Original Article

Fine needle aspiration cytology of soft tissue tumors with its histopathological correlation in a rural hospital of South India: A retrospective study

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ABSTRACT

Background: Fine needle aspiration cytology (FNAC) is often considered as the initial mode of investigation in the evaluation of the soft tissue tumors (STTs). This study was undertaken to explore the utility and accuracy of FNAC in STT by correlating their histopathological diagnoses. **Materials and Methods:** A total of 220 FNAC of STT was retrieved and evaluated retrospectively between January 2012 and June 2015 and correlated with their subsequent histopathological diagnoses. **Results:** On FNAC, 175 (79.6%) were benign, 26 (11.8%) were malignant and 19 (8.6%) were inconclusive. On the correlation of subsequent histopathology, 173 cases were confirmed as benign (true negative) and 22 cases were confirmed as malignant (true positive). There were four false positive and two false negative results. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of FNAC for diagnosing malignant STT were 91.7%, 97.7%, 97%, 84.6%, and 98.9%, respectively. **Conclusion:** The present study concluded that FNAC can be used as a reliable diagnostic tool for preoperative triaging of benign and malignant STT with fair sensitivity, specificity, and accuracy, even though a specific diagnosis may not be possible in all cases. In addition, we have found a considerable proportion of difficulties in the diagnosis of certain STT; hence, care should be taken while interpreting these challenging FNAC cases.

Key words: Fine needle aspiration cytology, histopathology, soft tissue tumors

INTRODUCTION

Soft tissue tumors (STTs) are a highly heterogeneous group of tumors and are classified on a histogenetic basis according to their resemblance to adult tissue.[1] Fine needle aspiration cytology (FNAC) is considered as an inexpensive, easy to perform, safe procedure with fair sensitivity and specificity in the diagnosis of primary, recurrent, and metastatic STT.[2] FNAC offers many advantages in different clinical scenarios. It can provide a predictive diagnosis of a benign or malignant neoplasm. If the diagnosis of benign neoplasm is made, surgery can be avoided in the elderly and in patients who are of poor surgical fitness. In high-grade malignancy or in recurrent cancers, it allows the administration of palliative treatment.[1,3] This study was undertaken to explore the utility and accuracy of FNAC in STT by correlating with subsequent histopathological results and also to compare the consistency of results with published literature.

MATERIALS AND METHODS

The study was conducted over the period of 3 years from January 2012 to June 2015. Approval from the Institutional

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Ethical Committee was obtained. Clinically suspected cases of STT, both in superficial and deep location sent for FNAC evaluation were included in the study. Cases which did not have histopathological diagnosis, skin, and their adnexal lesions were excluded. The technique used to aspirate material from STT was palpation and was performed by pathologists in all cases. Multiple numbers of passes/aspirates (depending on the size and consistency) were made for all the lesions. If adequate material was aspirated, both May–Grünwald–Giemsa (dry fixed) and hematoxylin and eosin (H and E) (wet fixed) stains were employed. If aspirate was scanty, only H and E stain was employed. The diagnosis was categorized into three groups-benign, malignant, and inconclusive. Benign group consisted of reactive proliferations along with unequivocally benign neoplasms without any atypical features. Malignant group included all the definite malignant diagnoses. Inconclusive group consisted of hemorrhagic and hypocellular smears. Special stain such as periodic acid–Schiff (PAS) was performed as and when required. On the correlation of FNAC diagnoses with histopathological diagnoses the sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive values of FNAC were calculated. All the statistical analysis was performed using International Business Machines Corporation (IBM) Statistical Package for the Social Sciences (SPSS) Statistics for Windows (SPSS version 20.0, IBM Corporation, Armonk, New York, USA).

RESULTS

The age range of study population ($n = 220$) was 1–80 years. The most common age groups for benign and malignant STT were second to fourth decades and fourth to fifth decades respectively. On FNAC, benign were 175 (79.6%), malignant were 26 (11.8%), and inconclusive were 19 (8.6%). On histopathology, there were 195 (88.6%) benign and 25 (11.4%) malignant tumors [Table 1].

Of the 195 patients with benign STT, 126 (64.6%) were male and 69 (35.4%) were female. Among 25 patients with malignant STT, 19 (76%) were male and 6 (24%) were female. The highest number of benign tumors was in upper extremities and trunk (96/195, 49.2%) followed by head and neck region (61/195, 31.3%). However, maximum number of malignant lesions was in the lower extremities (17/25, 68%).

After exclusion of inconclusive results (19 cases), the correctly cytotyped benign STT were 173 (true negative) and malignant STT were 22 (true positive). One case of lipoma was misdiagnosed as liposarcoma and two cases of benign fibrous histiocytoma and a case of schwannoma were misdiagnosed as malignant spindle tumors on FNAC [Figure 1a and b]. Hence, there were four false positive results. Two cases of fibrosarcoma were misdiagnosed as benign spindle cell tumors on FNAC [Figure 2a and b]. These were considered as false negative results [Table 2]. Ewing's sarcoma showed PAS-positive cytoplasmic materials. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of FNAC for diagnosing malignant STT were 91.7%, 97.7%, 97%, 84.6%, and 98.9%, respectively. The false positive rate was 2.3%, and the false negative rate was 8.3%.

DISCUSSION

STT can be diagnosed by a variety of methods namely FNAC, core needle biopsy or open biopsy; each of them having their own advantages and disadvantages. In comparison to open biopsy, FNAC is a simple, outpatient, low morbid, cost-effective procedure. Multiple passes to different areas of the lesion can be applied in FNAC, to

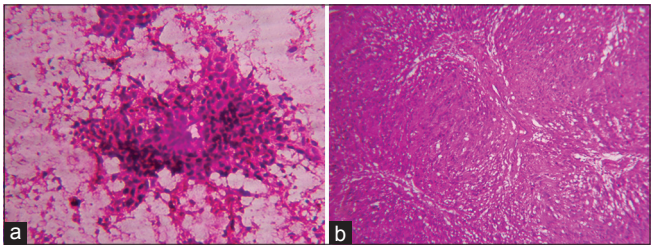

Figure 1: False positive case – Malignant spindle cell tumor turned out to be benign. (a) Single cluster of spindle cells with moderate to severe nuclear pleomorphism diagnosed as malignant spindle cell tumor (H and E, ×100). (b) Follow-up histopathological section revealing cellular Antoni A area with verocay bodies formed by Schwann cells diagnosed as schwannoma (H and E, ×100)

Table 1: Comparison of fine needle aspiration cytology and histopathological diagnoses of soft tissue tumors

FNAC diagnoses	FNAC (%)				Histopathology		
	Benign	Malignant	Inconclusive	Total	Benign	Malignant	Total
Lipomatous tumors	111 (97.4)	3 (2.6)	-	114 (51.8)	125 (97.7)	3 (2.3)	128 (58.2)
Vascular tumors	18 (100)	0 (0)	-	18 (8.2)	23 (100)	0 (0)	23 (10.5)
Spindle cell tumors	41 (78.8)	11 (21.2)	-	52 (23.6)	42 (80.8)	10 (19.2)	52 (23.6)
Myxoid tumors	5 (71.4)	2 (28.6)	-	7 (3.2)	5 (71.4)	2 (28.6)	7 (3.2)
Pleomorphic tumors	0 (0)	5 (100)	-	5 (2.3)	0 (0)	5 (100)	5 (2.3)
Round cell tumors	0 (0)	5 (100)	-	5 (2.3)	0 (0)	5 (100)	5 (2.3)
Inconclusive	-	-	19 (8.6)	19 (8.6)	-	-	-
Total	175 (79.6)	26 (11.8)	19 (8.6)	220 (100)	195 (88.6)	25 (11.4)	220 (100)

FNAC: Fine needle aspiration cytology

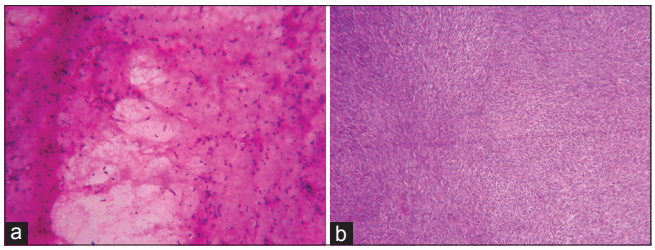

Figure 2: False negative case – Benign spindle cell tumor turned out to be malignant. (a) Cellular cytosmear showing plenty of benign appearing spindle cells without nuclear pleomorphism and necrosis diagnosed as benign spindle cell tumor (H and E, ×100). (b) Corresponding histopathological section showing interlacing fascicles forming herringbone pattern formed by malignant spindle cells, diagnosed as fibrosarcoma (H and E, ×100)

sample large tumors contrasting to core needle biopsy or open biopsy.[4]

FNAC diagnosis of STT is mainly based on cytological details such as cell types-lipomatous, spindle, round or pleomorphic and the background material-lipomatous, myxoid or metachromatic stromal fragments.[5]

On FNAC, benign STT formed 79.6% and malignant STT, 11.8% of our series which were almost comparable to Beg *et al*. study (82.5% and 17.5% respectively).[5] Whereas Soni *et al*.,[6] observed more number of benign (95.3%) and very less number of malignant cases (3.34%). Similar to Beg *et al*.,[5] we found 88.6% of benign and 11.4% of malignant STT on histopathology and it was contrasting to Dey *et al*.[7] who observed 32.9% (27/82) of benign and 67.1% (55/82) of malignant STT. The proportion of the benign and malignant cases in FNAC may vary widely between institutions depending on the evaluation protocol followed by them. Some of them may prefer FNAC in all cases while others may opt for excision/core needle biopsy in suspicious cases. This may explain the variation in the proportion of cases.

The present study observed that benign and malignant tumors were more common between second to fourth decades and fourth to fifth decades respectively, similar to Soni *et al*. study.[6] Roy *et al*.,[1] noted that benign STT were common in above the third decade of life, and malignant STT observed in all ages. Similar to Soni *et al*.,[6] we found the highest number of benign STT in upper extremities and trunk and malignant STT in lower extremities.

Beg *et al*.,[5] have shown in their series that lipoma was most common benign STT, and spindle cell sarcoma was the most common malignant STT. The current study also showed similar findings in both FNAC and histopathology. In contrast to the present study, Nagira *et al*.,[8] reported that most common benign STT was spindle cell (31.5%) followed by lipomatous tumor (14.6%) while the most common malignant STT was pleomorphic cell sarcoma (35%) followed by round cell sarcoma (19.3%). Institutional protocol regarding FNAC may be responsible for variation in the distribution of various histological subtypes. For example, some institutions may not resort to do FNAC of clinically obvious lipoma.

Out of all the FNAC diagnosis, one malignant lipomatous tumor, and three malignant spindle cell tumors were confirmed as benign (1, lipoma and 2, benign fibrous histiocytoma and 3, schwannoma) on histopathological examination. These were considered as false positive. On review, cytologically diagnosed malignant lipomatous tumor showed predominantly mature adipocytes with occasional suspicious lipoblast-like cells which were mistaken as lipoblast and erroneous diagnosis was made. On review of two cases reported as malignant spindle cell tumors showed spindle cells with high cellularity and mild to moderate nuclear atypia. However, no evidence of necrosis observed. The presence of high cellularity and nuclear atypia might have led to the diagnosis of malignant spindle cell tumor. In case of ancient schwannoma, smears were hypercellular with large bizarre cells and nuclear atypia which led to diagnosis of malignant spindle cell tumor.

We reviewed two cases of fibrosarcoma were underdiagnosed as benign spindle cell tumor. Smears of both cases revealed predominantly monomorphic spindle cell clusters with questionable hyperchromasia. This was missed during the initial cytological examination leading to a mistaken diagnosis of benign spindle cell tumors. All the false positive and false negative results in our series were due to interpretation errors.

The current study observed a false positive rate of 2.3% and a false negative rate of 8.3%. These results were comparable with most of the published studies, where the false positive and false negative rates for FNAC varied from <1% to 5% and 2% to 15%, respectively.[2] Wakely and Kneisl,[9] revealed a single case of false negative and nil false positivity. In contrast to this study, Nagira *et al*.[8] identified higher figures for false positivity and false negativity. Less number of false positive and false negative rates in our study could be due to categorization of inconclusive results.

A number of lesions with unclear etiology are grouped together under the category of tumor-like lesions of the STT. Although these lesions are grouped under neoplasms in the WHO classification, they are still considered by tradition as being tumor-like or reactive conditions. Of these, the most important are nodular fasciitis, proliferative fasciitis, proliferative myositis, and myositis ossificans. These lesions can be mistakenly diagnosed as sarcoma due to presence of cells often with the appearance of the tissue

Table 2: Correlation of fine needle aspiration cytology diagnoses with histopathological diagnoses in soft tissue tumors

FNAC		Histopathology	
Diagnoses	**Number of cases**	**Diagnoses**	**Number of cases**
Lipomatous tumors	114		
Benign	111	Benign	112
		Lipoma	87
		Lipomatosis	5
		Angiolipoma	7
		Fibrolipoma	12
Malignant	3	Malignant	2
Liposarcoma	3	Lipoma	1
		Well differentiated liposarcoma	2
Vascular tumors	18		
Benign	18	Benign	18
		Hemangioma	16
		Lymphangioma	2
Spindle cell tumors	52		
Benign	41	Benign	42
		Nodular fasciitis	1
		Fibroma	2
		Angiofibroma	2
		Fibrous hamartoma of infancy	2
		Benign fibrous histiocytoma	9
		Giant cell tumor	2
		Leiomyoma	2
		Neurofibroma	11
		Schwannoma	8
		Fibrosarcoma	2
Malignant	11	Malignant	10
		Benign fibrous histiocytoma	2
		Ancient schwannoma	1
		Fibrosarcoma	3
		Undifferentiated pleomorphic sarcoma	2
		Synovial sarcoma	1
		Leiomyosarcoma	1
		Malignant peripheral nerve sheath tumor	1
Myxoid tumors	7		
Benign	5	Benign	5
		Myxoid neurofibroma	5
Malignant	2	Malignant	2
		Myxofibrosarcoma	2
Pleomorphic tumors	5		
Malignant	5	Malignant	5
		Undifferentiated pleomorphic sarcoma	4
		Rhabdomyosarcoma	1
Round cell tumors	5		
Malignant	5	Malignant	5
		Ewing's/primitive neuroectodermal tumor	3
		Rhabdomyosarcoma	2
Inconclusive	19	Benign	18
		Lipoma	13
		Hemangioma	5
		Malignant	1
		Well differentiated liposarcoma	1

FNAC: Fine needle aspiration cytology

culture fibroblasts with striking cytoplasmic basophilia due to presence of abundant rough endoplasmic reticulum and large vesicular nuclei with prominent nucleoli and numerous mitotic figures. However, tumor-like or reactive lesions do not show atypical mitotic figures or nuclear atypia. The proper diagnosis of these lesions can be achieved by correlation with location, radiological and clinical findings. In this study, we diagnosed a case of tumor-like lesion (nodular fasciitis) as benign spindle cell tumor without posing any difficulty on FNAC.[10,11]

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of FNAC for diagnosing malignant STT were 91.7%, 97.7%, 97%, 84.6%, and 98.9%, respectively. These results were comparable to results of most of the published studies [Table 3].[5-7,12-14] Even though FNAC serves as a valuable tool in the preoperative assessment of STT, it has some limitations. Obtaining of poorly cellular smears due to nature of STT is an important limitation leading to either inconclusive report or wrong diagnosis. Categorization of benign or

Table 3: Comparison of statistical data of present study with published studies

Study	Number of patients	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Beg *et al.*[5]	126	98.1	96.7	-	97.2	-
Soni *et al.*[6]	150	70	100	98	97.9	100
Dey *et al.*[7]	82	91.5	92.5	-	95.5	-
Ng *et al.*[12]	432	89.2	89.8	-	96.1	98.1
Domanski *et al.*[13]	130	98.7	96.2	-	97.5	98
Kasraeian *et al.*[14]	57	79.2	72.7	75.4	67.9	82.8
Present study	220	91.7	97.7	97	84.6	98.9

PPV: Positive predictive value, NPV: Negative predictive value

malignant STT cannot be possible in certain neoplasms. Furthermore, it may not be possible to predict the grade or exact type of many STT on smears. However, use of ancillary diagnostic procedures can help to refine the cytological diagnosis.[2,3]

CONCLUSION

The present study concluded that FNAC can be used as a reliable diagnostic tool for preoperative triaging of benign and malignant STT with fair sensitivity, specificity, and accuracy, even though specific diagnosis may not be possible in all cases. In addition, we have found a considerable proportion of difficulties in the diagnosis of certain STT; hence, care should be taken while interpreting these challenging FNAC cases.

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Conflicts of interest
There are no conflicts of interest.

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