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Original Research Article

Role of FNAC in palpable soft tissue tumors with emphasis on its correlation with histopathology

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Abstract: Background: Soft tissue tumors (STTs) and tumor-like lesions have fascinated clinicians and pathologists for years. Due to their wide variety and close histopathological similarities between certain tumors, they pose a diagnostic challenge. They most commonly present as masses and are rarely associated with pain. Fine-needle aspiration cytology (FNAC) has been documented as a reliable preoperative diagnostic tool to broadly differentiate them into benign and malignant categories. Histopathology is still considered the gold standard for STTs.

Aim of the Study: The aim of this study is to classify and subcategorize soft tissue tumors and to correlate the findings of FNAC of soft tissue tumors with histopathology.

Methods: This prospective study was carried out on patients with palpable soft tissue masses attending the surgical OPD between January 2021 and June 2022. FNAC of soft tissue lesions was performed, and only cases with subsequent histopathological examination were included in the study. Cytopathological and histopathological diagnoses were correlated.

Results: Out of 90 soft tissue tumors, 83 (92.22%) were benign, 1 (1.11%) was intermediate, and 6 (6.6%) were malignant. The male to female ratio was 1.7:1. The most common site was the trunk (34.4%), followed by the lower extremity (30%). Of all benign lesions, lipoma was the most common (71.1%). There was a concordance of FNAC with histopathology in 88 out of 90 cases (97.8%).

Conclusion: Benign soft tissue tumors outnumber malignant tumors. FNAC is an effective method for the rapid diagnosis of STTs, and preoperatively, it helps differentiate between benign and malignant lesions in most cases. Although histopathology is the gold standard, FNAC has high specificity in diagnosing malignant tumors, thereby preventing unnecessary extensive or radical surgery for benign lesions.

Keywords: Benign; Fine needle aspiration cytology; Histopathology; Malignant; Soft tissue tumors.

1. Introduction

Soft tissue tumors (STT) are defined as mesenchymal proliferations that occur in extra-skeletal, non-epithelial tissue, excluding the glia and lymphoreticular system. They are a heterogeneous group classified based on the line of differentiation, according to the adult tissue they resemble. Soft tissue is a specialized form of tissue composed of non-epithelial, extra-skeletal tissue, which includes adipose, fibrous tissue, smooth muscle, and vascular tissue [1–10].

The pathogenesis of STT is still unknown, but possible recognized causes are chemicals, ionizing radiation, and immunological effects [1,8]. STT can occur anywhere in the body, with a predilection for extremities, trunk, and head and neck [1,5,6]. They usually present as painless masses, and an accurate diagnosis can be made by detailed clinical history and physical examination. A few parameters such as age, location, and size can help in narrowing down the differential diagnosis [2].

The absence of recognizable architectural patterns in cytology smears makes the diagnosis of STT by fine needle aspiration cytology (FNAC) difficult [2,11]. However, FNAC is easy to perform, relatively painless, safe, cost-effective, and a useful diagnostic technique in the initial diagnosis of STT [2]. Many studies have documented that FNAC is highly specific and fairly sensitive in distinguishing benign from malignant tumors [2–12]. Although histopathology is the gold standard [1,4,9,11], the most important preoperative information for a surgeon is whether the STT is benign or malignant, which is provided by FNAC [1–3].

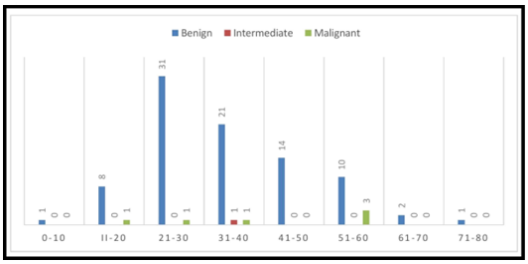

Figure 1. Age wise distribution of STT

2. Materials and Methods

All patients with clinically palpable soft tissue masses who visited the surgical department at VIMS, Ballari between January 2021 and June 2022 (18 months) and were referred to the Cytology section, CDL, VIMS Ballari for FNAC were included in the study. The decision to operate or observe by follow-up was made by the surgeon. Only cases that were operated and subjected to histopathology were included in the study.

2.1. Statistical Analysis

Data was collected using a structured proforma and entered into an MS Excel sheet. The data was analyzed using ratios and percentages.

2.2. Exclusion Criteria

The following cases were excluded from the study: inflammatory skin lesions, bone tumors involving soft tissue, and recurrent soft tissue tumors.

2.3. Procedure

Ethical clearance was obtained from the Ethics Committee of the Institute. A detailed history and physical examination of the cases were performed and recorded in the proforma.

Under strict aseptic precautions, FNAC was performed using a 21-23 gauge needle. The mass was located, examined, and fixed between the thumb and index finger. The needle was passed in a swift motion through the mass, and multiple passes were made to obtain material into the hub of the needle. This was then transferred onto a previously cleaned and labeled glass slide using a 10 ml syringe, and slides were made. Two slides were air-dried, and two were fixed in 95% alcohol to be stained with Leishman's and Hematoxylin-Eosin, respectively.

Subsequent surgery was performed at the discretion of the surgeon. The excised tumor was fixed in 10% formalin. After adequate fixation, representative bits of a standard size were taken and processed routinely to obtain 4-micron paraffin sections. These were stained with Hematoxylin and Eosin, and the histopathological features were analyzed by the pathologist.

3. Observations and Results

The study was conducted at VIMS, Ballari, over a period of 18 months from January 2021 to June 2022, during which 716 neoplastic lesions were received in the Department of Pathology, out of which 90 were soft tissue masses.

The majority of benign tumors were observed in the 3^{rd} to 6^{th} decades with a peak incidence in the 3^{rd} to 4^{th} decade. The majority of malignant tumors occurred in the 6^{th} decade.

The male to female ratio was 1.7:1 in the present study, indicating a slightly higher incidence of soft tissue tumors in males.

3.1. Benign and Malignant Cases

Both benign and malignant STTs showed male preponderance.

Out of the 90 cases studied, 83 (92.30%) were benign, 6(6.6%) were malignant, and one was of intermediate grade.

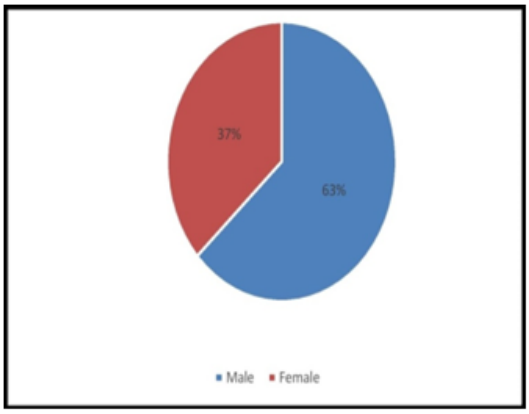

Figure 2. Gender distribution of STT

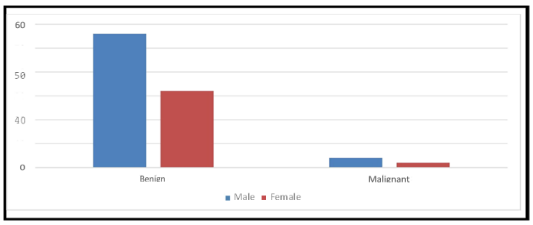

Figure 3. Gender based distribution

As shown in the table, STTs were predominantly located in the trunk (34.44%), followed by the lower extremity (30.0%). Adipocytic tumors were common in the trunk, while peripheral nerve sheath tumors showed a preference for lower limbs. The other types were equally distributed throughout the body.

In the present study, adipocytic tumors formed the majority (73.31%) followed by nerve sheath tumors (14.4%) and fibro-histiocytic tumors (5.55%). Other tumors identified included Nodular fasciitis, Pleomorphic sarcoma, Alveolar RMS, etc.

The youngest patient in the present study was 9 years old, diagnosed with Alveolar RMS, while the oldest patient was 73 years old, diagnosed with Pleomorphic sarcoma.

In the present study, 5 cases had inadequate FNAC sampling, of which 4 cases turned out to be lipoma and one case turned out to be Schwannoma on HPE. These cases were not included in the statistics.

One case diagnosed as Benign fibrous histiocytoma on FNAC turned out to be Pleomorphic sarcoma on HPE (false negative). This could be due to sparse cellularity or sampling errors.

Another lesion diagnosed as a malignant spindle cell lesion on FNAC was diagnosed as dermatofibrosarcoma protuberans on HPE (false positive). This could probably be due to the highly cellular smears with large pleomorphic cells.

Table 1. Relative occurrence of STT

Category	Number of cases	Percentage (%)
Benign (B)	83	92.3
Intermediate (I)	1	1.1
Malignant (M)	6	6.6
Total	90	100

Table 2. Anatomical site wise distribution of STT

Site	Frequency	Percentage
Head & Neck	12	13.33
Upper extremity	20	22.22
Lower extremity	27	30.00
Trunk	31	34.44
Total	90	100

Table 3. Age wise distribution of STT with respect to histological classification & subtypes

Age→ Soft tissue tumors	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**Total**	**%**
Adipocytic tumor Lipoma Liposarcoma	0	1	28	18	11	5 1	1	1	66	73.3
Fibroblastic and Myofibroblastic tumors Nodular fasciitis DFSP Fibrosarcoma	0	0	1	1	0	1	0	0	3	3.33
Fibrohistiocytic Tumor Benign fibrous Histiocytoma	0	2	1	1	0	1	0	0	5	5.55
Skeletal muscle Tumor Alveolar RMS	1	0	0	0	0	0	0	0	1	1.11
Peripheral nerve sheath tumor Neurofibroma & Schwanomma	0	4	2	1	3	3	0	0	13	14.4
Tumors of uncertain Differentiation Pleomorphic sarcoma	0	0	0	0	0	1	0	1	**2**	2.22
Total	1	7	32	21	14	12	1	2	90	
Percentage	1.11	7.7	35.5	23.3	15.5	13.3	1.11	2.22		100

Table 4. Correlation of fine needle aspiration cytology and histopathology diagnosis

FNAC Diagnosis	**NO**	**Histopathology Diagnosis**	**NO**	**Concordance**
Lipomatous tumor	**64**	Lipoma	**64**	100%
Atypical lipomatous tumor	**2**	Liposarcoma	**2**	100%
Nodular facsiitis	**1**	Nodular facsiitis	**1**	100 %
Malignant spindle cell	**1**(FP)	Dermatofibrosarcoma Protuberens	**1**	0%
Malignant spindle cell tumor	**1**	Fibrosarcoma	**1**	100 %
Benign Fibrous histiocytoma	**6**(FN)	Benign fibrous histiocytoma	**5**	83.33%
Benign spindle cell tumor	**9**	Neurofibroma	**9**	100%
Benign spindle cell tumor	**4**	Schwannoma	**4**	100%
Malignant spindle cell tumor	**1**	Pleomorphic sarcoma	**2**	50%
Malignant small round cell tumor	**1**	Alveolar Rhabdomyosarcoma	**1**	100 %

4. Discussion

Soft tissue tumors (STT) and tumor-like lesions have been of interest to clinicians and pathologists for years due to their remarkable diversity and the close histopathological similarities between certain tumors, making their diagnosis difficult. They usually present as painless masses, which can be diagnosed through a detailed clinical history, examination, and investigations.

FNAC has been shown to be a reliable pre-operative diagnostic tool for broadly differentiating them into benign and malignant categories. However, histopathology remains the gold standard for STT diagnosis.

In the present study, the frequency of benign tumors was 92.22%, and malignant tumors formed 6.66% out of the 90 cases studied. This is comparable with other studies.

Table 5. Comparison of frequency of soft tissue tumors

Author	No. of Cases	Benign (B)	%	Malignant (M)	%	B : MRatio
Arul & Masilamani [12]	220	195	88.6	25	11.4	7.8:1
Pandit et al., [4]	74	70	94.6	4	5.4	17.5:1
Dash et al., [5]	463	347	74.9	116	25.05	3:1
Bhatt et al., [7]	100	96	96.0	2	2	14.4:1
Solanki & Mangar [9]	170	158	92.4	10	5.88	15.8:1
Present Study	90	83	92.22	6	6.66	13.8:1

4.1. Comparison of incidence of STT by age

In the present study, the majority of benign soft tissue tumors were observed in the age group of 21-40 years, while malignant soft tissue tumors were commonly seen in the age group of 51-60 years. Similar findings were reported in previous studies by Janaki et al. [1], Soni et al. [2], Dhanya & Sateesh [11], Arul & Masilamani [12], and Uma et al. [10].

In the present study, there were 57 males and 33 females with a male to female ratio of 1.7:1, which is consistent with the above-mentioned studies, except for the study conducted by Pandit et al. [4] which showed a reversal of the ratio. This difference could be attributed to variations in the sample population studied and other confounding factors.

Regarding the location of soft tissue tumors, the most common site was the trunk (32.6%), followed closely by the lower extremity. There were variable findings with respect to location in previous studies, as some studies combined the upper extremity with the trunk or head and neck, or separately calculated the occurrence of benign and malignant STT by location.

In summary, the preference for the location of various tumors differs among different studies, possibly due to the rarity of STT and incomplete documentation of data. Most studies showed conformity regarding the incidence of benign lesions, which accounted for nearly 70-80% of STT, with adipocytic tumors being the most prevalent type. Additionally, there was agreement regarding age and gender, with benign lesions occurring before 40 years of age and malignant lesions occurring between 50-60 years of age, with a male predilection in both types of tumors.

The present study found lipoma to be the most common benign tumor diagnosed on FNAC and histopathology, followed by nerve sheath tumors, which is consistent with the findings of Pandit et al. [4], Dash et al. [5], and Arul & Masilamani [12].

In some studies, spindle cell lesions or fibrohistiocytic lesions were found to be the most frequent, which may be due to differences in their selection process or study criteria.

In the present study, the most common malignant tumor was tumors of uncertain differentiation, accounting for 2.1% of soft tissue tumors, which was similar to the findings of Umarani et al. [10] and Arul & Masilamani [12]. However, Dash et al. [5] and Pandit et al. [4] found fibroblastic/myofibroblastic tumors to be the most common malignant tumors.

In [4], one tumor was diagnosed as a benign spindle cell tumor on FNAC, but was confirmed to be low-grade myxofibrosarcoma on histopathology. This discrepancy was likely due to the limited tissue sampling in FNAC.

In [12], one case of lipoma was misdiagnosed as liposarcoma, and two cases of benign fibrous histiocytoma and one case of schwannoma were misdiagnosed as malignant spindle tumors on FNAC,

resulting in four false positive results. Two cases of fibrosarcoma were also misdiagnosed as benign spindle cell tumors on FNAC (false negatives). Two cases reported as malignant spindle cell tumors on FNAC showed spindle cells with high cellularity and mild to moderate nuclear atypia but no evidence of necrosis.

In [5], five cases showed discordance between FNAC and histopathology, with three false negatives and two false positives. Two cases diagnosed as lipoma were actually low-grade liposarcoma on histopathology, and two cases labelled as malignant spindle cell sarcoma were diagnosed as ancient Schwannoma on HPE.

In the present study, one case diagnosed as a malignant spindle cell lesion on FNAC was confirmed to be dermatofibrosarcoma on HPE. The FNAC showed only spindled tumor cells, absence of mitotic figures, atypia, and necrosis, possibly due to our inexperience in the cytology of this diagnosis and sampling errors.

In summary, various studies have shown issues with inadequate smears, false negatives, and false positives in the FNAC diagnosis of STT, highlighting the need for caution and expert interpretation in the diagnosis of these tumors.

1. Scanty aspirate due to high collagen or fibrous content, cystic areas within the tumor, or improper technique/site of FNAC can lead to inadequate smears. Vascular tumors are sparsely cellular, and tumor cells may be missed when embedded within a blood clot.
2. Aspirates from cellular areas of benign lesions may display high cellularity and mild to moderately atypical tumor cells, leading to an erroneous diagnosis of a malignant soft tissue tumor (false positives).
3. Aspirates from less cellular areas of malignant tumors may be mistakenly diagnosed as a benign tumor (false negatives).

Table 6. Comparison of sex wise distribution of STT

Authors	Males	%	Females	%	M: F Ratio
Janaki et al., [1]	106	50.47	104	49.52	1.2:1
Dhanya & Sateesh [11]	69	55.64	55	44.35	1.23:1
Arul & Masilamani [12]	145	66	75	34	1.9:1
Pandit et al., [4]	24	32.4	50	67.5	0.48:1
Dash et al., [5]	268	57.88	195	42.11	1.37:1
Present study	57	63.2	33	36.8	1.72:1

Table 7. Comparative analysis of anatomical site distribution of STT

Authors	Upper extremity	Lower extremity	Trunk	Head and Neck
Dwivedi et al., [3]	17.9%	25.3%	20%	18%
Pandit et al., [4]	35.13%	14.86%	8.40%	21.62%
Dash et al., [5]	26.56%	40.38%	19.22%	13.82%
Present study	**23.15 %**	**28.42 %**	**32.6 %**	**15.78 %**

Table 8. Comparative analysis of benign STT according to histological types

Tumors	Pandit et al., [4]	Dash et al., [5]	Arul & Masilamani [12]	Present study
Adipocytic tumors	68.9%	76.8%	50.9 %	68.8 %
Nerve sheath tumors	13.5%	19.4%	8.6 %	14.4%
Fibrohistiocytic tumors	6.75%	2.3 %	5%	5.55%
Fibroblastic / Myofibroblastic tumors	1.3%	2.3 %	1.3 %	2.22 %

Table 9. Comparative analysis of malignant STT according to histological types

Tumors	Arul & Masilamani [12]	Pandit et al., [4]	Dash et al., [5]	Uma et al., [10]	Present study
Adipocytic tumors	0.9%	1.3%	2.8%	1.4%	2.2%
Skeletal muscle tumor	1.3%		0.4%	0.9%	1.1%
Fibroblastic- myofibroblastic	2.2%	2.7%	4.1%		1.1%
Tumors of uncertain differentiation	2.7%		1.7%	1.8%	2.2%

Table 10. Comparative analysis of correlation of fine needle aspiration cytology and histopathology diagnosis

	Arul & Masilamani [12]	Pandit et al., [4]	Dash et al., [5]	Present study
Total cases(with histopathology correlation)	220176(B),24(M)19 (inconclusive)	74 71(B), 3(M)	463346(B),117(M)	9083(B),6(M)1(I)
Concordance	195	73	458	88
Discordance	6 (4 FP & 2 FN)	1 (FN)	5 (2 FP & 3 FN)	1(FN) 1 (FP)

5. Conclusion

Soft tissue tumors (STT) are rare, constituting less than 1% of tumors compared to carcinomas. However, early diagnosis is crucial for better management. In resource-poor settings, fine needle aspiration cytology (FNAC) plays a vital role in differentiating benign from malignant tumors. FNAC is a simple, rapid, relatively painless, cost-effective, outpatient procedure with good sensitivity, specificity, and diagnostic accuracy, and it correlates well with histopathological diagnosis. Thus, it obviates the need for unnecessary invasive surgical procedures for the diagnosis of a benign lesion.

Although histopathology is the gold standard for confirmed diagnosis with subtyping, it is mostly needed in cases of malignant tumors which are very rare. Sampling errors or low cell yield leading to inadequate smears were mostly due to cystic lesions, high fibrous and collagen content, and areas of necrosis/hemorrhage. The complex heterogeneity of STTs, overlapping histomorphology with limited documented studies, is a limiting factor for exact characterization of STTs.

6. Limitations

The study was limited by the reduced number of samples available due to the COVID-19 pandemic, our own inexperience with the cytology of the wide variety of STTs, and not using ancillary techniques.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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Appendix Images

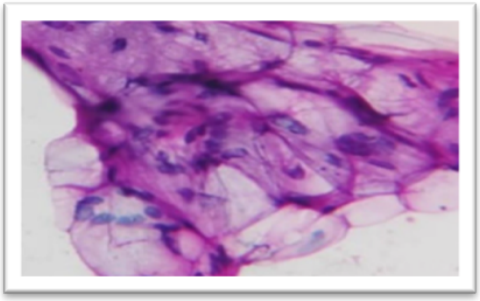

Figure 4. FNAC of Lipoma: sheets of mature adipocytes (H&E 40x)

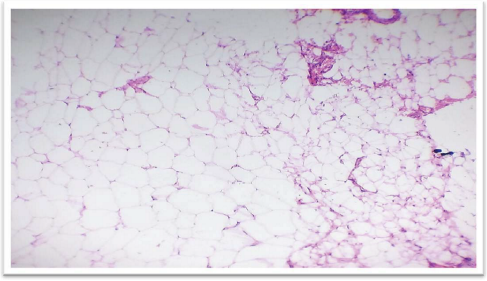

Figure 5. HPE of Lipoma: mature adipocytes separated by fibrous septae (H&E100x)

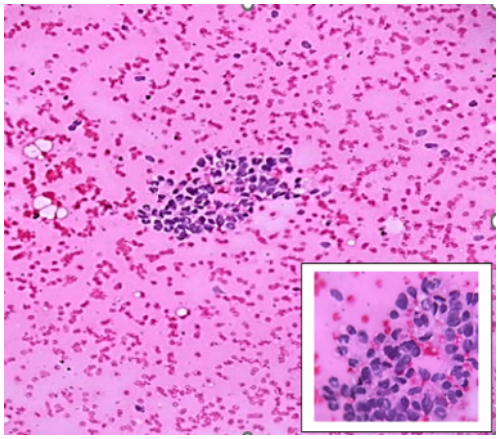

Figure 6. FNAC of Liposarcoma: Clusters of atypical cells showing large irregular hyperchromatic nuclei, occasional lipoblast (H&E.100x) Inset : (H&E 400x)

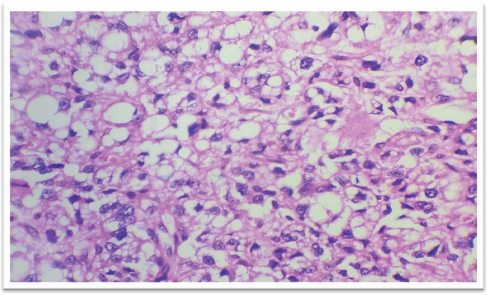

Figure 7. HPE of well differentiated Liposarcoma: Atypical cells showing large irregular hyperchromatic eccentric nuclei, vacuolated cytoplasm and occasional lipoblast (H&E.100x)

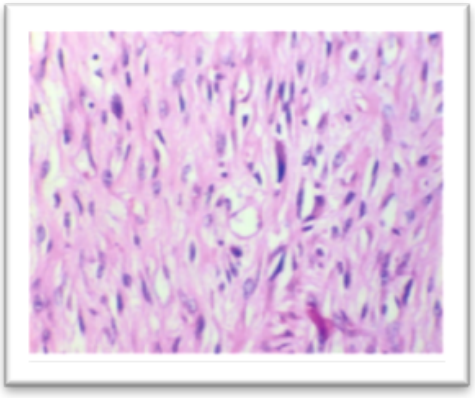

Figure 8. HPE of Pleomorphic liposarcoma showing lipoblasts and bizzare giant cells (H&E 100x)

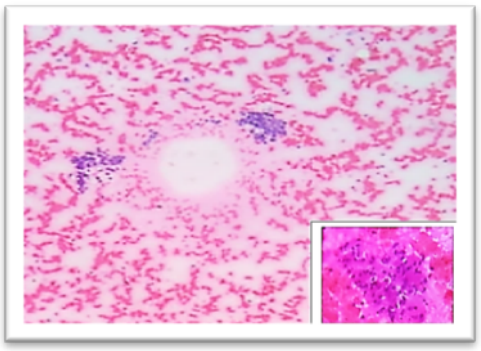

Figure 9. FNAC of Nodular fasciitis: spindle shaped cells (H&E.100x)Inset :(H&E 400x)

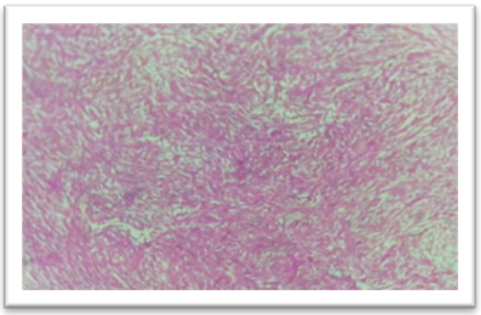

Figure 10. HPE of Nodular fasciitis showing spindle shaped cells loose fascicular pattern to storiform pattern(H&E.100x)

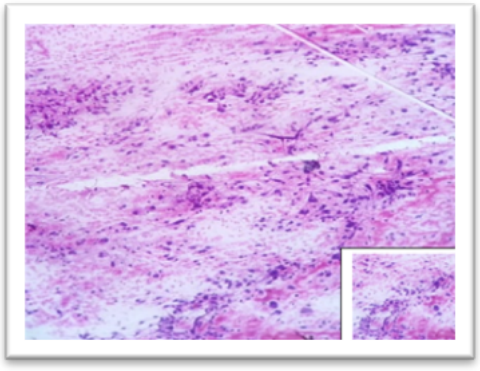

Figure 11. FNAC of Dermatofibrosarcoma Protuberans: shows clusters of spindle cells with poorly defined cytoplasm and round to ovoid hyperchromatic nuclei (H&E.100x)Inset :(H&E 400x)

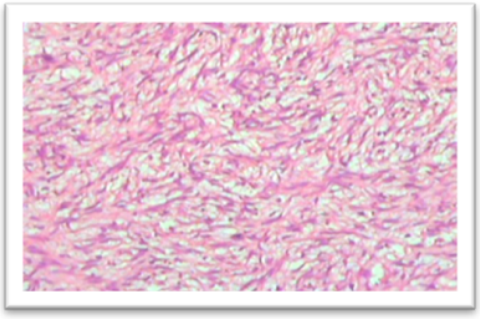

Figure 12. HPE of Dermatofibrosarcoma Protuberans: oval to spindle shaped cells with abundant eosinophilic cytoplasm. (H&E, 10x)

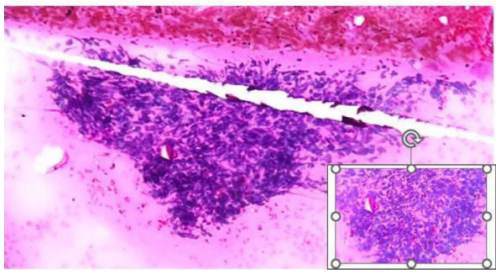

Figure 13. FNAC of Fibrosarcoma: atypical spindle cells with elongated hyperchromatic nuclei.(H&E.40x) Inset : H&E 100x

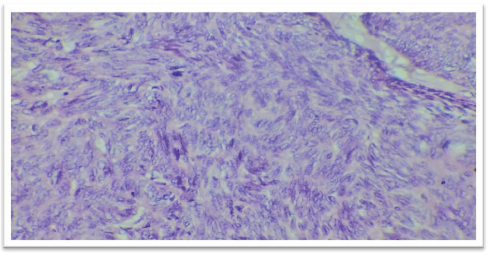

Figure 14. HPE of Fibrosarcoma: atypical spindle cells with elongated, hyperchromatic nuclei and scant cytoplasm arranged in herringbone pattern (H&E.40x)

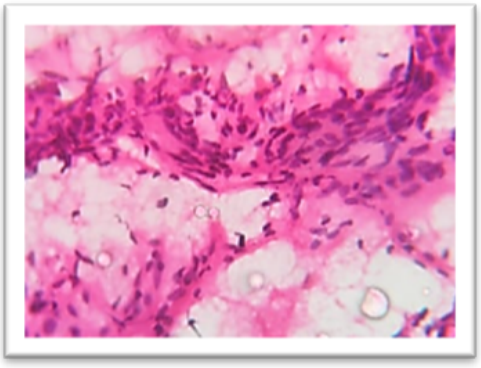

Figure 15. Benign fibrous histiocytoma showing spindle to plump ovoid cells (H&E 40x)

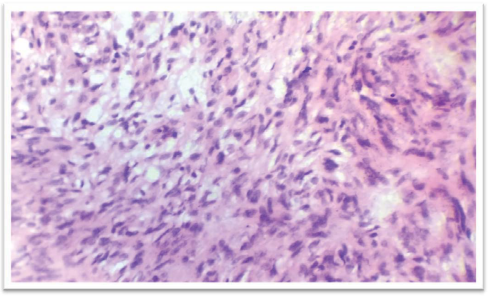

Figure 16. HPE of Benign fibrous histiocytoma: spindle to plump ovoid cells with indistinct cytoplasm in storiform pattern (H&E 40x)

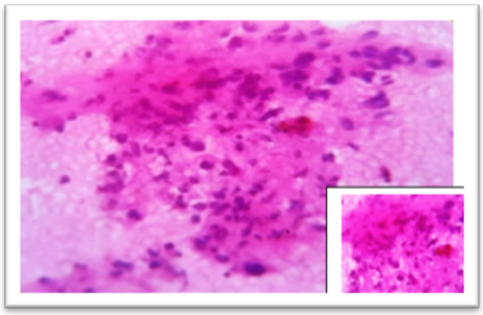

Figure 17. FNAC of Rhabdomyosarcoma: uniform atypical cellular pattern (H&E 40x)

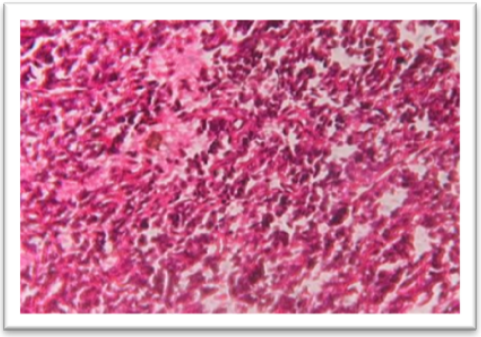

Figure 18. HPE of Rhabdomyosarcoma: sheets of neoplastic cells separated by thin fibrovascular septae (H&E 40x)

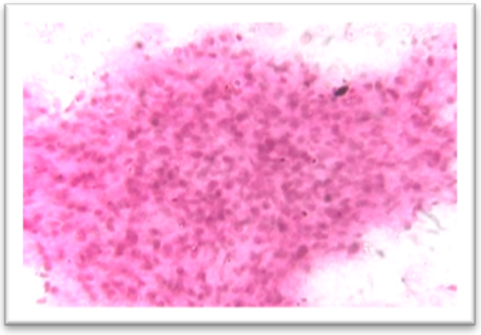

Figure 19. FNAC of Neurofibroma: spindled cells with oval elongated and regular nuclei (H&E.40x)

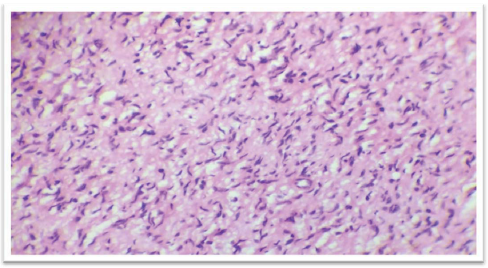

Figure 20. HPE of Neurofibroma: spindled cells with wavy nuclei with indistinct cytoplasm & occasional mast cells (.H&E.40x)

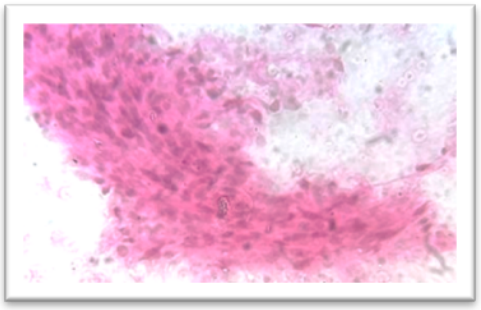

Figure 21. FNAC picture of Schwannoma: aggregates of spindle cells with elongated nuclei with blunt pointed ends.(H&E 40x)

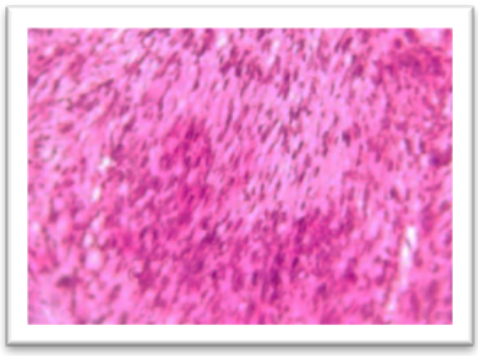

Figure 22. HPE of Schwannoma : Antoni type A and B patterns.(H&E 40x)

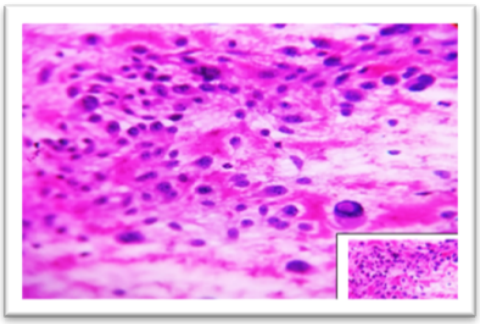

Figure 23. FNAC of Undifferentiated Pleomorphic Sarcoma: shows spindled, pleomorphic cells with irregular nuclei(H&E.100x)Inset :(H&E 400x)

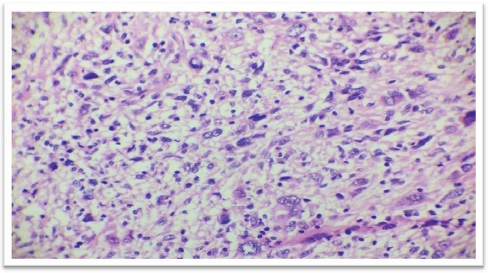

Figure 24. HPE of Undifferentiated Pleomorphic Sarcoma: irregular fascicles, pleomorphic and bizarre tumor cells with foamy cytoplasm, atypical mitotic figures and gaint cells.(H&E 40x)