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Original Research Article

To Study Sensitivity, Specificity, Predictive Values of Fine needle aspiration by Comparing with Histopathology of Soft Tissue Tumors

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Abstract:

Today, fine needle aspiration has become a definitive prerequisite prior to operative procedures in many cases, soft tissue tumors or otherwise, as it gives the surgeon and insight as to what they are dealing with and so surgery can be planned accordingly.

Fine needle aspiration is a diagnostic procedure used for examination of a superficial or deep seated mass (guided radio logically), by sampling a minute amount of the tissue representative of the mass and examining it microscopically after smear preparation & proper staining. The aspirate can be examined for individual cells (cytology/FNAC) or histologically by sampling a greater amount of tissue (biopsy/FNAB).

Keywords: FNAC, Tumors.

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Introduction

Soft tissue tumors encompass a very large of benign and malignant neoplasms arising from the various soft tissue components of our body, right from the very commons lipomas to some diagnostically challenging tumors whose origin is still shrouded in mystery. Soft tissue tumors are morphologically vast and various attempts at categorization has been made in the past. It is this diverse morphology and relative rarity of soft tissue tumors that makes their diagnosis challenging.

FNAC of soft tissue tumors has evolved over time and it is an effective tool for diagnosis of primary, recurrent and metastatic soft tissue tumors. Due to its low cost, less incidence of complications and relative rapidity of reaching a diagnosis, FNAC is a valuable diagnostic tool in the pre-operative stage.

Fine Needle Aspiration in General: Today, fine needle aspiration has become a definitive prerequisite prior to operative procedures in many cases, soft tissue tumors or otherwise, as it gives the surgeon and insight as to what they are dealing with and so surgery can be planned accordingly.

Fine needle aspiration is a diagnostic procedure used for examination of a superficial or deep seated mass (guided radio logically), by sampling a minute amount of the tissue representative of the mass and examining it microscopically after smear preparation & proper staining. The aspirate can be examined for individual cells (cytology/FNAC) or histologically by sampling a greater amount of tissue (biopsy/FNAB).

Advantages of Fine Needle Aspiration

1. Safe & less painful- can be performed on an OPD basis
2. Cost effective – does not require OT facilities or hospitalization.
3. Diagnosis can be given at the earliest sample does not need elaborate processing.
4. Cosmetically beneficial- does not leave any scar.
5. Easily repeated if needed and can be done from multiple sites in the same sitting
6. Highly diagnostic if the aspirate is good.
7. Can be performed on patients declared unfit for surgical biopsis
8. Deep-seated lesions can be easily reached with radiological guidance.

Drawbacks of FNA

1. Blind procedure-sample may not be representative (unless guided radiologically)
2. Can be dangerous in patients with bleeding diathesis (proper history is a must)
3. Complications-air embolism, bleeding, infections, pneumo/hemothorax, cardiac, tamponade, damage or major vessels/nerves-can occur rarely.

4. Tumor implantation-especially when large guage needle are used or multiple passes are made.
5. May cause changes in the tissue/lesion under focus, making subsequent histopathological diagnosis difficult.
6. Aspirate may lack architectural arrangement of cells/tissue, making diagnosis difficult.

However, success of FNAC mostly depends on :

1. Adequate cellular aspirate representative of the lesion under investigation
2. Adequate history and clinical examination of the patient
3. Adequate experience of the persons aspiring, processing the sample and reporting

Role of FNA In Soft Tissue Tumors

FNA has taken over as one of the first steps in diagnostic protocols, as it give a rapid preliminary diagnosis. FNA has a role to play in the diagnosis of many soft tissue lesions but its use should be limited as one cannot definitively discern the grade and histologic type of a tumor from the relatively small sample. Even core needle biopsies that are used sometimes for grading the soft tissue tumors, have the drawback of not getting the entire histological picture required for complete diagnosis.

However, M. Ackerman et al, in 1985 found 66 out of 75 tumors correctly diagnosed as malignant and 260 out of 271 as correctly benign, in a study of 365 patients. There were 19 false cytodiagnosis in the study of which only 2 were of consequence to the patient. They concluded that final pre-operative diagnosis should be based on all pre-operative data to minimize the effect of any misjudgement as regards cytodiagnosis and aspiration cytology used in this way is a valuable adjunct to determine the further management of soft tissue tumors.

In a study done by REkhi et al at Tata Memorial Hospital and published in 2007, FNAC on 127 patients with soft tissue tumors also showed high sensitivity and specificity. They concluded that FNAC is fairly specific and sensitive in Soft Tissue Tumor diagnoses for primary, recurrent and metastatic lesions. The cytological types, especially round cell and pleomorphic sarcomas, can be quickly identified, Clinicopathological correlation with immunocytochemistry as an adjunct, are valuable in exact sub typing.

The benefits of FNA in the definitive diagnosis of soft tissue sarcoma outweigh the limitations when

1. there is a close co-operation between cytopathologist and surgeon (referral of patients to multidisciplinary centers).
2. the diagnosis is based on reliable and reproducible criteria
3. ancillary methods are part of the diagnosis
4. the diagnostic pitfalls are identified.

Soft Tissue Tumors: Soft tissue has been defined as ‘the non-epithelial, extra-skeletal tissue of the body exclusive of the Reticulo-endothelial system (RES) glia & supporting tissue of various parenchymal organs’. It also includes peripheral nervous system as they present as soft tissue masses. Embryologically they are derived from mesoderm and some part from neuro-ectoderm.

The benign tumors outnumber the malignant ones by a great margin. With a few exceptions, such as lipoblastoma, hemangioblastoma, and angiofibroma, benign soft tissue tumors are diseases of young and middle aged adults.

Soft tissue sarcomas may occur anywhere but three fourths are located in the extremities (most common in thigh) and 10% each in the trunk wall and retro peritoneum. There is a slight male predominance. Like almost all other malignancies, soft tissue sarcomas become more common with increasing age; the median age being 65 years.

Retroperitoneal tumors are often much larger before they become symptomatic. One tenth of the patients have detectable metastases (most common in the lungs) at diagnosis of the primary tumor. Overall at least one-third of the patients with soft tissue sarcoma die because of tumor, most of them because of lung metastases.

In the present study we have tried to compare the effectiveness of Fine Needle Aspiration (FNA) methods in the diagnosis of soft tissue tumors. With histopathological correlation where ever possible. The study was conducted in the Department of Pathology, Goa Medical college, over a period of 5 years (2008-2012) part retrospective and part prospective. Documented data and slides from the period were reviewed.

Materials and Methods

This study was undertaken for a 5 years period from January 2012 to December 2016. Part of the study was retrospective (Jan 2012 to Jun 2015) and part prospective (July 2015 to Dec 2016). Patients diagnosed with a soft tissue tumor on FNA (Retrospectively Jan 2012 to Jun 2015) & patients with suspected soft tissue swellings (prospectively July 2015 to Dec. 2016) were selected and clinical details noted. Details for the retrospective study was collected from registers maintained by our department.

A total of 726 cases of FNAC of soft tissue tumors were studied with histopathological correlation in 162 cases, over a period of

5 years. FNAC was performed, with informed consent of the patient, on the swelling using 23 G needle with a 10 ml disposable syringe and a

modified Cameco syringe holder, under aseptic precautions. A 22/23G lumbar puncture needle was used in cases of radiologically guided aspirations of deep – seated lesions. Proper clinical history was taken and appropriate lab investigations (Wherever required) were done on all patients especially on all guided FNAC's and deep seated lesions.

Observations & Results

Table 1: Distribution According to Site- 2012

STT	Head & Neck	Body/Trunk	Extremities	Total
Adipocytic	18	44	35	97
Fibroblastic	1	0	1	2
Neurogenic	1	1	4	6
Vascular	4	0	5	9
Fibrohistiocytic	0	0	1	1
Skeletal Mm	0	0	0	0
Spindle Cell Benign	0	2	1	3
Spindle Cell Malignant	0	2	0	2
Inconclusive	1	0	1	2
Total	**25**	**49**	**48**	**122**
Percentage	**20.50%**	**40.16%**	**39.34%**	**100.00%**

Table 2: Distribution according to site- 2013

STT	Head & Neck	Body/Trunk	Extremities	Total
Adipocytic	20	80	40	140
Fibroblastic	0	0	0	0
Neurogenic	1	0	0	1
Vascular	2	3	2	7
Fibrohistiocytic	0	2	2	4
Skeletal MM	0	2	0	2
Spindle Cell Benign	1	0	6	7
Spindle Cell Malignant	0	1	2	3
Inconclusive	0	0	0	0
Total	**24**	**88**	**52**	**164**
Percentage	**14.63%**	**53.66%**	**31.71%**	**100.00%**

Table 3: Distribution According to Site- 2014

STT	Head & Neck	Body/Trunk	Extremities	Total
Adipocytic	16	68	35	119
Fibroblastic	0	1	1	2
Neurogenic	1	0	2	3
Vascular	11	1	2	14
Fibrohistiocyti C	0	0	1	1
Skeletal MM	0	0	0	0
Spindle Cell Benign	0	2	6	8
Spindle Cell Malignant	0	0	3	3
Inconclusive	0	1	3	4
Total	**28**	**73**	**53**	**154**
Percentage	**18.18%**	**47.40%**	**34.42%**	**100.00%**

Table 4: Distribution According to Site - 2015

STT	Head & Neck	Body/Trunk	Extremities	Total
Adipocytic	17	54	36	107
Fibroblastic	0	0	0	0
Neurogenic	2	1	5	8
Vascular	1	1	1	3
Fibrohistiocytic	0	1	2	3
Skeletal MM	0	0	0	0
Spindle Cell Benign	0	3	5	8
Spindle Cell Malignant	0	1	2	3
Inconclusive	0	0	0	0
Total	**20**	**61**	**51**	**132**
Percentage	**15.15%**	**46.21%**	**38.64%**	**100.00%**

Table 5: Distribution According to Site- 2016

STT	Head & Neck	Body/Trunk	Extremities	Total
Adipocytic	16	67	42	125
Fibroblastic	0	2	2	4
Neurogenic	2	0	3	5
Vascular	3	2	2	7
Fibrohistiocytic	0	0	1	1
Skeletal MM	0	0	0	0
Spindle Cell Benign	3	0	2	5
Spindle Cell Malignant	0	0	2	2
Round Cell	0	1	0	1
Inconclusive	0	1	1	2
Total	**24**	**73**	**55**	**152**
Percentage	**15.79%**	**48.03%**	**36.18%**	**100.00%**

Table 6: Distribution of STTS according to site 2012-2016

STTs	Head & Neck	Body & Trunk	Extremities	Total
Adipocytic	87(14.77%)	313(53.31%)	188 (31.92%)	589
Fibroblastic	1 (12.5%)	3 (37.5%)	4(50%)	8
Neurogenic	7(30.43%)	2 (8.69%)	14(60.88%)	23
Vascular	21(52.5%)	7 (17.5%)	12(30%)	40
Fibrohistiocytic	0	3 (30%)	7(70%)	10
Skeletal	0	2 (100%)	0	2
Spindle Cell	4 (9.09%)	11 (25%)	29 (65.91%)	44
Round Cell	0	1 (100%)	0	1
Total	**120 (16.76%)**	**342 (47.77%)**	**254 (35.47%)**	**100%**

Table 7: Distribution of Benign and Malignant Tumors According to Site 2012- 2016

STTs	Head & Neck	Body/ Trunk	Extremity	Total
Benign	120	338	245	703
Malignant	0	4	9	13
Total	120	342	254	716

Discussion

This study was undertaken for a 5 years period from January 2012 to December 2016. Part of the study was retrospective (Jan 2012 to Jun 2015) and part prospective (July 2015 to Dec 2016). Patients suspected to have soft-tissue swelling were subjected to fine needle aspiration cytology. Few of them were eventually biopsied or operated, on which histopathological correlation was possible.

A total of 28145 FNACs were done during the 5 year period, out of which 726 were given a diagnosis of soft tissue tumor, which accounts for 2.58% of all FNACs. 162 patients among these, were operated and excision biopsies were available to us for histopathological correlation.

The possible reasons for the low turn up for histopathology are:

1. benign tumors such as lipoma, if not causing any trouble to the patient (due to its size or location) or are not cosmetically problematic, were left alone
2. patient compliance for operative procedures
3. patient referred by consulting doctor to a higher cancer referral center for further treatment
4. tumor cured on chemotherapy/ radiotherapy
5. only palliative chemotherapy/ radiotherapy done in aggressive tumors
6. surgically inoperable tumors

This study of 726 patients revealed a male preponderance with 372 males and 354 female patients, i.e. 51.24% were males and 48.76% were females, giving a male : female ratio of 1.05:1.

Table 8: Comparison of Age Distribution

Study	Year of Study	0-10	21-30	31-40	41-50	Mean Age Group with Maximum Incidence
Beg S et al	2012	14	36	23	19	21-40
Choukimath et al	2012	13	55	44	39	21-40
Roy S et al	2007	16	21	47		>40
Rekhi et al	2001-2006		27			21-30
Present Study	2012-2016	11	154	208	154	21-50

As per the above table showing the comparison of age in various studies, we see that STTs are most common in the middle age group with a mean age group of 21- 40 years, as is shown in studies by Beg S et al, Choukimath et al and Rekhi et al. Present study shows similar results. However Roy et al showed maximum cases aged above 40 years.

Table 9: Comparison of Sex

Study	Year of Study	Male	Female	Ratio
Beg S et al	2012	81	45	1.8 : 1
Choukimath et al	2012	103	97	1.06 : 1
Roy S et al	2007	66	39	1.7 : 1
Rekhi et al	2001-2006			1.8 : 1
Present Study	2012-2016	372	354	1.05 : 1

As seen above males outnumbered females by a slight margin in all studies. Present study also showed comparable results to other studies, with a ratio of 1.05 : 1.

Table 10: Comparison of STTS Based on Site

Study	Year of Study	Head & Neck	Body/Trunk	Extremity
Beg S et al	2012	39	32	53
Choukimath et al	2012	28	60	78
Roy S et al	2007	24	43	38
Present Study	2012–2016	120	342	254

As shown above, the extremities were the commonest site in studies done by Beg S et al and Choukimath et al. However in present study and that of Roy et al body/ trunk was the commonest. In all cases, head and neck was least involved site for STTs.

Table 4: Comparison of Histological Type of STTs

STUDY	ADIPO	FIBRO	NEURO	VASC	FIBROHIST	SPINDLE CELL	SKEL	OTHER
Roy S et al	34	5	18	6	5	-	6	26
Hiracha ND et al	23	12	9	0	3	-	0	3
Present Study	589	8	23	40	10	44	2	0

As shown in the table above, adipocytic tumors are the commonest tumors in all studies including the present study. Other histological types also are comparable with each other with slight variations in number of cases.

Table 5: Comparison of Benign/ Malignant on Cytology

Study	Year of Study	Total Cases	Benign	Malignant
Beg S et al	2012	126	104	22
Choukimath et al	2012	200	152	38
Roy S et al	2007	105	65	33
Present Study	2012-2016	726	701	17

Table shows that benign tumors outweigh malignant ones by a great margin. Beg S et al, Choukimath et al and present study showed 22, 38 and 17 malignant cases respectively out of 126, 200 and 726 cases. However Roy et al study showed 33 malignant cases out of 105, i.e. about a third of the patients in the study were positive for malignancy.

Table 6: comparison of statistical values of FNAC of soft tissue Tumors

Study	Sensitivity	Specificity
Rekhi et al	100.00%	83.00%
Dey et al	92.00%	93.00%
Hirachand et al	25.00%	100.00%
Choukimath et al	100.00%	100.00%
Layfield et al	95.00%	95.00%
Bommer et al	96.00%	99.00%
Wakley et al	100.00%	97.00%
Jorda et al	92.00%	99.00%
Nagira et al	92.00%	97.00%
Kitagawa et al	100.00%	100.00%
Present Study	99.36%	75.00%

The studies by Rekhi et al showed 100% sensitivity and 87% specificity and that by Nagira et al, 92% and 97% respectively. In other series, Wakely et al reported 100% sensitivity and 97% specificity in STT diagnosis with FNAC. Layfield et al achieved 95% sensitivity and specificity while dealing with these lesions. Studies by Choukimath et al and Kitagawa et al had sensitivity and specificity of 100%. Hirachand et al got a low sensitivity of 25% but the study showed FNAC to be highly specific. Present study statistics were comparable with a high sensitivity of 99.36%, however specificity was 75%. Parajuli et al had observed a sensitivity and specificity of 97.36% and 66.67% for benign STTs, and 66.67% and 97.36% for malignant STTs respectively, and was comparable to present study.

Due to unavailability of immunocytochemistry and other ancillary techniques at our institution, many patients could not be evaluated further and the follow up was not possible, as they were referred to tertiary cancer referral centers for further course of treatment. This is one of the reasons for a low turnout rate of malignant cases for excision/ operative procedures in the present study, indirectly responsible for a low specificity.

In the present study there was 1 false positive and 1 false negative case. Predictive values obtained in the present study were, 99.36% positive PV and 75% negative PV. Among bone and soft tissue tumors, false-positive and false-negative rates range from less than 1% to approximately 5% and approximately 2% to 15%, respectively. 61,62,68,69

The large variability in the reported sensitivities and specificities is related to the variable number of cases available in the different studies, the type of lesions biopsied, presence of ancillary techniques and other factors. Different factors like poor localization of the lesions, poor aspiration techniques, tangential aspiration whereby the needle misses the tumor and only the inflammatory reaction are sampled, secondary changes like necrosis, hemorrhage and cystic change and desmoplastic tissue reaction which makes cells difficult to aspirate can lead to errors in cytological diagnosis, and hence should be carefully avoided.

However, many recent and past studies have shown that FNAC has been an effective and reliable diagnostic tool in the evaluation of soft tissue tumors, with a high sensitivity and specificity. Problems arise in the exact subtyping of tumors especially the low grade sarcomas, but these can easily be averted by corroborating with appropriate clinical, radiological and ancillary data.

So, to conclude, FNAC is a highly sensitive and specific first line diagnostic approach for STTs especially when done by an experienced cytopathologist by sampling from different areas and correlating with histopathology (core needle biopsy/ excision biopsy), clinical and radiological data simultaneously/ concurrently. Ancillary techniques when available can be utilised for exact subtyping, prognosis, and further treatment purpose.

Conclusion

- This study was carried out at our institution for a period of 5 years, 2012-16, part prospective and part retrospective, to find the efficacy of FNAC in STTs.
- A total of 726 cases of STTs were diagnosed cytologically, out of which 162 were available for histopathological examination. Cyto-histopathological correlation of these cases was done.
- Maximum number of patients were in the age group of 20-50 years.

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