Role of Fine Needle Aspiration Cytology in the Initial Diagnosis of Superficial Soft Tissue Lesions

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ABSTRACT

Introduction: The diagnosis with exact categorization of superficial true soft tissue lesions has been mired in controversy. With time FNAC has proven a useful tool for the diagnosis of soft tissue lesions for primary workup and planning treatment options of soft tissue lesions.

Material and Methods: A prospective 1 year study was conducted to evaluate the efficacy of FNAC as a primary initial investigation for the diagnosis of superficial soft tissue lesions.

Result: The sensitivity and specificity for benign lesions was 100% and 93% respectively whereas malignant soft tissue lesions showed sensitivity of 94% and specificity was only 50%. FNAC is highly reliable as an initial diagnostic tool for the diagnostic workup of superficial soft tissue lesions. A definite cytological diagnosis must be based on precise correlation of the cytological findings and results of ancillary studies with the clinical and radiographic data. To increase the specificity of malignant lesions, ancillary techniques like immunocytochemistry, FISH are recommended and can only be dealt at a specialized sarcoma center.

Conclusion: FNAC in the primary work-up of soft tissue lesions has definite several major advantages that certainly outweigh its limitations

Keywords: Cytology, Soft Tissue, Lipomas, Malignant Fibrous Histocytoma, Hemangioma, Malignant.

INTRODUCTION

The true frequency of soft tissue lesions is difficult to estimate, as most of non-neoplastic and benign lesions are not removed or not subjected to histopathological examination. A conservative estimate is that benign tumors outnumber their malignant counterparts by ratio of about 100: 1 in hospital population and their annual incidence is approximately 300 per 1,00,000 population. Though a high degree of accuracy in distinguishing malignant from benign soft tissue tumors has been reported, cytological methods have been less successful in establishing a histological diagnosis and grading of soft tissue sarcomas. The accuracy of FNAC in distinguishing benign from malignant soft tissue neoplasm and sarcoma from other malignancies has been shown to be comparable to that of surgical biopsies, while its accuracy in establishing a specific subtype diagnosis has been inferior to surgical biopsies.

However, failure in classifying the exact histological subtype of a soft tissue sarcoma does not always mean that correct therapy cannot be initiated as surgical intervention is similar for almost all adult sarcomas.[1]

A reliable initial diagnosis of sarcoma with exclusion of metastatic carcinoma, melanoma or lymphoma is often sufficient for the planning of surgical treatment.

In addition different treatment options for pseudosarcomatous lesions such as nodular fascitis, proliferative fascitis, proliferative myositis, and pseudomalignant myositis ossificans as well as for some low grade, locally aggressive but benign soft tissue tumors such as desmoid fibromatosis frequently require an exact histological diagnosis.

Ancillary techniques are used extensively today as diagnostic help in morphological diagnosis of soft tissue lesions. Essentially the same ancillary techniques are used for cytological as for histopathological diagnosis. The most commonly used is Immunocytochemistry. In addition cytogenetic and molecular biological techniques as well as electron microscopy play an important role. Techniques such as polymerase chain reaction (PCR) and fluorescence in situ hybridization have been proved to be suitable for fine needle.[1,2]

The technique for FNA of soft tissue tumors is the same as for other types of lesions. A good aspirate is essential for accurate diagnosis. Frequent problems occurring can be due to missing of the lesion altogether by aspirator and reactive changes mimicking sarcomas. In addition representative diagnostic areas may be difficult to aspirate from cystic, necrotic or hemorrhagic masses. With few exceptions, soft tissue tumors are heterogeneous in their composition. Besides neoplastic cells, they also contain an admixture of cells of local host tissue which can lead to errors of interpretation. The capacity of connective tissues to indulge in exuberant reactive and reparative growth is also remarkable. Thus many non-neoplastic lesions of soft tissues may mimic neoplastic conditions. Therefore, a thorough familiarity with the histological diversities of soft tissue lesions and experience with interpretation of different cell types in cytology smears along with awareness of fallacies of FNAC are required to achieve high diagnostic accuracy in these tumors. However, due to absence of tissue architecture

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in FNAC smears, it may be very difficult to categorize these lesions exactly by FNAC.[3]

Now, FNAC is valuable in the diagnosis of soft tissues tumors with sensitivity, specificity and positive predictive value 91.5%, 92.5% and 95.5% respectively.[4] A combination with ancillary techniques and a multidisciplinary approach is proving invaluable in the diagnosis/evaluation of soft tissue tumors.[5]

The benign soft tissue tumors comprise of lipomas, benign fibrous proliferations (fibroma, fibroepithelial polyp, nodular fasciitis, dermatofibroma, benign fibrous histiocytoma) leiomyomas, rhabdomyomas, haemangiomas, schwannomas, neurofibromas, giant cell tumor of tendon sheath.Among the malignant soft tissue tumors, malignant fibrous histiocytoma is the most common soft tissue sarcoma of late adult life followed by liposarcoma. Other common soft tissue sarcomas include rhabdomyosarcomas, leiomyosarcomas, synovial-sarcomas, and haemangiopericytomas affecting individuals in late adult life except rhabdomyosarcoma, which is common in children less than 15 years of age. The incidence rate, however, varies in different age groups and depends on the definition of soft tissue sarcomas and the types of neoplasm's that are included among these tumors.

Soft tissue sarcomas can occur anywhere in the body. Approximately 40% of soft tissue sarcomas occur in lower extremity, 30% in trunk/retroperitoneum, 20% in upper extremity and 10% in head and neck.

MATERIAL AND METHODS

The study was conducted on patients who presented to the Cytology section of the Department of Pathology, Govt. Medical College, Srinagar with superficial soft tissue masses over a period of one year from 01-12-2014 to 30-11-2015. Lesions of breast, lymph node, salivary glands and thyroid were excluded from the study. Franzen's type aspiration handle, 20cc syringes, were used for aspiration.

MGG and PAP stains were mainly used for staining the slides. The biopsies were fixed in 10% formalin and processed as per standard histopathological techniques.

STATISTICAL ANALYSIS

The collected data was processed through Microsoft Excel and tabulated in the form of tables and graphs.

RESULTS

A total of 2250 patients presented to the cytology section in the period. Amongst them 106 patients presented for FNAC of superficial soft tissue masses. After excluding lymph nodes, breast, thyroid and salivary gland lesions, Franzen aspiration technique was applied. Smears were stained by May Grunwald Giemsa and Papinicalaou stains mainly.6 cases were not considered for various reasons viz. insufficient scanty aspirate, lack of clinical data, lack of histological correlation The diagnosis was arrived after studying the fine needle aspiration smears. Subsequently confirmation of the diagnosis was done by histopathological examination of all the malignant lesions. Special stains e.g. Von Gieson, Masson Trichome along with immunohistochemistry was

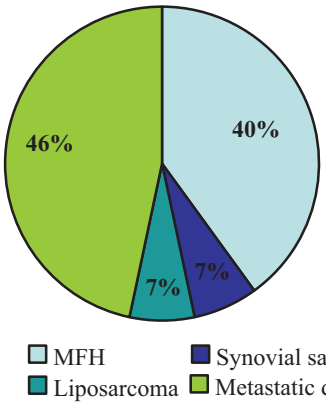

Figure-1: Percentages of Malignant Soft Tissue Lesions

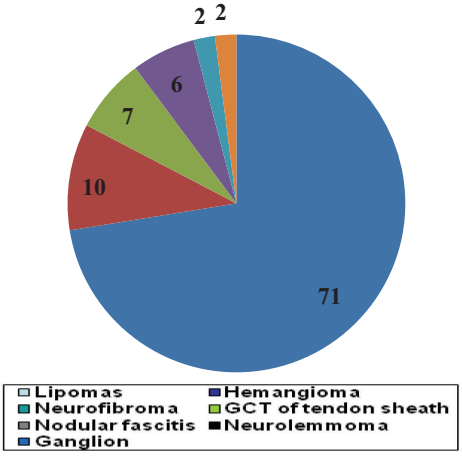

Figure-2: Percentages Of benign Soft Tissue Lesions

used in two cases of sarcomas.

The remaining 100 cases comprised of 85% benign lesions and 15% were found to be malignant. The 85 benign superficial soft tissue were mostly comprising of lipomas 60 cases (71%of benign cases) followed by Hemangiomas 8 cases (10%) and Neurofibromas 6 cases (7%). The other benign lesions diagnosed were Giant Cell Tumour of Tendon Sheath 5 cases (6%), Nodular fascitis 2 cases (2%), Neurilemmoma 2 cases (2%), ganglion cyst comprising of 2 cases (2%).

The commonest superficial soft tissue malignant lesion was found to be Malignant Fibrous Histiocytoma, 6 out of 15 malignant cases (40%). Metastatic deposits were found in 7 cases (46%). One case of liposarcoma and synovial sarcoma (7%) were found during the duration of the study. The diagnosis of the sarcomas was done on cytology and was confirmed by histopathological examination.

Lipomas constituted the commonest superficial soft tissue lesion. The age group of lipomas ranged from 11 yrs to 70 years. Males comprised 34 cases (56%) and females constituted 26 cases. (44%). The age group ranged from 11-70 years. Thorax was the commonest site involved in our study (31%) followed by extremities (28%) and thorax. (23%) Head and neck region accounted for least number of cases (16%). Five cases were categorized as spindle cell lipomas. Three cases were categorized as fibrolipomas in histopathology which were diagnosed as lipomas on

cytology. This could be because of the fibrous component of the lesion.

Hemangiomas comprised the next commonest superficial soft tissue lesion diagnosed on fine needle aspiration cytology. The diagnosis of the hemangiomas was confirmed on histopathology. 6 neurofibromas (7%) were observed in the study amongst the benign lesions. Males were affected more 66% (4 cases) compared with females 34% (2 cases).

Five cases (6%) of Giant Cell Tumor of tendon sheath were observed during this study. The cases were seen in the age group of 19-65 years. Cytological findings on smears were rather characteristic and included a mixture of oval or polygonal mono-nuclear cells showing vaculation and/or pigment deposition along with a population of multinucleated giant cells. The diagnosis was arrived at on cytology and histopathology done for confirmation purposes only. Careful attention was paid to cytological findings and correlation with clinical and radiographic data made which ruled out other giant cell-lesions viz GCT of bone, aneurysmal bone cyst and granulomatous inflammation.

15 cases were observed to be malignant lesions out of 100 superficial soft tissue lesions. The commonest malignant soft tissue lesion was found to be Malignant Fibrous Histiocytoma comprising of 6 cases (40%).Males were affected more as compared to females. Cellularity was variable with 66% having high cellularity and 34% having moderate cellularity. Bloody background occurred in 4 (66%) cases. Inflammation was minimal in most cases (83%). A stromal component was found in three cases (50%) with two cases having myxoid stroma.Nuclei displayed malignant characteristics with anisonucleosis, nucleomegaly increased N/C ratio, notched nuclear membranes and abnormal chromatin distribution. Nucleoli were variably present and were either single or multiple.

One false positive case was seen in a 17 year female with lesion over lower extremity. It was subsequently found to be osteogenic sarcoma on histopathological examination.

One case of synovial sarcoma was observed in a forty six year old male and the lesion was located on forearm. Smears were highly cellular comprising of mixture of tissue fragments and dispersed cells. The cells were small to medium sized with rounded nuclei and finely granular bland chromatin. Nucleoli were small and inconspicuous.

A single case (7%) of liposarcoma was observed in a 52 year old male affecting the upper extremity. Smears studied showed network of capillary vessels along with atypical lipoblasts. Lipoblasts observed were mostly univacoulated with multivacoulated at places. Scalloped nuclei were also identified. The diagnosis of pleomorphic liposarcoma was arrived at on histopathological examination.

Seven cases of metastatic deposits were observed in the study. Four cases (58%) were observed in males and three cases (42%) were observed in females. Deposits of squamous cell carcinoma were observed in 4 cases whereas deposits of adenocarcinoma were seen in 2 patients. Deposits of malignant melanoma were observed in anterior axillary fold of 28 years old female.3 patients were known cases of squamous cell carcinoma on Radiotherapy, whereas one patient presented with neck deposits of squamous cell carcinoma. Both patients with deposits of adenocarcinoma had known primary adenocarcinoma of lung. Similarly, deposits of malignant melanoma were observed in a known case of Malignant Melanoma.

DISCUSSION

The usefulness of FNAC in the diagnosis of soft tissue tumors has been a matter of controversy and this very fact became the aim of this study so as to assess the importance of fine needle aspiration cytology. Management of the lesions requires positive identification of the benign or malignant nature of a process and the degree of differentiation of sarcomas. A tissue diagnosis was and is still considered necessary for exact categorization and sub typing of the lesion in some cases. The aim of this study was to highlight the importance of FNA as an initial diagnostic tool for the diagnosis of superficial soft tissue lesions. Numbers of studies that have been done for assessing the efficacy of fine needle aspiration for soft tissue lesions have show high sensitivity and specificity for the diagnosis. Layfield et al, in their study on soft tissue lesion had sensitivity and specificity of 95% respectively for the diagnosis of soft tissue lesions.[6] False positive and false negative diagnosis was recorded at 2%. P Dey et al in their study had sensitivity and specificity of 91.5% and 92.5% respectively. 46.8% lesions were correctly categorized on FNAC. Amongst benign lesions 72% could be correctly subtyped on cytology alongwith 83% of correct subtyping of malignant lesions.[4] Keiko et al, in their retrospective study had a sensitivity and specificity of 92% and 97% respectively for the diagnosis of malignant lesion.[7]

In our study the sensitivity and specificity for the diagnosis of superficial soft tissue lesions was 100% and 93% for benign lesions. For malignant lesions the sensitivity and specificity was found to be 94% and 50%. One false positive and one false negative case were observed amongst malignant lesions.

Lipomas were commonest lesion comprising 60 cases (60%). Lipomas comprised of 40% of benign lesions in study of Dey P et al.[4] Layfield et al found 78% lipomas in their study.[3] These findings are in agreement with those studies where lipomas comprised the commonest soft tissue lesion.

Hemagiomas comprised of 8 cases (10%) of benign superficial soft tissue lesions. Hemangioma comprised 20% of benign superficial soft tissue lesions in study done by Keiko Nagira et al.[7] Our findings are in concordance with the study of Keiko Nagira et al.[7] As FNA yielded only hemorrhagic material and few spindle cells, histopathological examination is required for unusual, very large lesions. In study done by Keiko Nagira et al[7], only blood was obtained from hemangiomas and was judged to be cytologically non-diagnostic. MRI of hemangiomas provided helpful information for diagnosis in his study.

Six neurofibromas were observed in this study and are in concordance with studies in involvement of neurofibromas

equally in both the sexes and mostly seen in extremities.[8] Five cases (6%) of Giant Cell Tumor of tendon sheath (GCTTS) were observed during the study. GCTTS comprised 8 cases (8/137) (7%) in study done by Keiko Nagira et al.[7] The findings are in concordance with this study. The diagnostic accuracy was 100% and in concordance with other studies Keiko Nagira et al.[7]

Two cases of nodular fascitis were observed in the study. Nodular fascitis smears displayed cellular material comprising of plump, spindle and stellate cells with large reactive, often eccentric nuclei showing mild hyperchromasia and one to two nucleoli. As the cytomorphology is fairly characteristic diagnosis can be made on cytological smears. The findings are similar to that of Akerman M et al, and diagnostic accuracy was 100%.[9] In cases of nodular fascitis also adequate clinical information was found to be valuable. Nodular fascitis comprises the most common pseudosarcomatous proliferative lesion of the soft tissue.[10]

Two cases seen in the study of Neurlilemoma were observed in 35 years old and a 22 yr old female with swelling in abdominal wall and upper extremity respectively. The smears comprised of spindle cells with wavy nuclei embedded in a fibrillar, ocassionaly collagenous and/or myxoid matrix. Nuclear palisading was also observed.

Diagnostic difficulty in diagnosing neurilemmoma on cytology is due to high frequency of poor cellularity or lack of cells, particularly from cystic degenerated lesions.[11] Also, the similarities between FNA aspirates from neurilemomas and their malignant counterpart MPNST, or other soft tissue spindle cell neoplasms may, however, occasionally cause considerable diagnostic problems.[1,2] The most common differential diagnosis includes solitary fibrous tumour, leiomyosarcoma, MPNST, monophasic synovial sarcoma, intramuscular myxoma, perineuroma, low grade fibromyxoid sarcoma and spindle cell lipoma.[12]

Two cases of ganglion cysts were observed during the study. One case was found in male and other in female. The aspirated material comprised of thick jelly like glassy material. The diagnosis can even be made from this characteristic appearance smears showed drying artifacts of varying shapes. The distinction can be easily made from other soft tissue lesions viz juxtraarticular myxoid lesions, intramuscular myxoma.[13]

Amongst the malignant soft tissue tumors, the commonest lesion that was Malignant Fibrous Histiocytoma (MFH). These comprised of six cases in the study. The age group ranged from 21-70 years with males affected more (4 out of 6) in this study. MFH is accepted as most common soft tissue sarcoma in adults.[14]

The false negative case that was diagnosed as Malignant Melanoma comprised of pleomorphic round to oval and spindle cells with intracytoplasmic pigment and many binucleated cells. Malignant Melanoma is one of entities that can be confused with sarcoma.[1] One false positive case of MFH was seen in a 17 years old female with lesion in the knee region. X Rays revealed minimal bone involvement. The diagnosis of osteogenic sarcoma was made on the histopathological examination of the lesion. The differential diagnosis of MFH includes any pleomorphic mesenchymal tumour, and pleomorphic non-mesenchymal tumour such as anaplastic carcinoma and malignant melanoma. If lymph node metastasis is involved then anaplastic/ large cell lymphoma and lymphocyte depleted Hodgkin's disease should be considered, particularly because these two entities can have MGC's and scant lymphoglandular bodies. The distinction from MFH typically requires clinical and radiographic correlation with cytopathology as well as ancillary testing.[14]

Amongst mesenchymal tumours, classical leiomyosarcoma has to be included in the differential diagnosis of pleomorphic MFH as cellular pleomorphism is a common feature of both leiomyosarcoma and MFH. Immunohistochemistry using muscular markers helps to differentiate between these tumours.[15]

FNA has a definitive role in documenting the presence of malignancy and in determining the mesenchymal nature of the lesion. It however, may have a low specificity for identifying the histological subtype of sarcoma.[16] In study by Hal E Palmer et al sarcoma was recognized in 59 of 64 adequate cases (92%) with available histology, however the specific histopathological subtype was identified in only 9 cases (14%). [16] These findings are in concordance to this study.

One case of liposarcoma was observed in a 55 year old male. The lesion was located on the forearm. The smears comprised of polymorphous population comprising of round to spindle cells with occasional lipoblasts. The diagnosis of liposarcoma was made on cytology and histologic examination subtyped it as pleomorphic liposarcoma.

As it was located in extremity, atypical lipoma was included in the differential diagnosis. The distinction of well differentiated liposarcoma from atypical lipoma by cytological methods is presumptuous as both entities share similar morphological features. Another important differential diagnostic problem is hibernoma and spindle cell lipoma. Hibernoma may have cytological characteristics that overlap with well differentiated liposarcoma. Dedifferentiated liposarcoma without lipoblasts or pleomorphic liposarcoma on cytology smears may be misdiagnosed as other high grade sarcoma especially pleomorphic MFH.

One case of synovial sarcoma was observed in a forty six year old male with lesion on forearm. The smears are characteristically highly cellular with irregular papillary configurations. The synovial cell sarcoma was correctly identified in this case due to presence of characteristic oval to plump spindle cells with pale chromatin and inconspicuous nucleoli. P.Dey, Malik et al observed six cases of synovial sarcoma five of which were correctly categorized on FNAC which presented with similar cytological features.[4] The subgrouping of soft tissue lesions by cytomorphological features may be helpful in formulating a differentiated.[17,18]

Exact histological sub classification is not always necessary for therapy planning for adult soft tissue sarcomas. A reliable malignant diagnosis of sarcoma combined with radiographic

data and clinical staging is often sufficient when treatment includes primarily surgery. Exact histological diagnosis is required only for some low grade, borderline or locally aggressive but benign soft tissue lesions and some small cell sarcomas of pediatric age group.[19]

The histological subtyping of soft tissue tumors in FNA smears is more reliable when dealing with well differentiated tumors showing specific cytomorphological diagnostic and immunocytochemical criteria. Conversely, poorly differentiated soft tissue sarcomas can represent a difficult diagnostic group because of lack of distinctive morphological and immunocytochemical criteria. Definitive cytological diagnosis can often be obtained from FNA smears complemented by clinical data in lesions where cytological diagnostic criteria have been well characterized.[19]

If exact categorization of sarcomas is not possible on FNAC, then one can classify the tumours as

(1) **Sarcoma with spindle cell morphology** (Fibrosarcoma, MPNST, leiomyosarcoma etc)
(2) **Sarcoma with round cell morphology** (embryonal rhabdomyosarcoma, Ewing's Sarcoma)
(3) **Pleomorphic sarcoma** (pleomorphic MFH, pleomorphic liposarcoma, poorly differentiated fibrosarcoma etc)

Myxoid sarcomas present the greatest challenge in an attempt to make a diagnosis with cytological methods. These include myxoma, myxoid chondrosarcoma, chordoma, myxoid leiomyosarcoma and myxoid MFH.

Seven cases of metastatic deposits in the age group of 21-70 years were observed. Clinically, they presented as fixed, immobile swellings with known primary in all the cases. The primary comprised of malignant melanoma (1 case), Adenocarcinoma (2 cases), Squamous cell carcinoma (4cases).

The chest wall and axilla are the sites of very wide range of inflammatory and neoplastic.[20] The diagnosis can be made with confidence on cytological examination and most studies have a cytological – histological agreement of 100%. The findings are in concordance with this study.

CONCLUSION

We conclude, from our observations that FNAC is highly reliable as an initial diagnostic tool for the diagnostic workup of superficial soft tissue lesions. A definite cytological diagnosis must be based on precise correlation of the cytological findings and results of ancillary studies with the clinical and radiographic data.

To increase the specificity of malignant lesions, ancillary techniques like immunocytochemistry, FISH and DNA cytometry are recommended and can only be dealt at a specialized sarcoma center. FNAC in the primary work-up of soft tissue has definite several major advantages that certainly outweigh its limitations.

ABBREVATIONS

FNAC: Fine needle Aspiration Cytology, IHC: Immunohistochemistry, FISH: Fluorescent In-situ Hybridization, MFH: Malignant Fibrous Histiocytoma, MPNST: malignant peripheral nerve sheath tumor, GST: Giant cell tumor

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