheral nerve sheath tumour were under diagnosed as benign nerve sheath tumours. A case of synovial sarcoma in a child was reported as round cell sarcoma on FNAC (Table-6). Smears of synovial sarcoma are highly cellular with both single cells and cohesive clusters. Single cells are often stripped of their cytoplasm and appear as round to oval naked nuclei. Keeping in view of the age of the patient, the diagnosis of round cell sarcoma was made. Of the 11/105 (10.47%) cases with intermediate grade malignancy, only two cases showed correlation, and nine were inconclusive (Table-5). The correlation rate was comparable with that of Keiko Nagira et al [15].

In the present study an accuracy of 95%, sensitivity of 82.6% and 100% specificity were observed which were similar to Maitra et al [13]. False negativity was seen in four cases, two liposarcomas, and two malignant peripheral nerve sheath tumors.

Limitations of the present study: Small sample size. The diagnosis on FNAC can be challenging because of interpretation and sampling issues.

Conclusion

From the present study, it was concluded that FNAC is an important tool in the preoperative diagnostic work up of soft tissue tumors with certain limitations and FNAC diagnosis is supplementary but not a substitute for histopathological examination.

What the study adds in the existing knowledge?

FNAC distinguishes benign and malignant tumors of soft tissue with few limitations.

Author's contribution

Dr. Lakshmi Saraswathi Boni: Conception of idea, took lead in writing the manuscript, done investigations

Dr. Sumalatha Kasturi: Verified the analytical methods, done investigations, manuscript writing

Dr. Prasad Uma: Data analysis, analytical calculations, interpretation of results

Dr. Bhagyalakshmi Atla: Supervising the project

All authors provided critical feedback and helped shape the research analysis and manuscript.

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