www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i3.187

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Fine Needle Aspiration Cytology of Mesenchymal Tumours

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Abstract
Introduction: *FNA of musculosketal masses provides a number of advantages and disadvantages. However FNA of soft tissue and bone is not widely accepted to obtain a definitive diagnosis for tumours. This study aims to establish the diagnostic accuracy of fine needle aspiration cytology in diagnosing mesenchymal tumours with reference to the subsequent histopathology report.*
Material and Methods: *634 patients were studied over a period of 2 years. A comparison was made between cytological and histological findings whenever possible. On correlation the sensitivity, specificity, accuracy and positive predictive value were calculated*
Result: *Out of 634 cases, 54.36% of benign mesenchymal and 62.5% of malignant mesenchymal tumours were seen in males. 45.63% of benign and 37.5 % of malignant mesesnchymal tumours were seen in females. Soft tissue tumours (91.95%) were found to be much more common as compared to bone tumours (8.05%). The Sensitivity, Specificity and diagnostic accuracy of FNA of malignant lesions was found to be 90%, 97.72% and 95.31% respectively.*
Conclusion: *The present study concluded that FNA is fairly reliable for correct preoperative diagnosis and management of mesenchymal tumours.*
Keywords: *Cyto-histo correlation, FNAC, Histopathology, Mesenchymal, Soft tissue tumours.*

Introduction

Mesechymal tissue refers to the part of the embryonic mesoderm from which connective tissue, bone, cartilage and circulatory and lymphatic systems develop[1,2]. Mesenchymal lesions are a highly heterogenous group of tumours that are classified on a histogenetic basis according to the adult tissue they resemble.

FNA of musculosketal masses provides a number of advantages. FNA is a rapid outpatient procedure which permits on site evaluation of specimen adequacy and may provide an immediate diagnosis. The procedure is usually well tolerated. A major advantage is that much greater sampling is possible by altering the direction of the needle during a single puncture. Multiple portions of the mass may be aspirated as compared to a core needle biopsy. If necessary multiple passes may be taken in a single setting. Almost no instance of needle tracking of sarcomatous tumour cells by a fine needle has been documented[3]. Finally compared to all other

diagnostic techniques, FNA is relatively inexpensive[4].

FNA however also has several distinct disadvantages, some of which are relatively specific to mesenchymal lesions. There is dispersion of individual cells and loss of recognizable diagnostic tissue patterns. There may be difficulty in distinguishing among benign cellular lesions and low grade sarcomas. In densely collagenised or sclerotic masses or highly vascular lesions FNA may provide only a sparse cellularity, making a benign versus malignant distinction impossible[4].

Despite the long history of musculoskeletal fine needle aspiration (FNA), FNA of soft tissue and bone is not widely accepted to obtain a definitive diagnosis for tumorous lesions[5].

This study aims to establish the diagnostic accuracy of fine needle aspiration cytology in diagnosing mesenchymal tumours with reference to the subsequent histopathology report.

Material & Methods

The study was conducted over a period of 2 years. Approval from the Institutional Ethical Committee was obtained. Patients who were clinically and radiologically suspected to have a mesenchymal tumour sent for FNA were included. Patients who were subsequently diagnosed as adnexal, lymph node, inflammatory or cystic on cytological examination were excluded. Specimens considered unsatisfactory for evaluation were also excluded.

Multiple passes were taken if found necessary. The smears were stained with Haematoxylin and Eosin (H and E), Papanicolaou and May-Grunwald Giemsa stain. Special stains were used whenever required. The paraffin sections of biopsy or surgically resected specimen were stained with H and E. Immunohistochemistry was used for confirmation of diagnosis whenever considered necessary.

A comparison was made between cytological and histological findings whenever possible. On correlation the sensitivity, specificity, accuracy and positive predictive value were calculated. The diagnosis was categorized into three groups: benign, malignant and suspicious for malignancy. Benign group consisted of uniequivocally benign neoplasms without atypical features. The last subgroup consisted of cases where a definite categorization could not be done and the differential diagnosis included at least one malignant lesion.

Observations & Results

In the study 634 cases were subjected to FNA. The age range of the study population was 1 month to 85 years. The most common age groups for benign and malignant mesenchymal tumours were fourth and fifth decade respectively. Out of 634 cases, 54.36% of benign mesenchymal and 62.5% of malignant mesenchymal tumours were seen in males. 45.63% of benign and 37.5 % of malignant mesesnchymal tumours were seen in females. Soft tissue tumours (91.95%) were found to be much more common as compared to bone tumours (8.05%).

Table 1 Site wise distribution of Benign Mesenchymal tumours

Anatomical site	No of cases	Percentage
Trunk	235	42.72
Head & neck	100	18.18
Upper extremity	83	15.09
Lower extremity	67	12.18
Multiple	65	11.81
Total	**550**	**100**

Most common site of occurrence of benign mesenchymal tumors was found to be trunk (39.91%) followed by lower extremity (17.95%).

Table 2 Site wise distribution of Malignant Mesenchymal tumours

Anatomical site	No of cases	Percentage
Lower extremity	39	48.75
Trunk	21	26.25
Head & neck	09	11.25
Retro-peritoneum	07	8.75
Upper extremity	03	3.75
Multiple	01	1.25
Total	**80**	**100**

Most common site of occurrence of malignant mesenchymal tumors was found to be lower extremity (48.75%) followed by trunk (26.25%).

Table 3 Prevalence of benign bone tumours

Tumour	No of cases
Giant cell tumour of bone	04(0.63%)
Osteochondroma	02(0.31%)
Enchondroma	02(0.31%)
Chondromyxoid fibroma	01(0.15%)
Osteoid osteoma	01(0.15%)
Osteoblastoma	01(0.15%)
Total	**11**

Most commonly encountered benign bone tumour in present study was giant cell tumour of bone (0.63%) followed by osteochondroma (0.31%) and enchondroma (0.31%).

Table 4 Prevalence of malignant bone tumours

Tumour	No of cases
Osteosarcoma	15 (2.36%)
Ewing's Sarcoma	08 (1.26%)
Chondrosarcoma	05 (0.78%)
Multiple myeloma	04 (0.63%)
Chordoma	04 (0.63%)
Metastasis	02 (0.31%)
Total	**38**

Most common malignant bone tumour found in the study was Osteosarcoma (4.16%) followed by Ewing's Sarcoma (2.22%).

Table 5 Prevalence of benign soft tissue tumours

Tumour	No of cases
Lipoma	452 (71.29%)
Neural tumours	32 (5.04%)
Benign spindle cell tumour	18 (2.84%)
Giant cell tumour of tendon sheath	09 (1.41%)
Benign Fibrous Histiocytoma	08 (1.26%)
Pseudosarcomatous process	06 (0.94%)
Fibromatoses	04 (0.63%)
Lymphangioma	03 (0.47%)
Hemangioma	02 (0.31%)
Fibroma	02 (0.31%)
Myxoma	01 (0.15%)
Lipoblastoma	01 (0.15%)
Ectomesenchymal chondromyxoid fibroma	01 (0.15%)
Total	**539**

Most common benign soft tissue tumour in the present study was Lipoma (71.29%) followed by neural tumours (5.04%).

Table 6 Prevalence of Malignant soft tissue tumours

Tumour	No of cases
Sarcoma (Not otherwise specified)	14 (2.20%)
Malignant spindle cell tumour (Not otherwise specified)	05 (0.79%)
Malignant round cell tumour (Not otherwise specified)	05 (0.79%)
Liposarcoma	04 (0.63%)
Malignant fibrous histiocytoma	04 (0.63%)
Rhabdomyosarcoma	03 (0.47%)
Synovial Sarcoma	02 (0.31%)
Metastasis	02 (0.31%)
Malignant peripheral nerve sheath tumour	02 (0.31%)
Alveolar soft part sarcoma	01 (0.15%)
Total	**42**

As shown in table 6, out of the 40 cases of primary malignant soft tissue sarcoma, specific tumour typing could not be done in all cases. Seven cases required application of immunohistochemical markers for the confirmation of diagnosis. Most of the cases were of pleomorphic sarcomas where sub typing was not possible on light microscopy alone. Diffuse positivity for pancytokeratin and focally positive desmin helped clinching the diagnosis in 3 cases of malignant fibrous histiocytoma. A panel of markers consisting of vimentin, CD31, CD34, pancytokeratin, CD68, low molecular weight cytokeratin, desmin, smooth muscle actin, S100 and HMB45 was applied in a case of highly pleomorphic sarcoma. It came out to be positive for vascular markers like CD31 and CD34. Vimentin and focal Pan CK positivity was also observed. The case was subtyped as Epitheloid Angiosarcoma.

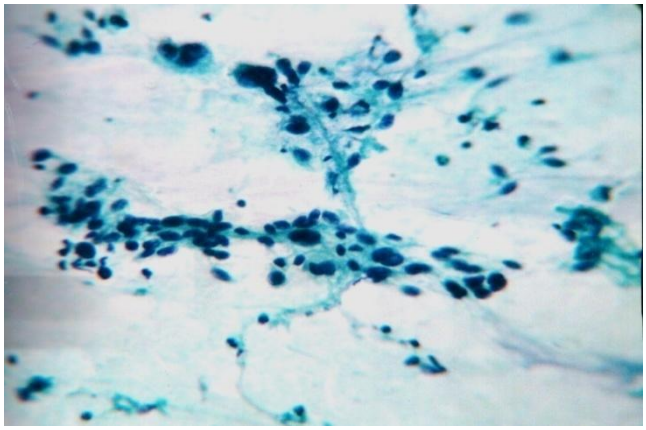

Fig. 1 Cytology smear of a case of Malignant Fibrous Histiocytoma showing hyperchromasia and pleomorphism (100x, pap)

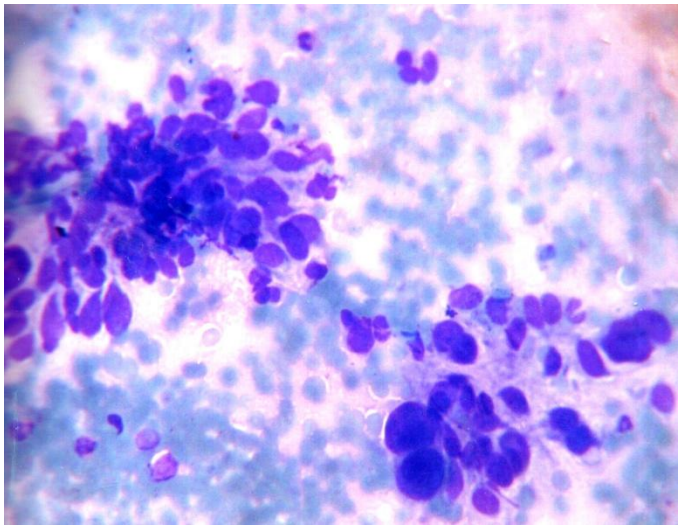

Fig. 2 Multinucleated tumour giant cells in the case of Malignant Fibrous Histiocytoma (400x, MGG)

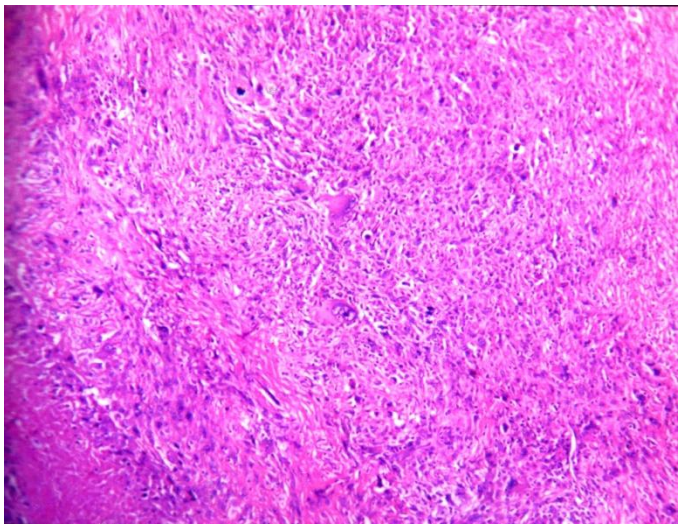

Fig. 3 Tissue section of the above case showing multinucleate and bizarre tumour giant cells (100x, H&E)

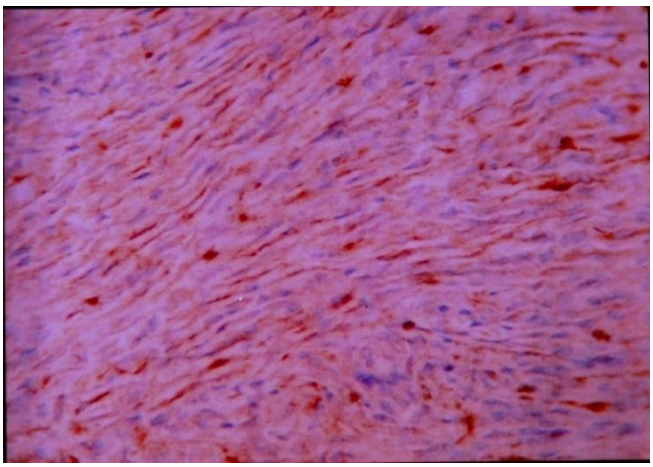

Fig. 4 Pancytokeratin immunostain showing diffuse positivity (400x, Pan-CK)

Table 7 Histopathological correlation according to predominant cell type

Cell Type	Histopathological Diagnosis		Total
	Concordant	Discordant	
Fatty	50	03	53
Spindle cell	27	04	31
Pleomorphic	08	0	08
Round cell	06	01	07
Giant cell	04	01	05
Osseous	06	0	06
Chondroid	04	01	05
Myxoid	03	01	04
Epitheloid	03	0	03
Vascular	02	0	02
Metastasis	04	0	04
Total	**117(91.4%)**	**11(8.60%)**	**128(100%)**

Table 8 Discordant Cases

Discrepancy	Cytology Diagnosis	Histology follow up
False Negative	Fibromatosis	Fibrosarcoma
	Lipoma	Dedifferentiated liposarcoma
	Benign myxoid spindle cell tumour	Myxofibrosarcoma
	Osteochondroma	Chondrosarcoma
False Positive	Giant cell tumour of bone	Aneurysmal Bone cyst
	Atypical lipomatous tumour	Lipoma

Out of the 11 discordant cases, 6 were truly discordant in respect of being false positive or negative. The remaining 5 cases were correctly categorized as benign or malignant but sub typing differed.

The Sensitivity, Specificity and diagnostic accuracy of FNA of malignant lesions was found to be 90%, 97.72% and 95.31% respectively.

Discussion

In the present study 81.60% masses were diagnosed as benign tumours and 11.86% were diagnosed as malignant on cytology. This finding was in accordance with those of Bezabih (2001)[6], Nagira et al (2002)[7], Roy et al (2007)[8] and Maitra et al (2000)[4] The present study observed that benign and malignat tumours were more common in third to fourth decades and fourth to fifth decades respectively similar to the study conducted by Soni et al[9].

Most common site of occurrence of benign mesenchymal tumours was found to be trunk while that of malignant mesenchymal tumours was lower extremities. These findings are in accordance to the findings of Bezabih (2001)[6].

In the present study, giant cell tumour was found to be the most common benign tumour followed by osteochondroma and enchondroma . This is in accordance with studies conducted by Jorda et al (2000)[10] and Handa et al (2005)[11]. Osteosarcoma was the most common malignant bone tumour followed by Ewing's Sarcoma. Kumar et al (1993)[12] and Kabukcuoglu et al (1998)[13] also studied bone tumours and reported similar findings.

In accordance with the studied conducted by Bezabih[6], Hirachand et al (2007)[14], Roy et al (2007)[8], lipoma was the most common benign soft tissue tumour. As stated that out of 40 cases of soft tissue sarcomas 60% of the cases could be diagnosed only as sarcoma. Specific sub typing was possible in 40% cases. Kilpatrick et al (2001)[15] studied 98 cases of soft tissue sarcoma out of which 46% cases were given a diagnosis of sarcoma (not otherwise specified). Similar findings were reported by Bezabih (2001)[6].

As shown in table 8, cases labeled as fibromatosis and lipoma on cytology turned out to be fibrosarcoma and dedifferentiated liposarcoma respectively. Clinically the tumours were large (>10 cm). Perhaps the areas of pleomorphism and increased mitotic activity were not represented in the smears. Hence aspirations from multiple sites are recommended.

The abundant myxoid background obscuring the morphology of cells and areas of atypia and increased mitotic activity being missed lead to misdiagnosing a myxofibrosarcoma. Differential diagnosis between a low grade chondrosarcoma and enchondroma is not possible on the basis of cytology alone and clinical and radiological correlation is mandatory.

The case diagnosed as giant cell tumour on cytology showed very few scattered haemosiderin laden macrophages apart from giant cells and clusters of stromal cells. These macrophages were missed. On histopathology a diagnosis of aneurysmal bone cyst was given. Finally the case labeled as atypical lipomatous tumour showed predominantly mature lipocytes along with few binucleate cells and cells showing cytoplasmic vacuoles and nuclear scalloping. On histopathology however, multinucleate giant cells and foamy histiocytes with areas of fat necrosis was seen. Hence a diagnosis of lipoma with fat necrosis was given.

The sensitivity, specificity and diagnostic accuracy in the present study is comparable with the studies conducted by Maitra et al (2000)[4]and Khalbuss et al (2010)[5]. Both of these studies have included soft tissue as well as bone tumours in their studies.

Conclusions

The present study concluded that FNA is fairly reliable for correct preoperative diagnosis and management of mesenchymal tumours. However, sampling from multiple sites and adequate clinicoradiological correlation is advised in fatty and spindle cell tumours. In cases of malignant round cell tumors use of ancillary techniques like immunocytochemistry is essential to arrive at a definite diagnosis. Expert radiological opinion is advised in cases of cartilaginous tumours to confirm/rule out low grade sarcoma on cytology.

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