

Diagnostic value of fine needle aspiration cytology in the evaluation of soft tissue tumours

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Abstract

Context: Fineneedle aspiration cytology (FNAC) is an important tool in the diagnosis of soft tissue tumours. The method is widely tested in recent years as it is easy, quick, safe and fast compared to histopathology.

Aims: Present study is being conducted to study the cytomorphological patterns of soft tissue tumours and find out the efficacy of FNAC when compared with histopathology aided with immunostains.

Settings and Design: Fifty six cases presented with soft tissue swellings were subjected to FNAC. The results were compared with histopathology aided with immunohistochemistry.

Materials and Methods: Present study was a prospective study conducted between July 2007 and December 2008 for a period of one and a half year in the department of Pathology of a tertiary care institute. Patients who presented with soft tissue tumours were included in the study. Patients with inflammatory swellings and those in which histopathology was not available were excluded. Fifty six cases presented with soft tissue swelling were subjected to fine needle aspiration (FNA). Findings were compared with histopathology. Immunohistochemistry was used in some cases for exact diagnosis.

Statistical analysis used: sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy.

Results: In the primary diagnosis of soft tissue tumours by FNAC, the study showed sensitivity and specificity of 93.75% and 94.4% for malignancy. Overall diagnostic accuracy was 94.4% for both benign and malignant neoplasms. Positive predictive value and negative predictive value was 88.24% and 97.3% for malignancy.

Conclusions: FNA of soft tissue tumours yields specific architectural patterns and cytological details. FNAC helps in the initial management of soft tissue tumours as it is rapid and fairly accurate.

Keywords: Soft issue tumours, Cytology, Patterns, Histopathology.

Key Messages: Careful interpretation of cytological findings is required for accurate diagnosis of soft tissue tumours. Different types of tumours having similar cell pattern poses diagnostic difficulties.

Introduction

FNAC is a valuable tool in the diagnosis of soft tissue tumours and has been widely tested in recent years.^{1-11,16-19} Benefits of FNAC over coarse needle or open surgical biopsy are rapid preliminary diagnosis without hospitalisation and anaesthesia, negligible complication and fear for tumour spread.⁵ Precise diagnosis of significant number of tumours is possible by taking into account architectural patterns, cytological details and clinical characters of lesion.¹¹

Present study is being conducted to ascertain the diagnostic value of FNAC in the evaluation of soft tissue tumours by studying various cytomorphological patterns and classify the tumours as benign or malignant and to subtype the tumour wherever possible. The results were compared with histopathology aided with immunostains.

Materials and Methods

Present study was conducted between July 2007 and December 2008 in the department of Pathology of a tertiary care institute. Fifty six cases presented with soft tissue swelling were subjected to FNA. Aspiration was done using 21-23 gauge needle and 20ml disposable

syringe. No local anaesthesia was used. Geimsa stain was used in all while per iodine acid schiffs (PAS) stain in few cases. All the cases were subjected for histopathological examination (HPE) aided with immunostains for final diagnosis. FNAC was then correlated with histopathology to ascertain the diagnostic accuracy of cytology.

Results

Of 56 cases with soft tissue swelling, 54 cases were of soft tissue tumours. One case was inconclusive due to hemorrhagic smears and other was organised abscess. Thirty nine (72%) were found to be benign and 16 (28%) were malignant on histopathology Table 1. Out of 54 cases, specific diagnosis was given to 52 cases while two cases were reported as benign spindle cell neoplasm. The age distribution showed that the benign tumours occurred above second decade of life, while soft tissue sarcoma occurred in patients of all ages Table 1. For benign tumours trunk was the commonest site followed by extremities whereas malignant tumours were common in lower extremities followed by trunk. Both on cytology and on histopathology benign tumours showed spindle and

mature tissue pattern while malignant tumours showed pleomorphic, spindle and round cell pattern Table 2. Histopathology of eight cases required immunohistochemistry for type specific diagnosis Table 3. The results of FNAC and histopathology were

compared and analysed Table 4 and Table 5. The study showed sensitivity and specificity of 93.5% and 94% respectively with overall diagnostic accuracy of 94.4%. FNAC was more specific than sensitive in diagnosing malignant tumours Table 6.

Table 1: Type and age wise distribution of soft tissue tumors

Type	Subtype	Age distribution (in years) and number				
		0-10	11-20	21-40	>40	All age groups
Benign tumour (B)	1 Lipoma			14	14	28
	2 Schwannoma			3	3	6
	3 Neurofibroma			2		2
	4 Cavernous hemangioma			2		2
	5 Fibroma			1		1
Malignant tumors (M)	1 Pleomorphic sarcoma			2	3	5
	2 Malignant Peripheral nerve sheath tumors(MPNST)			1	2	3
	3 Ewings sarcoma	1	1	1		3
	4 Synovial sarcoma			2		2
	5 Rhabdomyosarcoma(RMS)	1				1
	6 Leiomyosarcoma(LMS)				1	1
	7 Liposarcoma/Atypical lipoma			1		1

Table 2: Cytological patterns observed in soft tissue tumours

Pattern	No. and Type of tumour
Benign tumour (B)	
Spindle cell	11 (schwannoma, neurofibroma, fibroma, fibrolipoma, cavernous hemangioma)
Mature tissue	27 (lipoma)
Malignant tumours (M)	
Pleomorphic	Pleomorphic sarcoma (5),LMS(1),MPNST (1)
Spindle	MPNST (2), synovial sarcoma (2), atypical lipoma/liposarcoma (1)
Small round	Ewing's sarcoma (3), RMS (1)

Table 3: Tumors in which immunohistochemistry aided/confirmed the histopathological diagnosis

S. No	FNAC Diagnosis	Histopathological diagnosis	Markers used	Final diagnosis
1	MPNST	MPNST	S-100+	MPNST
2	Low Grade Myxofibrosarcoma	NEUROFIBROMA	S-100+	NEUROFIBROMA
3	Pleomorphic sarcoma	Pleomorphic sarcoma	SMA+, CD68-	LMS
4	MPNST	MPNST/SS	S-100+, SMA-	MPNST
5	Pleomorphic sarcoma	Pleomorphic sarcoma	S-100+	MPNST
6	Ewing's Sarcoma	Ewing's Sarcoma	MIC-2+, VIM+	Ewing's Sarcoma
7	Ewing's Sarcoma RMS	Ewing's Sarcoma/RMS	MIC-2+, MYOG-	Ewing's Sarcoma
8	RMS	RMS	MYOG+	RMS

Table 4: Comparative analysis of FNAC and histological diagnosis

Similarity between FNAC and histopathology			Disparity between FNAC and histopathology (HP)		
Nature	Diagnosis	No.	FNAC diagnosis	No.	HP Diagnosis
Benign	Lipoma	27	Nodular Fasciitis	1	Fibrolipoma
	Neurofibroma	1	Neurofibroma	1	fibroma
	Schwannoma	4	Benign spindle cell lesion (could not be specified)	2	1 Schwannoma
				1	1 Hemangioma
			Low grade Myxofibrosarcoma	1	Neurofibroma
			Spindle cell neoplasm of low malignant potential	1	Cellular Schwannoma
			Inconclusive	1	Hemangioma
Malignant	Rhabdomyosarcoma	1	Pleomorphic sarcoma	2	1.MPNST 2.LMS
	Pleomorphic sarcoma	4	Mesenchymal Neoplasm	1	Pleomorphic sarcoma
	Ewings Sarcoma	3	Nodular fasciitis	1	Synovial sarcoma
	MPNST	2			
	Synovial sarcoma	1			
	Atypical lipoma	1			

Table 5: Errors made in diagnosing soft tissue tumors

	FNA	Histopathology	Reason of error
Inconclusive FNA	Hemorrhagic	Cavernous hemangioma	Aspiration from blood filled spaces
False negative	Nodular fasciitis	Synovial sarcoma	History of rapid increase in swelling, tenderness Cytology showing myofibroblast like cells and myxoid background
False positive	Low grade myxofibrosarcoma	neurofibroma	Clinically large mass with history of rapid enlargement Cytology – spindle cells and cells with multiple cytoplasmic projections mimicking myofibroblast and intercellular myxoid substance
	Spindle cell neoplasm of low malignant potential	Cellular schwannoma	Atypia of nuclei and mitotic Fig.s
Typing error			
Mesenchymal tumour		Organized abscess	Pleomorphic nuclei, myxoid fibrocollagenous component and inflammation in the background
Subtyping error			
	Benign spindle cell tumor	Cavernous hemangioma	Scant cellular material, only few spindle cells aspirated
	Benign spindle cell tumor	schwannoma	Scant cellular material, only few spindle cells aspirated
	Nodular fasciitis	fibrolipoma	Aspiration from fibrous component and myofibroblast like cells
	neurofibroma	fibroma	Misinterpretation of cells
	Pleomorphic sarcoma	MPNST	Severe nuclear atypia
	Pleomorphic sarcoma	LMS	Severe nuclear atypia

Table 6: Accuracy, sensitivity, specificity, positive predictive value, negative predictive value of FNAC in primary diagnosis of mesenchymal lesion

Primary diagnosis	No. of cases/Total cases
True positive(FNAC M/HPE M)	15/54
True negative(FNAC B/HPE B)	36/54
False positive(FNAC M/HPE B)	2/54
False negative(FNAC B/HPE M)	1/54
Accuracy	51/54 (94.4%)
Sensitivity	93.75%
Specificity	94.74%
Positive predictive value	88.24%
Negative predictive value	97.3%

Discussion

The present study was aimed to find out the effectiveness of FNAC in the diagnosis of soft tissue tumours. Total of 56 cases were studied by FNAC. Out of 56 cases one case was excluded from the study as it turned out to be an organised abscess on histopathology. Out of 55 cases, 54 cases were reported while one (1.8%) case was inconclusive due to aspiration of blood. Out of 54 cases, specific diagnosis was given to 52 cases while two cases were reported as benign spindle cell neoplasm.

The inconclusive FNAC was found to be cavernous hemangioma on histopathology. Aspiration of blood was the cause for inconclusive FNAC. Fine needle aspiration of hemangioma of any type yields plenty of venous blood is cited by Ackerman.¹²

The excluded case was found to be an organised abscess on histopathological examination which was wrongly reported as malignancy on cytology. Wrong diagnosis of malignancy was made on cytology due to misinterpretation of the reactive fibroblasts and histiocytes as neoplastic malignant cells. Maitra et al⁷ in their study misinterpreted reparative fibroblastic activity as neoplastic atypia.

Of the two cases which were labelled as benign spindle cell neoplasm not specified on cytology, one was diagnosed as cavernous hemangioma whereas the other as schwannoma on histopathological examination. The patient diagnosed as cavernous hemangioma had a swelling in the calf region and was deep. Characterisation of this tumour was not possible on FNAC as the tumour aspirate was predominantly hemorrhagic and constituted few benign spindle cells. In this case the spindle cells represented the endothelial cells and the cause for haemorrhage was the blood filled spaces. The difficulty in diagnosing hemangiomas was cited by Siddharaju et al.¹³ Another case which was diagnosed as schwannoma on histopathology had lesion on her sacral lesion and the lesion was slow growing and was present for 20 years. Type specific diagnosis in this case was not possible on FNAC because of scant cellular smears and predominance of blood. Only occasional tightly cohesive spindle cell clusters and occasional stromal fragments were present in the

aspirate. The major problem in FNAC of neurilemmoma is to obtain sufficient material was also cited by Domanski et al.¹⁴

In this study, the majority of soft tissue tumours were found to be benign and of these, lipoma were the commonest variety (74%) consistent with the result reported in other studies.^{9,18} Lipomas commonly occur after the second decade of life. Soft tissue sarcomas occurred in all age group but common after the second decade of life. Upper extremity and trunk was the favoured sites for benign tumours. Lower extremities were the favoured site for malignant tumours as cited by other studies.^{9,18}

Accuracy was high for the diagnosis of lipomatous tumours and was comparable with studies of Akerman et al.²⁰ Roy et al.⁹ and Arul et al.¹⁸ One case of fibrolipoma was wrongly diagnosed as nodular fasciitis. Wrong diagnosis of nodular fasciitis was given due to small size of lesion and aspiration of fibrous areas. The cells aspirated showed bipolar to multipolar cytoplasmic processes of spindle cells as well as myxoid background which has led to erroneous diagnosis Fig. 1a.

Schwannoma was the second most common soft tissue tumour in the present study. Four (67%) cases were diagnosed correctly on cytology as neurilemmoma, one (16.6%) diagnosed as benign spindle cell neoplasm and one (16.6%) as spindle cell neoplasm of low malignant potential. The results were between the studies of Klijanienko et al.²¹ and Domnaski et al.²² where correct labelling of Schwannoma ranges from 38.2% to 84%. One case was diagnosed as benign spindle cell neoplasm due to scant cellular material and other was falsely diagnosed as spindle cell neoplasm of low malignant potential Fig. 1b. because of mitotic activity seen in cytological smears which turned out to be cellular Schwannoma on histopathological examination. Domnaski et al.²² also reported false positive diagnoses in their study. The diagnostic smears in most cases of schwannoma contained spindle cells with wavy nuclei embedded in a fibrillar, occasionally collagenous, and/or myxoid matrix and Antoni A/Antoni B tissue fragments. A moderate to abundant admixture of round to oval cells

was also frequent. Nuclear pallasading was also noted. Cytological findings correlated well with histological findings in the smears where cellularity was adequate.

Most of the malignant soft issue tumours were pleomorphic sarcoma. Malignant peripheral nerve sheath tumour (MPNST) constituted a significant proportion (19%) of soft tissue sarcoma in our institute. Kar M et al.²³ found 12% of soft tissue sarcomas as MPNST in their medical centre. In our study there were three cases of MPNST diagnosed histologically. Out of these two were diagnosed correctly. On FNAC, two were subtyped correctly while one was typed as pleomorphic sarcoma. One case presented with classical pattern, one with predominance of isolated cells and one as pleomorphic cell pattern. Well-differentiated MPNST comprised of cell-rich cellular fragments, spindle-shaped cells with wavy and comma-like naked nuclei, polymorphous oval to round cells mitotic figures, fibrillary, delicate stroma and background myxoid material. Anaplastic giant cells, intranuclear inclusions were found in one case. FNAC was a good test for the diagnosis of moderate to well differentiated tumours. However in poorly differentiated tumors exact subtyping was not possible. Klizanienko et al described the various cytomorphological features of MPNST in their study.²⁴

Three case (19%) of malignant soft tissue tumours in the present study belonged to Ewing's sarcoma group. Two were males and one female. The cytological appearance of this lesion was distinctive. Bakhos et al.²⁵ highlighted the characteristic cell morphology of this family of tumors. All cases of Ewing's sarcoma/PNET were correctly diagnosed on cytology. Immunohistochemistry was available in two cases against MIC-2 antigen aiding the diagnosis on histopathology. Ewings sarcoma/PNET of thoracopulmonary region is known as Askin's tumor. We had two cases of chest wall sarcomas. They had characteristic clinical, radiological and cytological features as described in case reports by Askin et al.,²⁶ Oruc et al.²⁷ and Gulati et al.²⁸ Two type of cell population of large light cells and small dark cells were seen Fig. 2a. The large light cells had cytoplasmic vacuoles which were PAS positive, the small round cells had tendency for rosette formation. Correct typing of these round cell tumours on cytology was possible due to characteristic morphology of cells and clinicoradiological correlation. PAS staining on cytological smears helped in the diagnosis. Antibody applied to MIC-2 antigen Fig. 2c was an important adjunct. In our study cytology correlated well with histology Fig. 2b and a type specific diagnose was possible due to characterstic morphologic appearance of cells. Better correlation was due to better differentiation of tumor cells.

We had two cases (12.5%) of synovial sarcoma (SS) in the present study. Both patients were young, one was male and other was female. The male patient

presented with swelling calf region Fig. 2d. Out of two only one was correctly diagnosed on cytology. In the male patient peripheral calcification on radiological investigation helped in the diagnosis. The false negative diagnosis of nodular fasciitis was given to other case because of rapidly growing tumour size, tender and small mass, myofibroblast like cells and myxoid background on cytology Fig. 1c. Classic patterns of monophasic synovial sarcoma observed cytologically as dispersed or small clusters of cells with bland chromatin, inconspicuous nucleoli, oval to spindle shaped cytoplasm and branching tumour tissue fragments, capillary network Fig. 2e. Similar findings were observed in the corresponding histopathology sections Fig. 2f. Klizanienko et al.²⁹ described the various cytomorphological features of synovial sarcoma.

In our study there was one case of rhabdomyosarcoma (RMS) in a six year female child in the right upper eyelid Fig. 3a. Almeida et al.³⁰ discussed the cytology of rhabdomyosarcoma. Clusters and isolated tumour cells were present. Smears revealed two types of cells - one with scant cytoplasm, pleomorphic nuclei, fine to coarse nuclear chromatin, occasional nucleoli and other type with large abundant cytoplasm and peripheral cytoplasmic vacuolation and evidence of rhabdomyoblastic differentiation Fig. 3b. Immunohistochemistry showed positivity for myogenin Fig. 3d. In the present study cytology correlated well with the histological findings Fig. 3c.

There was one case of leiomyosarcoma (LMS) near the right elbow joint Fig. 4a. The cytological findings were of pleomorphic sarcoma. This case was wrongly diagnosed as pleomorphic sarcoma on cytology. Histopathology supported with immunohistochemistry aided in the diagnosis of leiomyosarcoma. High grade tumours are difficult to typify. In the present case the cytological findings were not characteristic and the morphologic appearance on cytology suggested a high grade malignant neoplasm with spindle cell and histiocyte like pleomorphic tumour cells suggestive of pleomorphic sarcoma Fig. 4b. On histopathologic examination same pattern observed Fig. 4c and it show edimmunoreactivityto SMA (smooth muscle actin) Fig. 4d which led to the diagnosis of leiomyosarcoma. Klizanienko et al.³¹ highlighted the problem in differentiating high grade neoplasm.

Soft tissue tumours exhibited specific cell patterns which helped in their diagnosis and subtyping. Many classification schemes have been proposed that allow limited subclassification of soft tissue tumours. Nguyen et al. have proposed a three category scheme: 1) pleomorphic cell tumours, 2) spindle cell tumours and 3) small round cell tumours.¹⁵ In the present study, pattern of 54 cases were studied on cytology. In benign tumours, Twenty seven cases of lipoma recapitulated the mature tissue pattern. Rest of the benign tumours were having spindle cell pattern. In malignant tumours,

7 showed pleomorphic cell pattern, 5 showed spindle cell pattern and 4 showed round cell pattern. Study of tissue sections also revealed similar patterns as described on cytology. However, tissue sections had the advantage that large areas were examined and representative material from various areas were taken.

In the present study, total of 55 cases of soft tissue tumours were studied on FNAC and correlated by histopathology. Thirty seven were reported as benign, seventeen as malignant and one was inconclusive. One case of synovial sarcoma was reported as nodular fasciitis while false positive cases were neurofibroma and cellular schwannoma. The overall accuracy was 94.4% for both benign and malignant neoplasms. Diagnostic accuracy in the present study was comparable with the studies of Roy et al.⁹ and Arul et al.¹⁸

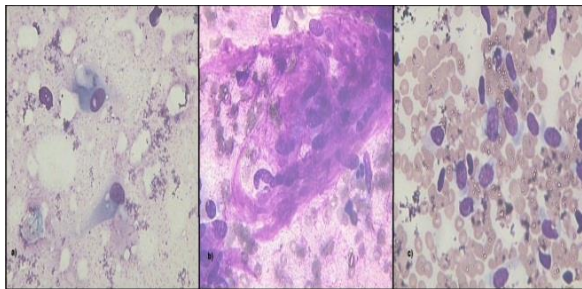


Fig. 1: (Giemsa stain, 400x). a) Myofibroblast like cells seen in fibrolipoma which were misinterpreted as a feature on nodular fasciitis. b) Spindle cells showing mild atypia and myxoid substance in the background in a case of schwannoma misinterpreted as sign of malignancy. c) Bland spindle cells and few myofibroblast like cells in synovial sarcoma misinterpreted as a feature of nodular fasciitis.

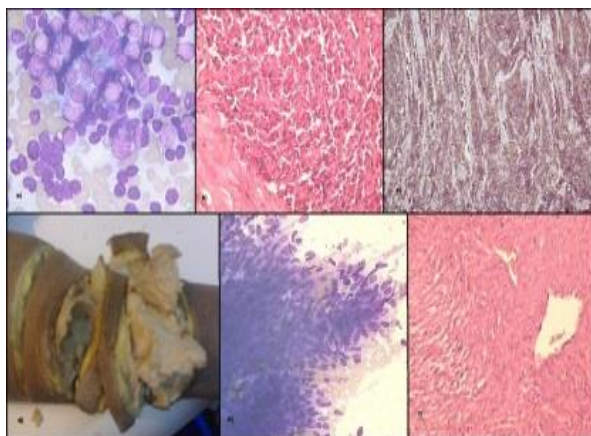


Fig. 2: (a-c, ewing's sarcoma), a) cytological smears showing large lighter cells and small darker cells (giemsa, 400x), b) corresponding histopathological section (h&E,200x), c) immunohistochemistry showing positivity for MIC-2. (d-f, synovial sarcoma), d) cut section of growth in calf region, e)

cytology showing branching fragments of bland spindle cells (giemsa,400x), f) corresponding histopathological section (h&E,400x).

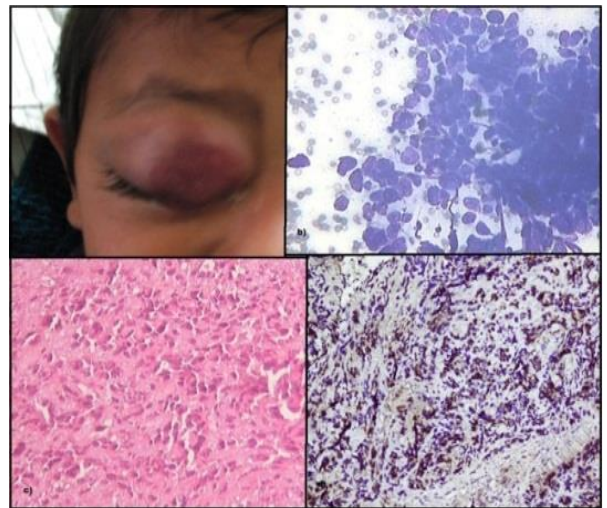


Fig. 3: Rhabdomyosarcoma. a) clinical presentation as swelling upper eye lid, b) cytosmears showing tumor cells in isolation and in clusters with pleomorphic nuclei and cytoplasmic vacolation (giemsa,400x), c) corresponding histopathological section (h&E,400x), d) immunohistochemistry showing positivity for myogenin (200x).

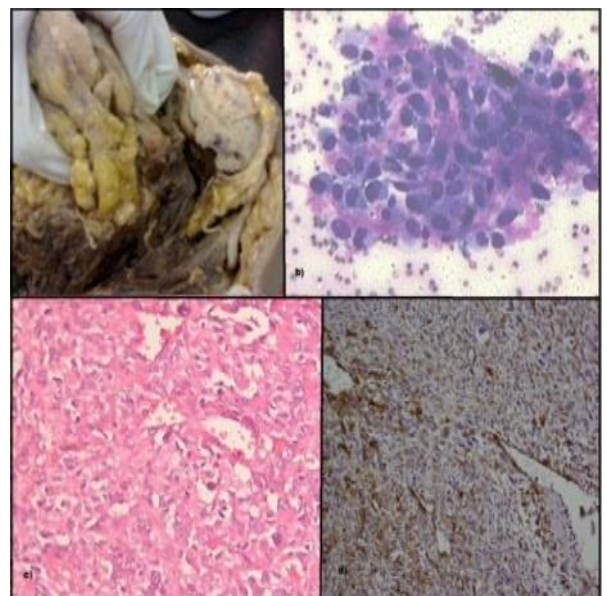


Fig. 4: Leiomyosarcoma. a) cut section of growth elbow, b) cytosmears showing pleomorphic spindle to polygonal cells (giemsa,400x), c) corresponding histopathology section (h&E,400x) d) immunohistochemistry showing positivity for smooth muscle actin (200x).

Conclusion

FNAC is a useful test in the initial management of soft tissue neoplasms as it is fairly accurate. FNA of soft tissue tumours yields specific cell pattern which help in their categorisation and subtyping. However, different types of tumours having similar cell pattern poses diagnostic difficulties and careful interpretation of cytological findings is required. Histopathological examination aided with immunohistochemistry is required for exact characterisation and grading which helps in deciding further treatment and final outcome.

Conflict of Interest: None

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