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Original Research Article

Diagnostic Accuracy of FNAC in Soft Tissue Tumors: Experience at a Tertiary Cancer Referral Centre in India

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ABSTRACT

Background: Soft tissue tumors (STT) are very rare in general population. They are always a challenging lesion for the pathologist to diagnose due to the wide morphological overlapping and the biological heterogeneity. Role of Fine needle aspiration cytology (FNAC) as a diagnostic tool for the suspected soft tissue mass is a matter of debate due to the conflicting observations reported in the literature world-wide.
Methods: We conducted this study on 89 patients to compute the diagnostic accuracy of the FNAC procedure as compared to the gold standard technique i.e. histopathological examination of the biopsied tissue.
Results: In this study we found that malignant and benign cases constituted 67.41% and 21.34% of all the cases. Malignant cases were most common in the age-group of 20-40 years and benign cases were common in the age-group of 40-60 years. Overall, the lower extremity was the most common site of involvement by STTs, followed by trunk and upper extremity. The most commonly diagnosed tumor was spindle cell type with slight predilection for males. The accuracy rate was of 92.40% for the nature of lesion (benignancy Vs malignancy) with sensitivity, specificity of 95% and 84.21% respectively, which was statistically significant ($p<0.0001$). The cytological diagnosis of 7.50% cases was found discordant with histopathological diagnosis.
Conclusion: FNAC proved to be a good diagnostic tool for diagnosing STTs and must be always considered as complementary tool for diagnosing suspected soft tissue mass, especially in healthcare set-up that has minimal access to the advanced diagnostic procedures.

Keywords: Soft tissue tumors, FNAC, histopathology.

INTRODUCTION

Soft tissue tumors are the mesenchymal proliferations that occur in the extra-skeletal, non-epithelial tissues of the body, excluding the viscera, coverings of the brain and lympho-reticular system. [1] They are derived from mesoderm with some contribution from neuro-ectoderm. They are an uncommon entity in general population. It is difficult to predict the actual incidence of soft tissue tumors especially benign soft tissue tumors because many benign tumors like lipoma and hemangioma do not undergo biopsy. Thus, direct application of any hospital based data on general population for determining the prevalence is invalid. In general, the ratio of benign to malignant STT is about 10:1 or higher & their annual incidence is approximately 300 per 1 Lac

population. [2,3] Soft tissue sarcomas occur more commonly in males, but gender and age-related incidences vary among the histologic types. [4] There is also no proven racial variation. STT are always challenging lesion for the pathologists due to wide morphological overlapping & the biological heterogeneity, [5] though ancillary techniques like ICC, IHC and cytogenetic analysis have come to rescue. The genetic studies are not routinely used but are immensely helpful in cases with equivocal diagnosis on histo-pathological examination (HPE) & immunohistochemistry (IHC). Domanskietal [6] presented fine needle aspiration cytology (FNAC) study of 130 primary soft tissue tumors with comparative histopathology, showed the diagnostic sensitivity 98.70% and specificity of 96.20%. Similar study of FNAC of soft tissue tumor in correlation with histopathology was done by Klipatricketal. [7] Comparative study of cytologic and histologic results of soft tissue tumors by Deyetal [8] showed sensitivity and specificity of 91.50% and 92.50% respectively with no inconclusive cases. Bennert and Abdul-Karim [2] conducted a study on 117 patients and reported the lowest sensitivity of 71.20% of the FNAC procedure. The lowest specificity is reported by Barth et al [9] as 36.40% only. The role of FNAC as a diagnostic tool for the suspected soft tissue mass is a matter of debate due to the conflicting observations reported in the literature world-wide. This study is an attempt to unearth this area of conflict. In this study we compared the cytological diagnosis with histo-pathological diagnosis so as to compute the diagnostic accuracy of the FNAC procedure in primary diagnosis of a suspected soft tissue mass. The lack of proper tissue architectural changes in cytological smear further limits the utility of FNAC as a primary diagnostic procedure.

MATERIALS & METHODS

This cross-sectional study was conducted from July 2012 to Dec 2013, over a period of 18 months after seeking the consent of the ethical and scientific committee of the institution. In this study, retrospective analysis of 89 patients with primary soft tissue masses was done, irrespective of the age and sex of the individual. These patients were referred to the Department of Pathology for the primary FNA diagnosis. All the patients underwent FNAC (unaided/guided) procedure after proper work-up, which included clinical examination, radiographic & routine laboratory investigations. In all the cases, informed consent was taken & aspiration was done by an experienced cyto-pathologist. Their cytological diagnosis was correlated with histo-pathological diagnosis. IHC was used for further histologic subtyping in 24 cases. Cytomorphological grading was done into the following six categories i.e. Spindle Cell tumor, Lipomatous tumor, Pleomorphic type, Round cell type, Myxoid and Epitheloid Cell type. It was based on the recommendations of Akerman and Domanski. [10] The cytosmears with more than one component was diagnosed on the basis of predominant subtype. Aspiration was carried out with 22-gauge needle coupled with 10cc disposable syringe in case of superficial masses and a 9 cm long, 22-gauge needle in case of deep-seated masses. Neither LA nor any pre-medication was used. The aspirate was deposited on to clean glass-slides & smeared. The air-dried smears were stained with May-GrunwaldGiemsa (MGG) stain. Smears wet-fixed with 95% ethanol were stained with Papanicolaou stain. Smears were then evaluated for cytological details. FNAC being a blind procedure may have sampling error & poor cellular yield at time. [11,12] Thus applying the correct technique is as important as correct interpretation of the sample.

In the series the accuracy rate was calculated for the nature of lesion (benign

vs malignant) as follows: Cases with concordant diagnoses/ Cases included in each specific consideration. Concordant cases were those in which both cytological and histo-pathological diagnoses were coherent. Statistical analysis of the data was performed by Graph-pad software using 2x2 contingency table. The false-positive diagnoses were defined as rendering of malignant cytologic diagnoses for the benign cases (HPE/IHC confirmed). False-negative diagnoses referred to the benign cytological diagnoses which were found to be malignant case on HPE/IHC. Inadequate/ inconclusive/ unsatisfactory smears were excluded from the analysis.

RESULT

In this study, eighty-nine cases of soft tissue mass were evaluated on the basis of their cytological features for primary cytological diagnosis. Out of 89 cases, 60 were malignant, 19 were benign & rest was found to be inconclusive on cytology (Fig 1). Majority of the benign STT were in the age group of 40-60 year while the malignant cases were in the age group of 20-40 year (Fig 2).

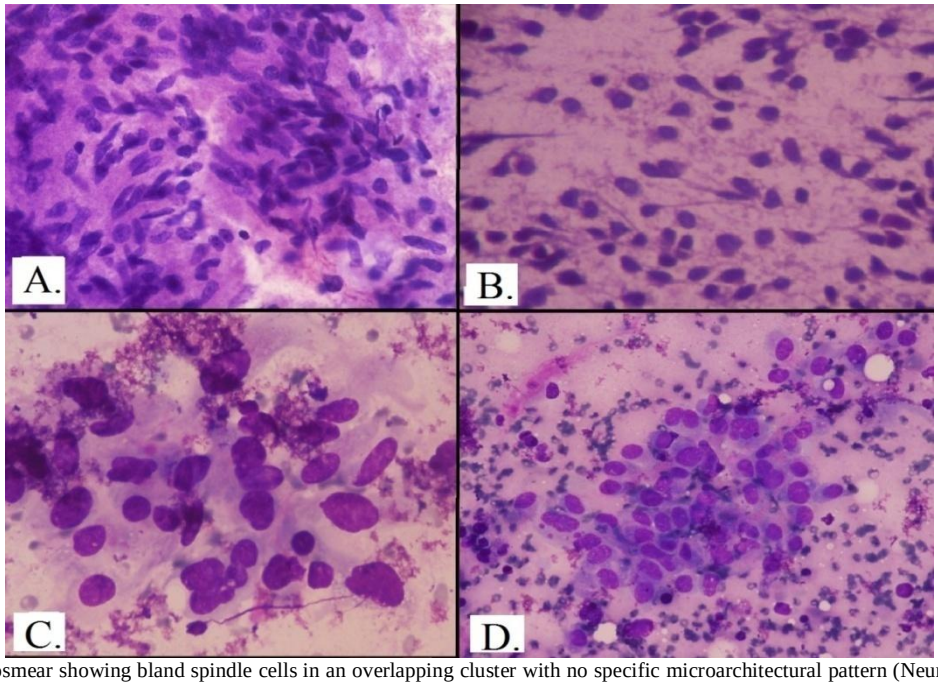

Fig 1: [A] Cytosmear showing bland spindle cells in an overlapping cluster with no specific microarchitectural pattern (Neurofibroma). [B] Dispersed population of small round cells with eccentrically placed nuclei and scanty cytoplasm (Ewings' Tumor). [C] Pleomorphic cells arranged in loosely cohesive cluster with hyperchromatic nuclei (Undifferentiated pleomorphic sarcoma). [D] Polygonal cells scattered singly and in loose clusters (Epithelioid sarcoma). MGG, 100X.

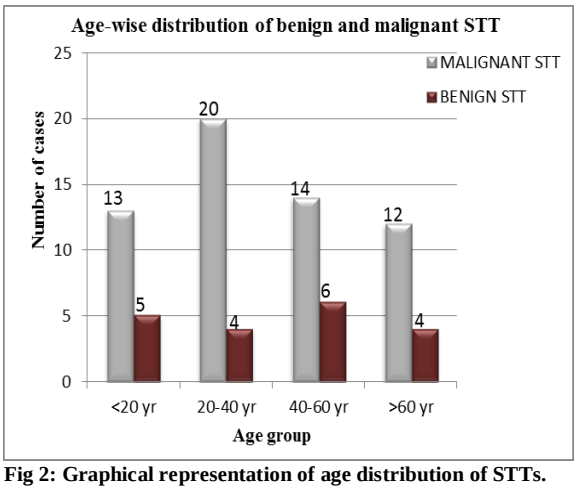

Fig 2: Graphical representation of age distribution of STTs.

In our study malignant tumors were found most commonly in lower extremity while benign tumors were equally distributed all over the body with slight variation. Overall it was found that lower extremity was the most common site of involvement by soft tissue tumors, followed by trunk and upper extremity. Thereafter primary FNAC diagnosis was correlated with the histopathological diagnosis (Fig 3) in each & every case to determine cyto-histopathological concordance. Out of 89 cases evaluated, 79 cases were categorized as benign or malignant and rests were inconclusive on

cytological examination due to various reasons like inadequate sampling, obscuration by blood elements etc.

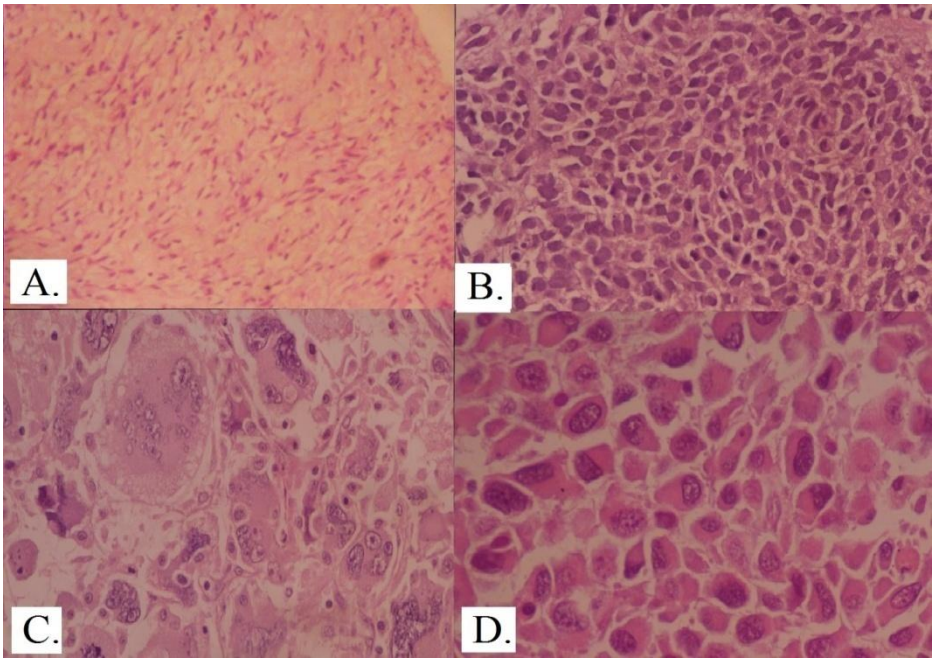

Fig 3: [A] Photomicrograph showing loosely arranged spindle cells in myxoid matrix (Neurofibroma). [B] Sheet of small round cells with round nuclei and scanty cytoplasm (Ewings' Tumor). [C] Anaplastic cell with high grade of nuclear pleomorphism and interspersing tumor giant cells (Undifferentiated pleomorphic sarcoma). [D] Polygonal tumor cells in abundance with eosinophilic cytoplasm giving carcinoma-like appearance (Epithelioid sarcoma). H&E, 400X.

Table 1: Categorization of STT into benign and malignant cases based on FNAC diagnosis

Cytological Diagnosis	No. Of Cases	Percentage Cases (%)	Benign Stt(%)	Malignant Stt(%)
Spindle Cell Tumor	36	40.44	11(57.89%)	25(41.66%)
Round Cell Tumor	14	15.73	-	14(23.33%)
Pleomorphic Tumor	13	14.60	-	13(21.66%)
Adipocytic Tumor	8	8.98	7 (36.84%)	1 (1.66%)
Myxoid Tumor	4	4.49	-	4 (6.66%)
Epitheloid Cell Tumor	4	4.49	1(5.26%)	3 (5.0%)
Other/Inconclusive	10	11.23	-	-
Total	89	100	19	60

Out of 19 benign cases, the spindle cell tumor constituted the majority (57.89%) followed by adipocytic tumor (36.84%). Among 60 malignant cases, the spindle cell tumor formed the major part (41.66%) followed by round cell tumor & pleomorphic tumor (Table 1).

Among all the cases, including the benign and malignant one, the most commonly diagnosed tumor was spindle cell type with slight predilection for males. All the pleomorphic, round cell, epithelioid cell tumor diagnosed cytologically were malignant. In this study we found the most common benign STT as spindle cell (57.89%) followed by adipocytic tumors (36.84%), while the most common malignant STT was spindle cell (41.66%) followed by round cell tumor (23.33%).Out of 19 cases of benign STT, 16 were found concordant with histopathological diagnosis while 3 cases turned out to be malignant, like benign adipocytic tumor was diagnosed to be liposarcoma on HPE. Among 60 malignant cases, 57 were concordant with histopathological diagnosis while 3 turned out to be tumor other than primary FNA diagnosis. Two of the malignant myxoid tumors were found to be benign on histopathological examination and diagnosed as Myxoid neurofibroma and Myxoid modular fasciitis while one case of malignant spindle cell tumor turned out to be schwannoma. Thus, overall 7.50% (6/79) of the cytological diagnoses were

found discordant with histopathological diagnoses (Fig 4).

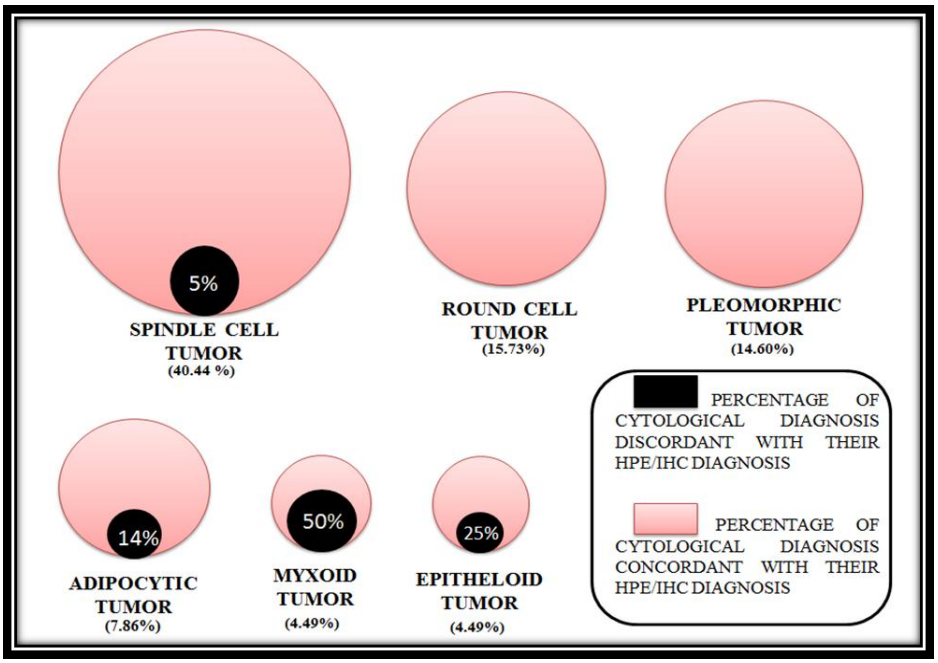

Fig 4: Pictorial representation of discordancy (%) in cytological and histopathological diagnosis of STTs.

Hence FNAC is found to be most reliable for diagnosing pleomorphic tumor and round cell tumor with no discordancy on correlation with HPE/IHC diagnosis in our study.

The accuracy rate was 92.40% (73/79) for nature of lesions (benign vs malignant). The sensitivity & specificity of primary cytological diagnosis was found to be 95% (57/60) & 84.21% (16/19) respectively, which is statistically significant ($p<0.0001$). In this study 89 cases of primary soft tissue tumors were analyzed, documenting 6 cases, of which 3 were incorrectly classified as malignant, yielding a 5% (3/60) false-positive rate and 3 were incorrectly classified as benign, yielding a 15.78% (3/19) false-negative rate. Unsatisfactory/ inconclusive/ inadequate smears were not included in this analysis.

DISCUSSION

In this study out of 89 cases, 60 (67.41%) were malignant, 19 (21.34%) were benign & rest (11.23%) were found inconclusive on cytology. In contrast the study of Dey et al [8] and Nagira et al [13] reported only 16.3% & 20.4% as malignant and 83.7% & 70.6% as benign. Referral bias might have contributed to this disparity, ours being one of the premier institute of oncology in Bihar providing comprehensive management services. In this study we found the most common benign STT was spindle cell (57.89%) followed by adipocytic tumors (36.84%), while the most common malignant STT was spindle cell (41.66%) followed by round cell tumor (23.33%). As in our study, Nagira et al [13] also reported spindle cell tumor (31.5%) as the most common benign STT followed by lipomatous tumor (14.6%) while most common malignant STT in their study was pleomorphic cell (35%) followed by round cell tumor (19.3%). Bezabih [14] reported lipoma (70.5%) as the most common benign STT and spindle cell tumor as the most common malignant STT (63.6%). Bennert et al [2] reported lipoma (69%) as the most common benign STT and MFH (27%) as the most common malignant STT, followed by lipomatous tumor (13.5%).

With the diagnostic accuracy of 94.20%, FNAC proved to be an accurate technique for categorizing a suspected

tissue mass into benign and malignant one. On-site evaluation of the lesion by cyto-pathologist and correlation with clinical and imaging findings are strongly recommended as they played the major role in yielding high accuracy rate in our study. Ackerman and Rydholm [15] analyzed 517 FNAC smears and reported 2.7% false-positive and 2.7% false-negative diagnoses with 5.6% inadequate smears. Bommer and colleague [16] analyzed 450 FNAC smears and reported only 0.2% false-positive and 2.2% false-negative rate with 1.7% inadequate smears.

The application of USG/CT-guided FNAC procedure for the deeply seated lesions proved fruitful, limiting the number of inadequate/ unsatisfactory smears to a small number (11.23%) in this study. Logan et al [17] study shows that 60% of the unsatisfactory smear are contributed by deep-seated lesion when sampled unaided. They reported 37.28% (22/59) cases to yield unsatisfactory smear on FNAC (unaided). However, Layfield et al [18] reported only 17.0% cases as inadequate for reporting suggesting factors like faulty aspiration technique in benign cases and necrotic and cystic changes in malignant lesions to be responsible for it. Numerous articles published in cytology journals create an impression that nothing is impossible with FNAC but the broad range of diagnostic pitfalls limit our view.

CONCLUSION

FNAC must be an integral component of the diagnostic approach to be followed for STTs. FNAC proved to be a good complementary tool for categorizing the lesions as benign and malignant STT, hence guiding the line of treatment. But its role in further sub-typing of tumor is not conclusive. Thus, both the techniques are complementary to each-other and it is not about choosing one method to the exclusion of other.

RECOMMENDATION

We recommend that the cyto-histological diagnosis must be correlated with clinic-radiographic findings and biologic behavior of the tumor before deciding the management protocol of the patient. Assistance of ancillary techniques must be taken for exact sub-typing of the tumor.

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Conflict of interest: The authors declare that they have no conflict of interest related to the publication of this manuscript.

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