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Pathology

Cytological, Histopathological and Immunohistochemical Correlation of Soft Tissue Tumours

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Abstract **Original Research Article**

The diagnosis of a soft tissue tumour, like other tumours, is always challenging. FNAC in the evaluation of primary soft tissue tumours, however, remains underutilized. FNAC of soft tissue masses possesses a number of distinct advantages. However, histologic grade is the most crucial factor in predicting prognosis. Immunohistochemistry (I.H.C) is an adjunctive diagnostic technique to histopathology. The aim of our study is cytological, histopathological and immunohistochemical correlation of soft tissue tumours involving the clinical parameters. This retrospective study was undertaken in histopathology laboratory of Department of Pathology, N. R.S Medical College and hospital, Kolkata for period of 2 years from October 2016 to September 2018. Fifty four (54) cases of soft tissue tumours were studied clinically, by FNAC, histology and immunohistochemistry. Results were statistically analyzed. Amongst 54 cases, 33 were benign, 17 malignant and 4 were inconclusive on FNAC. Comparing histopathology, the overall accuracy rate was 87.18%. Both the sensitivity and specificity of the study was 100%.
Key words: FNAC, Histology, Immunohistochemistry, Soft tissue tumours.

INTRODUCTION

Modern histological classification of soft tissue tumours is based on the presumptive cell of origin of the tumour. Continuous modification is needed to incorporate newly recognized tumour variety and respond to new information on cell derivation. Generally the cytological features of the vast majority of these new entities in pathology of soft tissue tumours have not yet been investigated sufficiently [1].The incidence of soft tissue tumours, especially the frequency of benign tumours comparing to the malignant one, is nearly impossible to determine because of the fact that many benign tumours e.g. lipomas and hemangiomas do not undergo biopsy. Malignant soft tissue tumours on the other hand ultimately come to medical attention [2]. Data from the National Cancer institute's Surveillance, Epidemiology and End Results Program (SEER) showed a marked increase in the age-adjusted incidence of soft tissue sarcomas between 1981 to 1987[3]. Fine Needle Aspiration Biopsy (FNAB) in the evaluation of primary soft tissue tumours, however, remains underutilized [4]. There are two main indications for FNAB of soft tissue and bone lesions; the diagnosis of primary lesions and the investigation of lesions clinically suspicious of tumour recurrence or metastasis [5]. FNAB of soft tissue masses possesses a number of distinct advantages. It is a rapid outpatient procedure and provides an immediate diagnosis. The aspiration procedure is well tolerated and local anesthesia is usually unnecessary. A much greater sample is possible; multiple portions of the mass may be aspirated as compared to needle core biopsy. It is relatively inexpensive and much cost effective [6]. On the other hand, FNAB possess several distinct disadvantages, some of which are relatively specific to soft tissue lesions. It results in relatively small samples of a tumor; there is dispersion of individual cells and loss of recognizable diagnostic tissue patterns. There may be even more difficulty in distinguishing among benign cellular lesions and low grade sarcomas. Accurate grading of many sarcomas may not be possible when utilizing current histopathologic classification schemes. In densely collagenized or sclerotic masses or highly vascular lesions, FNAB may provide only a sparse smear cellularity [7]. However, FNAC has its utility in accurately distinguishing between benign and malignant soft tissue tumors [8]. Histologic grade is one of the most significant and perhaps the most crucial single factor in predicting a patient's prognosis. The ability to assess mitotic figure counts, variability in cellular differentiations and the extent of tumor necrosis is very important for accurate grading [9]. It cannot be overemphasized that immunohistochemistry is an adjunctive diagnostic

technique to traditional morphologic methods in soft tissue pathology, as in any other area of surgical pathology [10]. The application of immunohistochemical techniques has had a major impact on the diagnosis of soft tissue lesions and it has come to be considered a routine procedure in many institutions [11]. Considering the above mentioned facts we undertook the study involving clinical parameters, cytology, histopathology assisted with immunohistochemistry.

MATERIALS AND METHODS

This retrospective study was undertaken in histopathology laboratory of Department of Pathology, N. R.S Medical College and hospital, Kolkata for period of 2 years from October 2016 to September 2018.The study included 54 cases of soft tissue tumours attending the surgical outpatient department. After proper history taking and clinical examination aspiration was carried out using a 21 gauge disposable needle and a 20 cc disposable syringe capable of producing good suction. No local anesthesia was used. Leishman-Giemsa (LG) and Papanicolaou (Pap) stains were used for the aspiration smears. Then after the operative procedure, a proper histopathological examination of the specimens was done in all the cases. Hematoxylin-Eosin (H&E) stain was used for the histopathological studies supported in some cases by periodic acid Schiff (PAS) and reticulin stains. A provisional diagnosis was made in each case. Immunhistochemistry was done as per the provisional diagnosis of routine histopathological examination. Monoclonal antibody against Actin was done in suspected cases of rhabdomyosarcoma [12], Neuron Specific Enolase (NSE) [13] was done in malignant peripheral nerve sheath tumors (MPNST) and factor VIII related antigen [14] in angioarcoma. After immunohistochemistry, final diagnosis of the cases was made. The FNAC report was then correlated with the final histopathological report. Statistical analysis was done by assessing sensitivity, specificity and diagnostic accuracy of FNAC with regard to benign and malignant lesion.

The study was approved by Institutional Ethical Committee (IEC).

RESULTS

A total of 54 cases were included in the study of which 33 were found to be benign soft tissue tumours, 17 were malignant and 4 cases were inconclusive on FNAC. The age distribution of the soft tissue tumours as diagnosed by FNAC (Table-1 and Table-2) showed benign tumours were relatively common above third decade of life, while soft tissue sarcomas occurred in patients of ages above 20 years. Male patients outnumbered the female patients in both benign and malignant categories (Table-3). Benign tumors were roughly equally distributed across all parts of the body with a slight predilection for the upper parts, in the head and neck and the trunk region especially for the lipomas (Table-4). The commonest site of involvement of the malignant tumors was the trunk followed by lower extremity. After the cytological diagnosis, the cases were followed up to get them operated and the histological examination of the lesions was done. Table 5 shows the comparative analysis of the cases diagnosed both by FNAC and histological examination. The immunohistochemical study confirmed the histological diagnosis of rhabdomyosarcoma by Actin, malignant peripheral nerve sheath tumors (MPNST) by Neuron Specific Enolase (NSE) and angiosarcoma by factor VIII related antigen.

DISCUSSION

A total of 54 cases were studied by FNAC of which 4 cases were inconclusive (7.4%) (Table-5). Thirty three (61.1%) were found to be benign soft tissue tumor and 17 (31.5%) were malignant. Out of 4 (7.4%) inconclusive FNAC cases, 2 were found to be benign and 2 were malignant on histopathological examination. The probable causes may be excessive fibrosis or necrotic / cystic change in the tumour. Akerman *et al.* [15] reported in their series of 517 cases, the aspirated material was insufficient for diagnosis in 6% cases. Lindell MM Jr. *et al.* [16] and Zornoza J *et al.* [17] found ultrasonography, computed tomography or magnetic resonance imaging to be helpful in finding viable tissue in extensively necrotic or cystic tumors. Table 1 to 4 show that male patients of more than 40 years age are mostly affected by benign lesions and trunk was the commonest location. Malignant lesions affected male patients of 20 to 40 years age group and here also trunk was the commonest site.

Out of 33 (61.1%) benign soft tissue tumors diagnosed on FNAC, 6 (18.18%) were labeled as benign mesenchymal lesion as they could not be specified to a definite group. On histopathological examination, 2 cases were benign fibrous histiocytoma (BFH); rest 2 was hemangioma and schwannoma respectively. Seventeen cases (17) were diagnosed as malignant soft tissue tumour on FNAC, of which 5 (29.41%) cases could not be specified to any particular group. Two were angiosarcoma and rest three was malignant peripheral nerve sheath tumor (MPNST), liposarcoma and malignant fibrous histiocytoma (MFH), respectively on histopathology. The immunoshistochemical study confirmed the histological diagnosis in rhabdomyosarcoma, malignant peripheral nerve sheath tumor and angiosarcoma. Akerman *et al.* [15] found an erroneous cytological diagnosis in 5% of adequate smears.

Considering the 33 benign soft tissue tumorus diagnosed by FNAC, specific diagnosis was made in 27 (81.81%) cases. Twenty four of them were confirmed by histopathology but 3 cases showed different diagnosis on histopathological examination. The

accuracy rate was 88.89%. In case of malignant lesions, out of 17 cases diagnosed by FNAC, 12 were of specific diagnosis. Ten cases showed similar diagnosis and 2 cases showed different diagnosis on histopathological examination. The accuracy rate came to 83.33%. The overall accuracy rate was 87.18% considering both benign and malignant conditions. Both the sensitivity and specificity of the study came to 100% with regard to benign and malignant lesions.

In the study of Akerman *et al*. [15] 85% of the benign tumors were reported as benign and 89% of the sarcomas were classified as malignant soft tissue tumors. In another study, Akerman and Wilen [18] were able to distinguish benign from malignant lesion in 94% of the patients. Brosjo *et al*. [19] in a retrospective study of 342 cases from the musculoskeletal tumor group at the Karolinsks Hospital, Stockholm evaluated that the cytologic diagnosis was conclusive in 88% cases, 5% was false negative and 2% was false positive. Wakely *et al*. [20] found 96% accuracy rate in FNAC. In another study, Oland *et al*. [21] found no false positive interpretation but one false negative case. In their study, total 196 cases were studied in which 16 were metastatiic carcinoma. Forty eight underwent surgery and 25 cytologically diagnosed sarcoma was confirmed on histology. Out of 17 benign tumors, one was false negative. In our study, no metastatic carcinoma was found. In a retrospective analysis of FNA material from the orthopedic oncology group, Lund University Hospital over the last 20 years revealed that diagnostic aspirates were obtained from 475 out of 517 soft tissue tumors (92%). These consisted of tumors of the extremities and trunk and included 315 benign tumors and 202 sarcomas. A correct diagnosis with regard to benign versus malignant lesions was made in 447 (94%) of the 475 diagnostic aspirates [22]. From the above observations, we can say that our study corroborates with the studies done by other authors. However, study involving more number of cases and utilizing broad panel of immunohistochemical agents will improve the histological diagnosis and authenticity of the results. So, we can conclude that FNAC evaluation of soft tissue tumors is a useful procedure, quite safe, cost effective and accuracy rate of our study is at par with the available literature.

Table-1: Showing age distribution of benign soft tissue tumours on FNAC

Benign soft tissue tumors	No.	0-10 years	10-20 years	20-40 years	>40 years
Lipoma	12	Nil	Nil	3(25%)	9(75%)
Neurofibroma	9	Nil	Nil	1(11.11%)	8(88.89%)
Hemangioma	3	2(66.67%)	1(33.33%)	Nil	Nil
Leiomyoma	3	1(33.33%)	Nil	1(33.33%)	1(33.33%)
Benign mesenchymal lesion (could not be specified)	6	1(16.67%)	2(33.33%)	1(16.67%)	2(33.33%)
Total	**33**	**4**	**3**	**6**	**20**

Table-2: Age distribution of malignant soft tissue tumours on FNAC

Malignant soft tissue tumours	No.	0-10 years	10-20 years	20-40 years	>40 years
Rhabdomyo- Sarcoma	3	1(33.33%)	1(33.33%)	1(33.33%)	Nil
Fibrosarcoma	3	Nil	1(33.33%)	2(66.67%)	Nil
Liposarcoma	1	Nil	Nil	1(100%)	Nil
Small round cell tumor	2	1 (50%)	1(50%)	Nil	Nil
MFH	3	Nil	Nil	1(33.33%)	2(66.67%)
Malignant mesenchymal lesion (could not be specified)	5	Nil	Nil	2(40%)	3(60%)
Total	**17**	**2**	**3**	**7**	**5**

Table-3: Showing sex distributions of soft tissue tumours on FNAC

Soft tissue tumours	Total no. of cases	No. of males	No. of females
Benign	33	20 (60.6%)	13 (39.39%)
Malignant	17	11 (64.70%)	6 (35.29%)
Inconclusive	4	3 (75%)	1 (25%)

Table-4: Showing anatomical distribution of different soft tissue tumours on FNAC

Soft tissue Tumours	Total no. of cases	Head & neck region	Trunk	Superior extremity	Inferior extremity
Benign	33	8(24.24%)	11(33.33%)	8(24.24%)	6(18.18%)
Malignant	17	2(11.76%)	9(52.94%)	2(11.76%)	4(23.52%)
Inconclusive	4	1(25%)	2(50%)	Nil	1(25%)

Table-5: Showing the comparative analysis of the cases diagnosed both by FNAC and histological examination

H/P diagnosis		FNAC diagnosis(54)											
		Benign(33)					Malignant(17)						
		Lipoma (12)	Neuro-fibroma (9)	Heman-gioma (3)	Leio-myoma (3)	Benign mesen-chymal lesion (6)	Rhabdo-myo-sarcoma (3)	Fibro-sarcoma (3)	Lipo-sar-coma (1)	Small round cell tumor (2)	MFH 3	Malig. mesen-chymal lesion (5)	Incon-clusive (4)
BENIGN 35	Lipoma (11)	11											
	Neuro-Fibroma (8)		8										
	Hemangioma(5)			3		1							1
	Leiomyoma (2)				2								
	Nodular fascitis (2)	1											1
	Dermato-fibroma (2)					2							
	BFH (3)				1	2							
	Schwannoma (2)		1			1							
MALIGNANT 19	Rhabdomyo-sarcoma (2)						2						
	Fibro-sarcoma (2)							2					
	Liposarcoma (2)								1			1	
	Small round cell tumor (2)									2			
	MFH (5)						1				3	1	
	MPNST (2)											1	1
	Leiomyo-sarcoma (2)							1					1
	Angiosarcoma(2)											2	

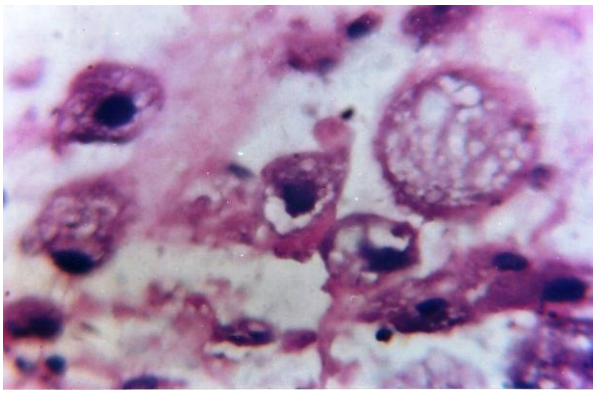

Fig-1: Photomicrograph of FNAC smear in liposarcoma showing multi vacuolated lipoblast (LG x400)

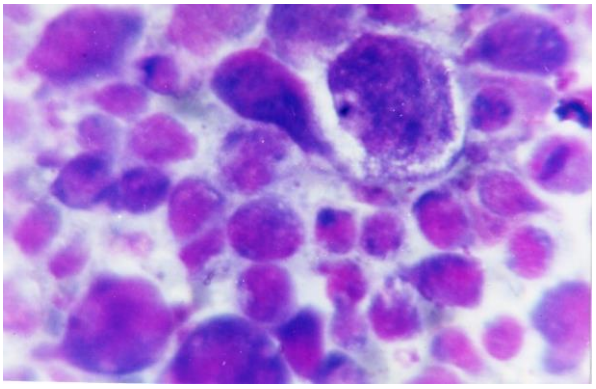

Fig-2: Photomicrograph of FNAC smear in MFH showing pleomorphic cells and large vacuolated cells (LG x400)

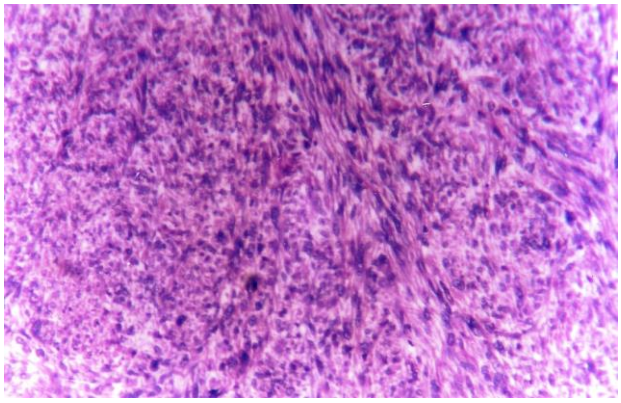

Fig-3: Photomicrograph of histology in MFH showing storiform pattern, pleomorphic cells and giant cells (H&E x100)

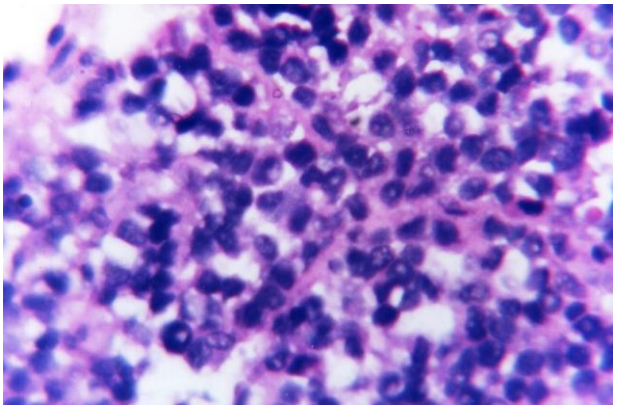

Fig-4: Photomicrograph of histology in small round cell tumor showing uniform population of round to oval cells (H&E x400)

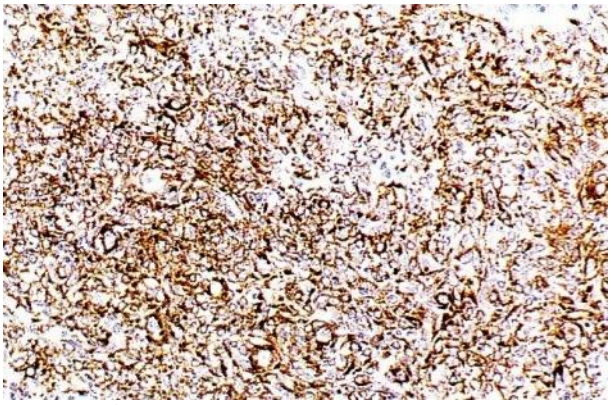

Fig-5: Photomicrograph showing positivity for actin in rhabdomyosarcoma (stained by monoclonal antibody against actin x100)

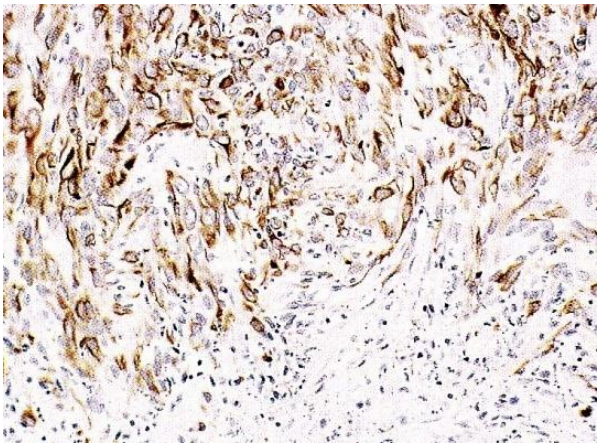

Fig-6: Photomicrograph showing positivity for NSE in MPNST (stained by monoclonal antibody against NSE x100).

CONCLUSION

FNAC evaluation of soft tissue tumours is a useful procedure, quite safe and cost effective.

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