Fine Needle Aspiration Cytology of Mesenchymal Tumours

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Abstract

Introduction: FNA of musculoskeletal 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 mesenchymal 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

Mesenchymal tissue refers to the part of the embryonic mesoderm from which connective tissue, bone, cartilage and circulatory and lymphatic systems develop¹.². 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 musculoskeletal 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 documented³. Finally compared to all other
diagnostic techniques, FNA is relatively inexpensive. 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. 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.

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 unequivocally 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 mesenchymal 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%).
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%).

| 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**      |

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 subtyping 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.

**Table 3 Prevalence of benign 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 benign soft tissue tumour found in the study was Lipoma (71.29%) followed by neural tumours (5.04%).

**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 commonly encountered malignant bone tumour in the 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 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 subtyping 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       | Fibromatosis       | Fibrosarcoma        |
| False       | Lipoma             | Dedifferentiated liposarcoma |
| False       | Benign myxoid spindle cell tumour | Myxofibrosarcoma |
| False       | Osteochondroma     | Chondrosarcoma      |
| False       | Giant cell tumour of bone | Aneurysmal Bone cyst |
| False       | 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 malignant 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 Bezabih⁶, 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 were not represented in the smears. Hence aspirations from multiple sites are recommended.

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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