Research Article

Fine Needle Aspiration Cytology as a Primary Diagnostic Modality in Evaluation of Mesenchymal Lesions


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Abstract

Since mesenchymal lesions (bone and soft tissue) are heterozygous and classified on histogenetic basis, it is difficult to cytologically categorize and subtype them into specific entities. Nevertheless, the necessity for determining at least the general category of these neoplasms as benign or malignant arises since, the management of these mesenchymal neoplasms involves definitive and even radical surgery. To meet this requirement, a study was undertaken by adapting Fine Needle Aspiration Cytology (FNAC) as a primary modality for diagnosis of mesenchymal lesions. 502 FNAC smears of mesenchymal lesions were reviewed to assess if FNAC was an appropriate tool for primary evaluation of mesenchymal lesions.

After excluding typical lipomas, fibrolipomas and smears with inadequate material from the study, the remaining 127 cases were taken up for the study. Histopathological correlation was available in 113 cases and only these cases were considered for calculation of various statistical indices. 89 cases were cytodiagnosed as benign, 5 cases as ‘suspicious of malignancy’ and 19 cases as malignant. The diagnostic accuracy rate was 92.2%, accounting for sensitivity and specificity of 83.3% and 95.51% respectively.

Keywords: Benign, FNAC, Malignant, Mesenchymal lesions, Primary diagnosis.

Abbreviations: DFSP: Dermatofibrosarcoma protuberans, BFH: Benign fibrous histiocytoma, IHC: Immunohistochemistry, FNAC: Fine needle aspiration cytology, MPNST: Malignant peripheral nerve sheath tumor.

Introduction

The diagnostic efficacy of FNAC in identifying recurrences and metastasis in mesenchymal lesions is undeniable. The use of FNAC in primary diagnosis of mesenchymal lesions, especially of the malignant category, is still open to a lot of scepticism among pathologists and clinicians. As the management of most of these lesions involves definitive and sometimes radical surgery, the necessity
arises for determining the category of the neoplasms as basically benign or malignant. If not the specific diagnosis, it becomes imperative for the surgeon to be aware of the primary diagnosis of mesenchymal lesion prior to surgery as basically benign or malignant, as it helps in subsequent patient management. Sensing this necessity, the present study is undertaken to determine the usefulness, limitations and diagnostic accuracy of FNAC in primary evaluation of mesenchymal lesions. FNAC as a pre-operative diagnostic technique is definitely an attractive alternative to open biopsy, since it is relatively inexpensive, non-invasive and does not require hospitalization, besides providing the clinician and patient with rapid preliminary diagnosis, allowing them to consider management decisions during the first hospital visit, without losing out on the precious time factor in diagnosis.

Materials and Methods

In this study, 502 patients who underwent FNAC for mesenchymal lesions during a period 5 years from 2007 to 2011 were reviewed. The cytology smears were obtained by standard FNAC procedure using 22-24 gauge needle, under aseptic precautions. The aspirates thus obtained were immediately fixed in 95% ethanol for subsequent staining by Papanicolaou method.

Amongst 502 cases, 256 cases of typical lipomas, 77 cases of fibrolipomas and 42 cases of cytological smears with inadequate material were excluded from the study. Of the remaining 127 cases, histological correlation was available in 113 cases and only these cases were taken up, for calculation of various statistical indices.

FNAC diagnosis were stratified into three general categories as benign, malignant and suspicious of malignancy. The last subset included those cases where the differential diagnosis included at least one malignant lesion, but specific categorization as benign/malignant was not possible. Since FNAC is a screening test with a relatively high sensitivity for the diagnosis of malignancy, the cases under the category of 'suspicious of malignancy' were considered in the category of malignant lesions for statistical analysis.

After reviewing the cytology smears and histopathology sections independently, cytohistological correlation was done.

Special Stains: Per-iodic acid Schiff (PAS) and Phosphotungstic acid hematoxylin (PTAH) were done in cases with histopathological diagnosis of Ewing’s sarcoma and Rhabdomyosarcoma.

IHC study was undertaken in 3 cases for confirmation of diagnosis to facilitate appropriate patient management.

Observations

Out of the 113 cases in which histopathological correlation was available, 89 (78.76%) cases were diagnosed as benign, 5(4.42%) as suspicious of malignancy and 19(16.81%) as malignant lesions (Table 1).The benign cases which correlated on histology were neurofibroma (38 cases), benign fibrous histiocytoma (8 cases), schwannoma (8 cases), benign spindle cell tumor (6 cases), neurofibrolipoma (5 cases), fibromatosis (5 cases), pleomorphic lipoma(3 cases), fibroma (3 cases), nodular fasciitis (2 cases), benign smooth muscle tumor (2 cases of leiomyoma), giant cell tumor of tendon sheath (2 cases), benign vascular tumor (2 cases) and xanthofibroma (1 case). The malignant cases included 4 cases of liposarcoma, 3 cases of malignant fibrous histiocytoma, 2 cases each of alveolar rhabdomyosarcoma, spindle cell sarcoma, pleomorphic sarcoma and myxoid sarcoma and 1 case each of osteosarcoma, small round cell sarcoma and epithelioid/polygonal cell sarcoma.
Table 1: Distribution of Lesions (Cytological)

<table>
<thead>
<tr>
<th>Lesions</th>
<th>No. of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>89</td>
<td>78.76%</td>
</tr>
<tr>
<td>Suspicious of malignancy</td>
<td>05</td>
<td>04.42%</td>
</tr>
<tr>
<td>Malignant</td>
<td>19</td>
<td>16.81%</td>
</tr>
</tbody>
</table>

Of the 89 cytologically benign cases, 85 (95.51%) correlated on histology. 4 (4.49%) cases which showed cytohistologic discordance included one case each of MPNST, synovial sarcoma, well-differentiated liposarcoma and low-grade fibrosarcoma. 18 of the 19 cases with cytodiagnosis of malignancy were subsequently confirmed as malignant on histopathology.

One false positive case of benign fibrous histiocytoma was cytologically diagnosed as DFSP (Table 2 & 3).

Table 2: Cytohistological Correlation

<table>
<thead>
<tr>
<th>FNAC Diagnosis</th>
<th>Histopathology Diagnosis</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>Benign</td>
<td>85</td>
</tr>
<tr>
<td>Benign</td>
<td>Malignant</td>
<td>04</td>
</tr>
<tr>
<td>Malignant</td>
<td>Malignant</td>
<td>18</td>
</tr>
<tr>
<td>Malignant</td>
<td>Benign</td>
<td>01</td>
</tr>
<tr>
<td>Suspicious of Malignancy</td>
<td>Benign</td>
<td>03</td>
</tr>
<tr>
<td>Suspicious of Malignancy</td>
<td>Malignant</td>
<td>02</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>113</td>
</tr>
</tbody>
</table>

Table 3: Summary of Cases with Cytohistologic Discordance

<table>
<thead>
<tr>
<th>FNAC DIAGNOSIS</th>
<th>HISTOLOGICAL DIAGNOSIS</th>
<th>NO. OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign tumors diagnosed as malignant (n=1)</td>
<td>Dermatofibrosarcoma protuberans</td>
<td>Benign fibrous histiocytoma</td>
</tr>
<tr>
<td>Malignant tumors diagnosed as benign (n=4)</td>
<td>schwannoma</td>
<td>Malignant peripheral nerve sheath tumor</td>
</tr>
<tr>
<td>Pleomorphic lipoma</td>
<td>Well differentiated liposarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Benign fibrous histiocytoma</td>
<td>Synovial sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Nodular fascitis</td>
<td>Low grade fibrosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Tumors reported as suspicious of malignancy cytologically (n=5)</td>
<td>Suspicious of malignancy</td>
<td>Benign fibrous histiocytoma</td>
</tr>
<tr>
<td></td>
<td>Ancient schwannoma</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Desmoid fibromatosis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>liposarcoma</td>
<td>2</td>
</tr>
</tbody>
</table>

As FNAC is used as a screening test with a relatively high sensitivity for malignancy, cases diagnosed as ‘suspicious of malignancy’ were included under the malignant lesions for statistical analysis.

Of the 5 cases diagnosed cytologically as ‘suspicious of malignancy’, 2 proved to be malignant (liposarcoma) and 3 benign (one case each of benign fibrous histiocytoma, ancient schwannoma and desmoid fibromatosis on histopathology).

Discussion

Neurofibroma, Benign fibrous histiocytoma, and Schwannoma were the most common benign tumors in this study similar to the study by Gonzalez-Campora R et al in 1992. Definite cytodiagnosis and subtyping was possible in well-
differentiated malignant lesions with distinct cytological features. In this category of well-differentiated malignancies, liposarcoma was the most common entity. The other lesions in this category comprised of Malignant fibrous histiocytoma, Alveolar rhabdomyosarcoma and Osteogenic sarcoma.

Malignant lesions in which cytological features did not permit definite subtyping were grouped under broader categories as ‘Spindle cell sarcomas’ (Fig 1), Small round cell sarcomas (Fig 2), Epithelioid / polygonal cell sarcomas, Pleomorphic cell sarcomas (Fig 3) and Myxoid sarcomas (Fig 4).
The subsequent histopathological examination and special stain (PAS) confirmed cytologically diagnosed Small round cell tumors as Ewing’s sarcoma/PNET. The Spindle cell tumors were confirmed as fibrosarcomas on histopathology. Epitheloid /polygonal cell sarcoma was confirmed as Granular cell tumor on histopathology. The Pleomorphic cell sarcomas were confirmed on histopathology as Pleomorphic rhabdomyosarcoma or Pleomorphic liposarcoma. The Myxoid sarcomas were confirmed as Myxoid liposarcoma or Fibromyxoid sarcoma.

IHC study of three cases confirmed the diagnosis of Malignant fibrous histiocytoma, Synovial sarcoma and Low-grade fibrosarcoma.

FNAC has several advantages over traditional open incisional biopsy for diagnosis and management of malignant neoplasms including little or no risk of tumor cell contamination of the needle track, less risk of morbidity and mortality, ease of performance and rapid turnaround time (Maitra A et al in 2000, Gonzalez-Camora R in 2000). FNA is less expensive, less invasive, can sample a lesion more extensively, and provides quicker results compared with needle core biopsy (Vincent Y Ng et al in 2010).

However, FNAC has certain limitations in the diagnosis of some reactive and benign connective tissue lesions with treacherous pleomorphism and ironically, in some sarcomas with monotonous appearance (Hadju S I and Melamed M R in 1984). The sensitivity and specificity of FNAC in correctly classifying primary mesenchymal lesions as malignant were 83% and 95% respectively in the present study, comparing favourably with the observations in other studies (Table 4).

Table 4: Comparative Statistical Analysis of Various Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beg et al</td>
<td>98%</td>
<td>96.5%</td>
</tr>
<tr>
<td>Bezabih M</td>
<td>88.5%</td>
<td>81.5%</td>
</tr>
<tr>
<td>Dey P et al</td>
<td>91.5%</td>
<td>92.5%</td>
</tr>
<tr>
<td>Khalbuss W E et al</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>Layfield et al</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Maitra et al</td>
<td>89%</td>
<td>87%</td>
</tr>
<tr>
<td>Nagira K et al</td>
<td>92%</td>
<td>97%</td>
</tr>
<tr>
<td>Vincent Y Ng et al</td>
<td>88.9%</td>
<td>84.4%</td>
</tr>
<tr>
<td>Wakely PE Jr, Kinsel Jr</td>
<td>100%</td>
<td>97%</td>
</tr>
<tr>
<td>Present study</td>
<td>83.3%</td>
<td>95.5%</td>
</tr>
</tbody>
</table>

The role of FNAC in differentiating a benign soft tissue lesion from a sarcoma is commendable (Kulkami D R et al in 2002, Rekhi B et al in 2007), an opinion which is in concordance with our observation. According to Wakely PE Jr, Kneidsl JS in 2000, FNA cytopathology was capable of specifically subtyping a large percentage of...
primary and metastatic soft tissue tumors if cellular material either in the form of a
cell block or flow cytometry is obtained in
addition to cell smears. Dey P et al in 2004
found that FNAC was very useful in
distinguishing benign from malignant soft
tissue tumors. However, it was not so
effective in exact categorization of tumors.
In our study, specific subtyping of
malignant lesions on cytology posed the
greatest challenge. The difficulties in
interpretation were probably due to
overlap in the cytologic features of these
entities. Well-differentiated malignant
lesions with distinct cytological features
could be diagnosed and specifically
subtyped with ease. One of the
liposarcomas in the present study was
located in the breast, an unusual site.

Bezabih et al in 2001 categorized
malignant lesions in which definite
subtyping was not possible on cytology
under 5 broader subgroups as, Small
round cell sarcomas, Spindle cell
sarcomas, Epithelioid/polygonal cell
sarcomas, Pleomorphic cell sarcomas
and Myxoid sarcomas according to
predominant cytomorphologic features.
Similar categorization was done in present
study to facilitate patient management.

In our study, cytological smears from`
round cell sarcomas 'were highly cellular
and were composed of discohesive tumor
cells and occasional small cellular clusters,
whereas, hypercellularity was a dominant
feature in 'spindle cell sarcoma' group. The
tumor cells tended to be discohesive and
individually dispersed with a few scattered
variably sized tumor cell clusters. In
contrast to round cell sarcomas, cytological
atypia was observed more often in spindle
cell sarcomas. Pleomorphism was marked
in the Pleomorphic cell sarcomas whereas
myxoid sarcomas showed focal myxoid
areas amidst tumor cells.

The four false negatives encountered in the
study comprised one case each of MPNST,
Well-differentiated Liposarcoma, Synovial
sarcoma and Low-grade fibrosarcoma. The
probable reasons being:

1) Low-grade MPNST may show spindle
cells with bland wavy nuclei, thus
mimicking a schwannoma as in our
case.

2) Well-differentiated liposarcoma may
be misdiagnosed as pleomorphic
lipoma due to the inability to
demonstrate lipoblasts with certainty
on cytological smears as in our case
and the presence of floret cells in
both.(Fig 4 and 5).

3) Synovial sarcoma may be diagnosed as
Benign fibrous histiocytoma due to
extreme uniformity of cells, lack of
nuclear pleomorphism , ovoid to
slightly round tumor cells with scant
tapering cytoplasm and absence of
epithelial cells as in the present case.

4) Low-grade fibrosarcoma may be
diagnosed as nodular fasciitis due to
paucity of mitotic figures and
pleomorphic nuclear characters in
nodular fasciitis which may mimic
Low-grade fibrosarcoma (Ackerman M
as in the present case.
Of the 5 cases reported as ‘suspicious of malignancy’, 3 were spindle cell lesions which were confirmed on histopathology as one case each of BFH, Ancient Schwanomma and Desmoid fibromatosis. On cytologic review, the probable diagnostic pitfalls in these cases were:

- High cellularity with occasional nuclear atypia in BFH.
- Presence of large atypical cells with occasional atypical mitosis in Ancient schwannoma.
- High cellularity with strands and clusters of cells with moderate anisokaryosis in Desmoid fibromatosis.

The other two cases reported under the ‘suspicious of malignancy’ category were subsequently diagnosed as Well-differentiated liposarcoma on histopathology.

The only false positive under the malignant category in the study was, a case of BFH diagnosed cytologically as DFSP, since they may have cytological similarities like high cellularity, presence of nuclear atypia and histiocytes.

In conclusion, FNAC is a valuable tool in the diagnosis of soft tissue lesions as it does not present major complications and permits a swift preliminary diagnosis in a large number of cases besides being a simple, inexpensive and rapid diagnostic modality. Given the high rates of accuracy, sensitivity and specificity that it offers, coupled with these additional advantages and minimal risks, FNAC represents a viable alternative to open biopsy for the primary diagnosis of soft tissue lesions at initial presentation as it facilitates early decisions and appropriate patient management.

References


