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Case Report

Clinical and Histopathological Insights Into Soft Tissue Tumors: A Case Series with a Review of the Literature

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ABSTRACT

Soft tissue sarcoma is an uncommon and highly heterogeneous group of malignant tumors. The annual incidence of soft tissue sarcoma is about 50 cases per 1 million people, i.e., 1% of all malignant tumors. The field of soft tissue tumors (STT) is extremely vast; the pattern of tumors is varied, both on benign tumors and on malignant soft tissue tumors. Therefore, it is a very challenging job for a pathologist to give a final diagnosis. Here we have discussed three rare cases of soft tissue tumors.

Keywords: Soft tissue sarcoma, Immunohistochemistry, Malignant.

INTRODUCTION

Soft-tissue sarcomas (STS) are a rare and diverse group of malignancies, accounting for approximately 1% of adult cancers.[1] Soft tissue tumors are non-epithelial extraskeletal tissue of the body exclusive of the reticuloendothelial system, glia, and supporting tissue of various parenchymal organs.[2] They most frequently arise in the trunk, extremities, and retroperitoneum. Giving a definitive diagnosis is a difficult task for a pathologist because the pattern of tumors varies, both in benign and malignant soft tissue tumors.[1, 3] we have covered three cases of soft tissue tumors in this article. **Table-1** displays the clinical details, FNAC finding, histomorphological, Immunohistochemistry diagnosis each of three cases.

Table- 1: Clinical case profile and diagnostic features on FNAC, Histopathology and Immunohistochemistry.

Case No.	Age/ Sex	Tumour Location	FNAC Diagnosis	Histopathology	Immunohistochemistry marker	Final Diagosis
1.	72/M	Left upper back, 6 cm in diameter	High grade spindle cell tumour	High grade sarcoma	Positive- CD99 , Desmin,SMA, Negative-S100,CD34,bcl2	Leiomyosarcoma (Grade –III)
2.	50/F	Swelling over left thigh, 4 cm x 2 cm in size	High grade spindle cell lesion	High grade sarcoma	Positive-Vimentin , CD 99 Negative-CK,SMA,S100, DESMIN,CD34	High grade pleomorphic sarcoma
3.	63/M	Right inguinal area, 10 x 6 x 5 cm	Low grade spindle cell tumor	Low grade fibromyxoid spindle Cell tumor.	Positive-vimentin, CD34 Negative- S-100,Desmin,SMA	Cellular Angiofibroma

CASE HISTORY

Case-1:

A 72-year-old male patient came to the surgery outpatient department (OPD) with a history of swelling over the left upper back. The swelling was small in size initially, but increased gradually over 6 to 7 months to the present size of 5x4x3 cm. There was no history of pain. On physical examination, the swelling was non-tender and not fixed to the underlying structure. On MRI of the left shoulder with the scapula shows a large, rounded, homogenously enhanced necrotic mass, suggestive of a neoplastic etiology. A fine needle aspiration (FNAC) was done at our hospital, and cytological examination shows highly pleomorphic malignant spindle cells arranged in discohesive clusters and scattered singly with a raised nuclear-cytoplasmic ratio (N/C) and a moderate amount of eosinophilic cytoplasm. Many bizarre tumor cells, tumor giant cells, and abnormal mitoses were seen. A diagnosis of high-grade spindle cell neoplasm was offered. The wide local excision was done, and the specimen was sent for histopathological examination. On gross examination, the specimens were large, measuring 12 x 6 x 5 cm. microscopically, the tumor was composed of spindle cells arranged in interlacing bundles and interweaving fascicles. Individual tumor cells were pleomorphic, with a hyperchromatic nucleus and a moderate amount of eosinophilic cytoplasm. Mitotic figures (MF) were abundant, with 33 mitoses per 10 high-power fields (HPF), surrounded by fibro-collagenous stroma. Lymphovascular Invasion: not identified The diagnosis of high-grade sarcoma, grade III, was given. Figures 1(a, b) and IHC were advised.

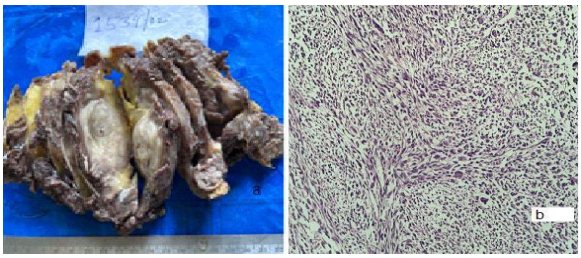

Figure -1: Photograph showing Gross (a) and Microscopic (b) Features of Leiomyosarcoma showing smooth muscle cells arranged in fascicles and whorls. (H&E stain,10x) (Case 1)

IHC revealed that it was leiomyosarcoma (Grade -III) with positive CD99 and Desmin and negative CK, SMA, S100, CD34, and BCL2.Aberrant expression of TLE1 in scattered cells with weak reactivity was seen.

Case-2:

A second case in our study was undifferentiated pleomorphic sarcoma (UPS). A 50-year-old female patient came with complaints of swelling over the left thigh for 5 months, which was small in size and gradually progressed to 4 cm x 2 cm in size. On examination, the swelling was non-tender, mobile, and not fixed to the underlying structure, with no history of trauma. On USG, swelling measuring 7x5x4 cm over the upper thigh showed a hypoechoic mass lesion with patchy vascularity. Radiological finding was not significant; the diagnosis of a high-grade spindle cell lesion was given based on cytology. The mass was surgically excised and sent to the histopathology department. Grossly, the tumor was irregular, ranging from soft to firm in consistency. On the cut surface, there was a grayish-white mass with a variegated appearance. Microscopic examination showed highly pleomorphic tumor cells. Individual tumor cells were round to oval with a high nucleocytoplasmic ratio and a moderate amount of eosinophilic cytoplasm. The tumor was highly mitotically active (mitosis > 27/10 HPF) with a large area of necrosis. No lymphovascular invasion was identified. Figure 2(a, b)

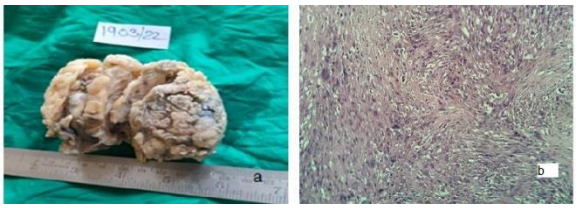

Figure-2: Photograph showing Gross (a) and Microscopic b) features of High grade-pleomorphic sarcoma showing spindle cells with marked nuclear pleomorphism .(H&E stain, 10x)

All margins were free of tumors. Therefore, based on the above findings, a diagnosis of high-grade sarcoma was offered and IHC was advised. On immunochemistry, vigintin and CD-99 were positive, and other markers like CK, SMA, S100, Desmin, and CD-34 were negative. Therefore, the final diagnosis of "high-grade pleomorphic sarcoma" was given.

Case-3: 65-year male patient came to OPD with history of swelling over Right inguinal area since 8 months, No history of trauma, No history of Diabetes mellitus and hypertension, Asthma. There is no similar history in past. USG finding were likely suggestive of desmoid tumour or sarcomatous change. On CT Abdomen and pelvic –Not significant. Patient underwent wide local excision with reconstruction excise complete. On grossly sectioning well circumscribed, soft, reddish-brown, gelatinous tumor is identified measuring 10 x 6 x 5 cm along with 05 lymph nodes identified. On histopathological diagnosis was given low grade fibromyxoid spindle Cell tumor, Figure 3(a, b).

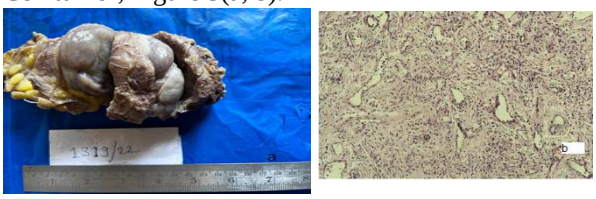

Figure-3: Photograph showing Gross (a) and Microscopic (b) features of cellular angiofibroma showing spindle cells with bland elongated nuclei and moderate amount cytoplasm (H&E, 10x)

On IHC vimentin and CD34 were positive and final diagnosis was offered as benign mesenchymal neoplasm suggestive of cellular angiofibroma.

DISCUSSION WITH REVIEW OF LITERATURE

Soft tissue sarcoma is a rare and highly heterogeneous group of cancers. A study by Blay et al. suggested the lower extremity to be the most common site for sarcomas, and the common histologic types of sarcoma in adults are leiomyosarcoma and undifferentiated pleomorphic sarcoma.[4] Leiomyosarcoma, which is our first case, is a tumor arising from smooth muscles. It accounts for only 5–10% of all soft tissue sarcomas.[1, 5, 6] Location-wise, LMS has commonly been seen in the extremities (particularly the lower extremities), uterus, abdomen/pelvis, trunk, blood vessel walls, and bone.[2, 7] Soft tissue leiomyosarcoma has an equal incidence in both genders. It can affect any age group but is more commonly seen in the 5th to 7th decades of life.[8] in our case, leiomyosarcoma was seen in a 64-year-old male and was located on the left upper back, a rare location as only 16% of leiomyosarcoma on a trunk has been reported in literature till now. [4, 9-13] LMS is found to be associated with Li-Fraumeni syndrome, hereditary retinoblastoma, and radiation exposure.[2] However, no such association was found in the present case. Radiological imaging techniques Such as ultrasonography, MRI, and CT scanning are useful in the detection of palpable. Superficial soft-tissue masses as well as non-palpable deeper lesions. Furthermore, it helped to determine the exact location, extent of the mass, and its relation to surrounding structures.[14] An MRI of the left shoulder with scapula revealed a large rounded homogenously enhancing necrotic mass, indicating a neoplastic etiology. Other than radiology, a cytologic examination is considered to be a necessary part of the diagnostic workup.[15] in our case, FNAC features of high-grade spindle cell lesions helped with an early presumptive diagnosis.

Grossly, leiomyosarcoma typically has a fleshy, gray-white to tan appearance along with whorled areas. Larger tumors can have areas of hemorrhage, necrosis, or cystic change. Tumor borders can be circumscribed or infiltrative.[2] The tumor in our case was large, measuring 10 x 6 x 5 cm, and was attached to the muscle posteriorly. Microscopically, LMS is an encapsulated and ill-circumscribed tumor composed of tumor cells arranged in fascicles and storiform patterns. Individual tumor cells were pleomorphic, spindly, and had a high NC ratio, as well as large, round to oval, plump, blunt-ended nuclei and scant to moderate pale to brightly eosinophilic cytoplasm. Hypercellularity, high mitotic activity, and the presence of coagulative necrosis differentiate LMS from its benign counterpart.[16] The same histological features were noted in our case. On immunohistochemistry, leiomyosarcoma shows positivity for SMA, desmin, or h-caldesmon. Out of these markers, at least one IHC marker is positive in all (100%) cases. For diagnostic purposes, positivity for a minimum of 2 myogenic markers is more supportive for diagnosis. Also, the diagnosis of leiomyosarcoma should not be made exclusively on the basis of IHC markers in the absence of appropriate morphological features.[2,17] in our case, immunohistochemistry was done on paraffin blocks and showed positivity for SMA patchy strong positivity, desmin-focally positive, CD99-positive, and TLE1-scattered weak reactivity. TLE1 has been recognized as a diagnostic IHC marker for synovial sarcoma.[18] The attributes of leiomyosarcoma in literature were summarized in Table 2.

Table 2- Clinical, morphological and diagnostic features of high-grade leiomyosarcoma- Literature review.

S.R	AUTHORS	AGE /sex	YEAR	TUMOUR LOCATION	SIZE	HISTO	IHC positive	IHC negative
1	Kusuma Venkatesh et al.[19]	55/F	2010	Kidney	20x15x20cm	Primary Leiomyosarcoma	Desmin, actin	Cytokeratin,HMB45,CD117
2	Giovanni Conzo et al.[20]	77/M	2014	Thyroid Gland	4.5-6.5 cm	Leiomyosarcoma	Vimentin, H-caldesmon, smooth muscle actin	AE1-AE3, CK7, CK19, CK5/6 and CK8/18), EMA, TTF-1, , CD31 and factor VIII
3	Taylan Senol et al.[21]	62/F	2015	Uterus	25 × 25 cm	Giant leiomyosarcoma	Ki-67	p16, p53 , Ki-67
4	Yi Yang et al.[22]	47/M	2017	Spine		Primary leiomyosarcoma	Actin,Desmin,Ki-67	EMA,s100,myogenin,pan-keratin
5	Sarra Mestiri et al.[23]	Median 52 /M	2019	lower limbs (45%),retroperitoneum(2 cases)	≥5cm	Leiomyosarcoma	h-Caldesmon, SMA,desmin,	EMA,s100,vimentin,CD34,CD117
6	Natalia Parisi Severino et al.[24]	67/F	2022	Rectal	6.5 cm in length	Rectal leiomyosarcoma	(SMA), beta-catenin, h-Caldesmon, ER,vimentin, and Ki-67	desmin, (EMA), S100, CD34, CD117

The second case in our study was high-grade pleomorphic sarcomas. It is a rare subtype that belongs to a heterogeneous group and accounts for less than 1% of all soft tissue sarcomas. Since pleomorphic sarcoma has a better prognosis when diagnosed early, it is crucial to immediately recognize and assess any enlarged mass or nodule, even though it is a rare diagnosis. The incidence of pleomorphic sarcomas is low; they have a variable presentation, behavior, and long-term outcomes.[25-27] Pleomorphic sarcoma is a subtype of undifferentiated soft tissue sarcoma. It can be found at a variety of sites and tends to occur in the extremities, retroperitoneum, and head and neck region. It can occur at any age, but is predominantly seen in the 6th and 7th decades of life. Both males and females can be equally affected.[2,28] Here we have reported a 50-year-old female with pleomorphic sarcoma on her left thigh. Radiological investigations are useful in preoperative diagnosis to learn about the character of the tumor and its anatomical site in the abdomen and pelvis.[13] Ultrasonography is not very useful in diagnosing a soft tissue tumor. In our case, a similar Finding was reported. Fine needle aspiration cytology is a useful technique that is cheap, easily available, and helpful for the early diagnosis of all soft tissue lesions.[29] in our case, an FNAC high-grade spindle cell lesion diagnosis was offered. This helped the clinician proceed with quick further management of this case. The patient was operated on, a wide local excision was done, and the mass was sent for histopathological examination. On gross examination, a tumor usually has a variegated appearance, with a large area of hemorrhage and necrosis or cystic changes.[2,30] on cut surface showed a grayish-white appearance. Microscopically, tumor cells can be pleomorphic, spindle cells, round cells arranged in storiform, fascicular, or sheet-like patterns, or atypical pleomorphic spindle cells with abundant mitotic figures and necrosis. Sometimes tumors extend to underlying structures.[2, 31] similar findings were noted in our case. However, no lymphovascular invasion was seen. Due to the high rate of recurrence and metastasis, chemotherapy and radiotherapy can be used in treatment, mainly in deep, high-grade lesions larger than 5 cm. Patients underwent radiotherapy after 6 months. Regular follow-up was done after surgery, and patients were stable. Table 3 shows the detailed features of undifferentiated pleomorphic sarcoma with literature view.

Table-3: Clinical, morphological and diagnostic features of undifferentiated pleomorphic sarcoma-Literature review

S.R	AUTHORS	AGE /sex	YEAR	TUMOUR LOCATION	SIZE	HISTO	IHC positive	IHC negative
1	Robert Diaz-Beveridge et al.[32]	75/M	2015	Colon mass	14cm x13cm	Primary Mesentric Undifferentiated pleomorphic sarcoma	Vimentin,CD68	Ck,EMA,CD34,S100,HMB45
2	Yohei Oguri et al.[33]	70/M	2018	Stomach	14 cm	Aggressive undifferentiated pleomorphic sarcoma	Vimentin	α-SMA, actin, cytokerat- (AE1/AE3), EMA, desmin, S-100 protein, c-Kit, CD34 and Melan-A
3	Austin H. Allen et al.[34]	62/F	2019	Thigh	24×9.5×7cm	Undifferentiated pleomorphic sarcoma	Vimentin	desmin, HMB-45, SMA, S100, myosin, CD34, CD45, TLE1, CD99, Keratin AE1/AE3
4	Fadi Taza.[35]	60/M	2020	Thigh Medially	7cm	High grade pleomorphic sarcoma	Desmin	fluorescence in situ hybridization (FISH) for anaplastic lymphoma kinase (ALK)
5	Christian Taylor Smith et al.[36]	64/M	2021	Upper Back	5 × 5 cm	Pleomorphic Leiomyosarcoma	Actin, Desmin	----
6	Wafa Almalki et al.[37]	58/F	2021	retro-gastric mass	30 × 22 × 11 cm	undifferentiated pleomorphic sarcoma	SMA, Vimentin	Desmoid, CD117, and CD34

Third case in our study was benign cellular angiofibroma. Cellular angiofibroma is a rare, painless, slow-growing benign stromal tumor, first described by Nucci et al.[38] the peak incidence of cellular angiofibroma is noted in the 5th decade in females and the 7th decade in males .[2,39] The tumors are commonly located in the subcutaneous tissue of the inguinoscrotal area in men and the vulva in women. However, no sex difference was found in its incidence. On gross examination, tumors vary in size (0.6–25 cm). Histopathological, it is usually a well-circumscribed tumor mass composed of spiral-shaped cells along with various-sized blood vessels and collagen bundles. On IHC, cellular angiofibroma usually expresses CD34 and SMA, and in Desmin, ER and PR are variably expressed.[40] Local recurrence is infrequent. In our case, the histological and immunohistochemical findings were similar to those previously reported. In Table 4, we discuss previously reported cases in literature of benign cellular angiofibroma.

Table 4- Clinical, morphological and diagnostic features of Cellular angiofibroma-Literature review

S.R	AUTHORS	AGE/ years /sex	YEAR	TUMOUR LOCATION	SIZE	HISTO	IHC positive	IHC negative
1	Xia-Qin Cai et al.[41]	47/F	2022	Left vaginal wall	2.5 × 2.0 cm	Cellular angiofibroma	CD34, SMA, desmin, ki-67,ER,PR	SMA , S-100,Actin
2	Omar F Altal et al.[42]	53/F	2022	Left vulvar region	13.1 × 10.9 × 10.7 cm	giant vulvar angiofibroma	CD34, SMA	Desmin
3	Sarah Van Mulders [43]	34/F	2020	vagina	5 cm	Cervicovaginal cellular angiofibroma	CD 34, ER positive	S100, SMA and desmin
4	Kamitani R[44]	77/M	2020	Left inguinal	40mm	Inguinal cellular angiofibroma	CD 34,SMA,Desmin	S100

A complete workup, including clinical history, radiological findings, and fine needle aspiration cytology, should be performed in all suspected soft tissue sarcoma cases. Histopathological examination and ancillary methods such as IHC and EM studies help make an accurate diagnosis of tumors.[45]

CONCLUSIONS

Soft tissue tumors can have varied clinical and histomorphological presentations. For timely diagnosis of rare soft tissue tumors, a comprehensive approach including radiology, cytology (FNAC), histopathology, and ancillary studies like IHC and molecular analysis are useful to make an accurate diagnosis of tumors. However, in lower resource areas like rural regions, histopathology remains the gold standard for the typing of tumors.

Informed Consent – Written informed consent was taken from all patients for publication of this case series.

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