Soft Tissue Sarcomas and Mimicking Lesions Encountered in Surgical Career: Unanswered Questions and Surgical Bewilderment

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Abstract:

Soft tissue sarcomas are malignancies which arise from the mesodermal tissues although in some cases they can be ectodermal in origin. Common sites of involvement include the extremities followed by intraabdominal and retroperitoneal regions. Clinical symptoms in the extremities typically include a painless enlarging mass while in the retroperitoneal region vague symptoms like dull pain, fullness and loss of appetite may also be encountered. Diagnostic guidelines include radiological followed by pathological examination for confirmation. Factors such as the size, grade, location, histology as well as patient related factors like age and comorbidities, determine the specific approach needed. Surgery is the mainstay of treatment for any sarcoma and radiation can be used in the adjuvant or neoadjuvant setting. Use of chemotherapy, although seen to be beneficial in certain patients, is controversial and hence no standardized protocol is available for the same. However, certain STS are highly chemo sensitive like Synovial sarcoma, as we have documented in this paper. This paper aims to highlight a series of sarcomas and lesions presenting as sarcomas over a course of fourteen years. The confirmatory diagnosis of each such case was cytopathological in order to decrease the chances of local recurrence after which they were managed accordingly. On follow up of four out of these five patients, there has been no local recurrence till date.

Keywords: *mesodermal, retroperitoneum, adjuvant, neoadjuvant*

1. Introduction:

Sarcomas constitute a heterogeneous group of solid tumors[1] of mesenchymal cell origin with distinct clinical, pathological and immunohistochemical features. They are usually divided into two broad categories- 'sarcomas of soft tissues'[2] and 'sarcomas of bone[3]'.

Soft Tissue Sarcomas (STS)[4] are the most frequent sarcomas. Collectively, sarcomas account for approximately 1% of all adult and 15% of pediatric malignancies. *Etiological*[5] causes for the same are varied and differ according to the various histopathological types. Prior 'Radiation Therapy' (RT)[6] given years before is a risk factor for the development of certain STS like UPS[7] (Undifferentiated Pleomorphic Sarcoma), angiosarcoma[8] and lymphangiosarcoma[9]. Hereditary syndromes like Gardener's Syndrome[10] for desmoid tumors, Von Recklinghausen's disease[11] for Malignant Peripheral Nerve Sheath Tumor (MPNST)[12] is also an *etiological* factor. More than 50 different histologic subtypes of STS have been identified; with UPS (previously known as malignant fibrous histiocytoma) being the most common followed by GIST[13], liposarcoma, leiomyosarcoma[14], synovial sarcoma[15], and malignant peripheral nerve sheath tumors[16]. Rhabdomyosarcoma[17] is the most common STS of childhood.

The most common primary sites are the extremities (60%) followed by visceral and retroperitoneal, trunk and head neck. The anatomic site of the primary disease is an important variable influencing treatment and outcome. STS in the extremity most commonly metastasize to the lung while those arising in the abdominal cavity or retroperitoneum commonly metastasize to the liver and peritoneum.

Management guidelines include confirmation of diagnosis by radiology and pathology, followed by surgical management in resectable cases. In extremity sarcomas, the trend towards limb salvage surgery has increased. Amputation of limb is reserved for very few cases with continued recurrence or very few high-grade tumors. Most high-grade sarcomas are treated with

[1] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/tumor
[2] https://www.cancer.gov/types/soft-tissue-sarcoma
[3] https://www.hopkinsmedicine.org/health/conditions-and-diseases/sarcoma/bone-sarcomas
[4] https://www.cancer.gov/types/soft-tissue-sarcoma
[5] https://www.dictionary.com/browse/etiology
[6] https://en.wikipedia.org/wiki/Radiation_therapy
[7] https://www.mayoclinic.org/diseases-conditions/undifferentiated-pleomorphic-sarcoma/symptoms-causes/syc-20389554
[8] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/angiosarcoma
[9] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/angiosarcoma
[10] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/gardner-syndrome
[11] https://rarediseases.org/rare-diseases/neurofibromatosis-type-1-nf1/
[12] https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-soft-tissue-tumors/mpnst
[13] https://www.mayoclinic.org/diseases-conditions/gastrointestinal-stromal-tumors/cdc-20387715
[14] https://www.mayoclinic.org/diseases-conditions/leiomyosarcoma/cdc-20387733
[15] https://www.mayoclinic.org/diseases-conditions/synovial-sarcoma/cdc-20387747
[16] https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-soft-tissue-tumors/mpnst
[17] https://www.cancer.org/cancer/rhabdomyosarcoma/about/what-is-rhabdomyosarcoma.html

radiotherapy which was be given both pre operatively or post operatively. Margin positive sarcomas are also followed up with radiation therapy. Sarcomas in general are chemo-resistant, however certain STS like synovial sarcoma[18] and osteosarcoma[19] are highly sensitive to chemotherapy hence they are included in their management protocol. Advancement in the field of targeted therapy is also being studied. STS has a variable potential for recurrence, the management guideline of such an event is always re-excision. If this is not possible, then salvage radiotherapy is usually preferred.

2. Definition of Terminologies Used:

A brief note about the Terminologies, which are used in this Article, are given below for ready references of the hon'ble readers.

- UPS*: Undifferentiated Pleomorphic Sarcoma (UPS*) is a rare type of cancer that begins mostly in the soft tissues of the body. Soft tissues connect, support and surround other body structures. UPS usually occurs in the arms or legs. Less often it can happen in the area behind the abdominal organs (retroperitoneum).
- Angiosarcoma and Lymphangiosarcoma: A type of cancer that begins in the cells that line blood vessels or lymph vessels. Cancer that begins in blood vessels is called hemangiosarcoma. Cancer that begins in lymph vessels is called lymphangiosarcoma.
- **Gardner's Syndrome:** A rare, inherited disorder in which many polyps (abnormal growths of tissue) form on the inner walls of the colon and rectum. It is a type of familial adenomatous polyposis and a type of autosomal dominant genetic disease.
- **Von Recklinghausen's Disease:** *Neurofibromatosis 1 (NF1)*, also called Von Recklinghausen's Disease, is a genetic disorder characterized by the development of multiple noncancerous (benign) tumours of nerves and skin (neurofibromas) and areas of abnormal skin colour (pigmentation).
- **MPNST**: *Malignant Peripheral Nerve Sheath Tumor (MPNST*) is a cancer of the cells that form the sheath that covers and protects peripheral nerves. Peripheral nerves are those outside of the central nervous system (brain and spinal cord).
- **GIST:** *Gastrointestinal Stromal Tumors (GISTs)* are soft tissue sarcomas that can be located in any part of the digestive system. Their most common sites are the stomach and small intestine
- **Leiomyosarcoma**: Leiomyosarcoma is a rare type of cancer that begins in smooth muscle tissue.

[18] https://www.mayoclinic.org/diseases-conditions/synovial-sarcoma/cdc-20387747
[19] https://www.cancer.org/cancer/osteosarcoma/about/what-is-osteosarcoma.html

- **Osteosarcoma:** osteosarcoma (also called *Osteogenic Sarcoma*) is the most common type of cancer that starts in the bones
- **Synovial Sarcoma**: is a rare type of cancer that tends to arise near large joints, particularly the knee, in young adults. Despite its name, it typically doesn't affect the interior of joints, where synovial tissue and fluid are located.
- **Rhabdomyosarcoma (RMS):** RMS is a type of sarcoma made up of cells that normally develop into skeletal (voluntary) muscles.
- **Dermatofibrosarcoma Protuberans (DFSP)**: Itis a very rare type of skin cancer that begins in connective tissue cells in the middle layer of your skin (dermis).

3. Objectives of the Study:

The purpose of the study are as follows-

i) To observe the Symptoms, Causes and related aspects behind different Soft Tissue Sarcomas and the Lesions Mimicking them through different Case-Studies;

ii) To find out the unanswered questions and the Surgical Bewilderment in Surgical Career.

4. Materials and Methods:

4.1. Methodology followed:

The case series reported here are a series of five patients. The first documented patient was studied in 2006 at our clinic and the rest were studied from June 2013 to November 2018 in KPC Medical College and Hospital[20], Kolkata. All these patients were diagnosed on preliminary examinations as a soft tissue tumour. Cytology was done which gave us our preoperative diagnosis and the patients were managed accordingly. Three of these patients were diagnosed with soft tissue sarcoma, one as a benign soft tissue tumour while one of the patients, though reported initially via initial cytological examination as a sarcomatous malignancy, was later re diagnosed as a carcinoid tumour after a review of the same slide. Of these patients, one was female while the rest four were male patients. Their age of presentation ranged from twenty-five to sixty-seven.

4.2 Tools used:

Following three sets of Tools have been prepared by the members of the study-group to observe, collect data and for analyzing the collected data to be revealed from different Case-Studies.

[20] http://kpcmedicalcollege.in/

i) **Questionnaire for Pre-history of the Patient:** Detailed history of the Patients, and their family members, particularly related to the disease; i.e., **Soft Tissue Sarcomas and the Lesions Mimicking them;**
ii) **Observation Schedule during Treatment:** List of Cytological Examinations and Laboratory Examinations to be made before and during treatment of the Patients;
iii) **Observation Schedule for Post Treatment:** List of Items to be observed related to follow up and major recurrence.

4.3 Sample Design:

Table-1: Sample Design of the Case Studies

Sl. No	Brief about the Sample/ Patients	Age	Sex	Date/ Year of Case Study		Place of Study	Remarks (If any)
				Beginning	Completion		
1	Painful Lesion Upper Left Thigh	31	F	2006	2008	clinic	Presented With Empyema Gall Bladder
2	Swelling on the Lower Two-Third of his Left Forearm	27	M	2012	2021	KPMCH	-
3	A Large Breast Mass on the Right	55	M	2017	2020	KPCMCH	No Fixity.
4	Huge Swelling of Right Gluteal Region	25	M	2017	2020	KPCMCH	Increased Slowly In 15years
5	Left Sided Dull Aching Chest Pain	67	M	2018	2020	clinic	-

5. Case Series:

All these patients were diagnosed on preliminary examinations as a soft tissue tumour. Cytology was done which gave us our preoperative diagnosis and the patients were managed accordingly. Three of these patients were diagnosed with soft tissue sarcoma, one as a benign soft tissue tumour while one of the patients, though reported initially via initial cytological examination as a sarcomatous malignancy, was later re diagnosed as a carcinoid tumour after a review of the same slide. Of these patients, one was female while the rest four were male patients. Their age of presentation ranged from twenty-five to sixty-seven.

5.1 Case Study No-1:

A 31-year-old female patient, presented in 2006 with a painful lesion of about 1.5X 1 cm on medial aspect of left upper thigh with no significant family history. The swelling was tender and not fixed to any underlying structures. There were no palpable lymph nodes. Cytology showed mitotic spindle cells[21] in vascular stroma of malignant etiology. Other reports including chest roentgenogram were normal. Patient was posted for wide local excision following pre anesthetic

[21] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2807548/

fitness and final histopathology report diagnosed the case as biphasic synovial sarcoma[22] with no area of necrosis. She was then referred to another Centre where she received adjuvant radiotherapy. She completed her radiotherapy cycle in August, 2006. Thereafter patient was followed up every 2 months for the first year and 6 monthly for the next two years. She presented with empyema gallbladder[23] after one year and subsequently underwent open cholecystectomy. Patient was followed up and was healthy with no further recurrences or metastasis. She also had a full-term pregnancy and delivered a female child in 2008. Thereafter patient has had no significant medical history on regular follow up.

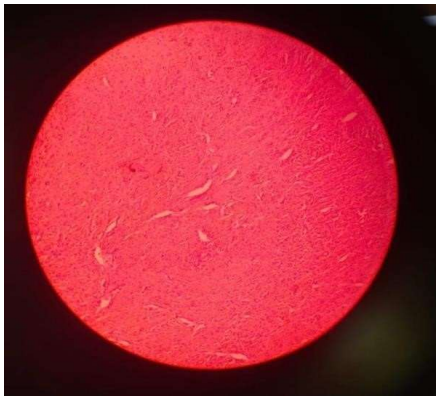

Figure- 1: microscopic study of mitotic spindle cell

(Photography by Authors of this Study Group)

5.2 Case Study No-2:

The second patient is a twenty-seven-year-old male who presented in 2012 with a swelling on the lower two-third of his left forearm which was slowly growing over the past three months. The swelling was around 2cm X 1cm, greyish, broad based with a smooth surface. Cytology was suggestive of spindle cells with mitosis. A wide local excision was done and final histopathology report was diagnosed as benign fibrous histiocytoma[24]. Patient was followed up and is doing well till date.

5.3 Case Study No-3:

The third case is that of a fifty-five-year-old male patient who presented in 2017 with a large breast mass on the right. It was mobile with no fixity to the underlying muscle or fascia. The left breast and both axillae were normal. Cytology was suggestive of cellular atypia with hemorrhage. Chest radiogram was normal as were the other blood parameters. Patient underwent mastectomy and axillary clearance. Final histopathology report was reported as

[22] https://www.mayoclinic.org/diseases-conditions/synovial-sarcoma/cdc-20387747
[23] https://emedicine.medscape.com/article/174012-overview
[24] http://tumorsurgery.org/tumor-education/bone-tumors/types-of-bone-tumors/benign-fibrous-histiocytoma.aspx

dermatofibrosarcoma protuberans[25] with low mitotic activity. He was then referred to a radiation oncologist. Patient was followed up for two and half years and reported no significant history.

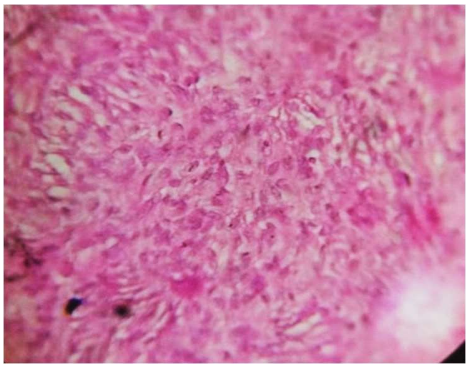

Fig – 2 : Cytopathological analysis of patient of dermatofibrosarcoma protuberans

(Photography by Authors of this Study Group)

5.4 Case Study No-4:

The fourth case is that of a twenty-five years old male who presented in 2017 with a huge swelling of right gluteal region which was gradually increasing in size for the last fifteen years. On examination, swelling was mobile and non-tender. Patient also gave a family history of malignancy of maternal uncle but could not specify. A cytology report was done which was suggestive of a low grade sarcomatous lesion[26]. Wide local excision with a 2cm margin was done and final histopathology and immunohistochemistry report was suggestive of low grade fibromyxoid sarcoma[27]. Patient did not require adjuvant radiotherapy and on regular follow up patient has presented with no fresh complaints and reported no recurrence.

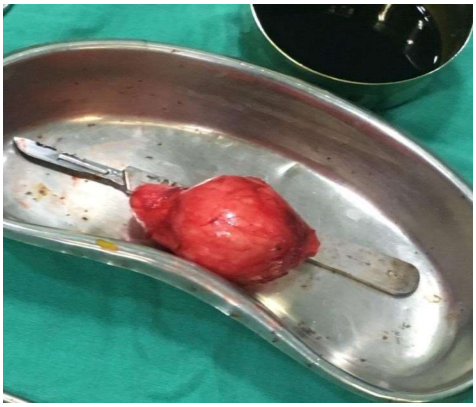

Fig-3 : Post Operative Specimen of Fibromyxoid Sarcoma

(Photography by Authors of this Study Group)

[25] https://www.mayoclinic.org/diseases-conditions/dermatofibrosarcoma-protuberans/cdc-20352949
[26] https://www.cancer.gov/types/soft-tissue-sarcoma
[27] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-grade-fibromyxoid-sarcoma

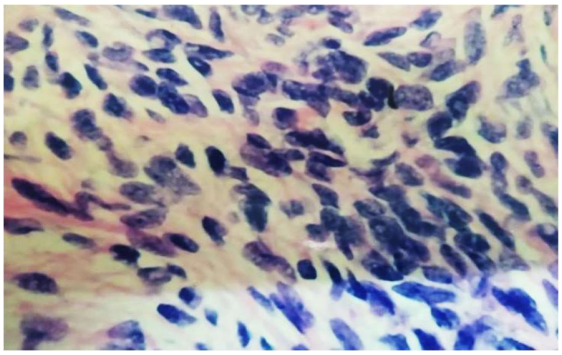

Fig-4: Cytopathological Analysis of Patient with Fibromyxoid Sarcoma

(Photography by Authors of this Study Group)

5.5 Case Study No-5:

Our fifth patient is a sixty-seven-year-old male who attended our clinic in 2018 with left sided dull aching chest pain. He also gave history of hemoptysis. Chest radiogram showed emphysematous[28] changes with a large space occupying lesion on the apex of his left lung. A CT scan was done thereafter which gave the impression of a soft tissue mass with lobulated margins covered by sub segmental atelectasis of adjacent lung segments in left upper lobe of lung. CT guided FNAC was done which suggested a sarcomatous lesion[29]. Since primary sarcoma of the lung is exceedingly rare, and on thorough investigation no other space occupying lesion was found, a repeat cytology was done to confirm the diagnosis. Patient was re-diagnosed as a case of carcinoid tumor[30] of lung on repeat cytology although he gave no history of flushing attacks or diarrhea. Unfortunately, patient was lost to follow up thereafter.

Table-2: Synopsis of the Case Studies

Case Study No	Brief about Sample / Patient	Age & Sex	Period of Case Study		Observations Noted	Treatment Suggested/ Done
			Beginning	Completion		
1	The patient, presented with **a painful lesion of about 1.5X 1 cm on medial aspect of left upper thigh** with no significant family history	31 Female	2006	2008	The swelling was tender and not fixed to any underlying structures. There were no palpable lymph nodes. Cytology showed mitotic spindle cells in vascular stroma of malignant etiology. Other reports including chest roentgenogram were normal	Excision surgery was done on the same year and radiotherapy was conducted as mentioned in the case report
2	The patient who presented **with a swelling on the**	27/M	2012	2021	The swelling was around 2cm X 1cm, greyish, broad based with a smooth surface. Cytology was	Excision surgery was done on the same year and radiotherapy was

[28] https://www.mayoclinic.org/diseases-conditions/emphysema/symptoms-causes/syc-20355555
[29] https://www.cancer.gov/types/soft-tissue-sarcoma
[30] https://www.mayoclinic.org/diseases-conditions/carcinoid-tumors/symptoms-causes/syc-20351039

	lower two-third of his left forearm which was slowly growing over the past three months				suggestive of spindle cells with mitosis	conducted as mentioned in the case report
3	The patient who presented in 2017 with a large breast mass on the right. It was mobile with no fixity to the underlying muscle or fascia.	55/M	2017	2020	The left breast and both axillae were normal. Cytology was suggestive of cellular atypia with hemorrhage. Chest radiogram was normal as were the other blood parameters.	Mastectomy with axillary clearance
4	A patient who presented with a huge swelling of right gluteal region which was gradually increasing in size for the last fifteen years	25/M	2017	2020	swelling was mobile and non-tender. Patient also gave a family history of malignancy of maternal uncle but could not specify. A cytology report was done which was suggestive of a low grade sarcomatous lesion	Wide local excision with a 2cm margin was done and final histopathology and immunohistochemistry report was suggestive of low-grade fibro myxoid sarcoma No adjuvant therapy was required.
5	a sixty-seven-year-old male who attended our clinic in 2018 with left sided dull aching chest pain	67/M	2018	2020	Chest radiogram showed emphysematous[31] changes with a large space occupying lesion on the apex of his left lung. A CT scan was done thereafter which gave the impression of a soft tissue mass with lobulated margins covered by sub segmental atelectasis of adjacent lung segments in left upper lobe of lung. CT guided FNAC was done which suggested a sarcomatous lesion	-

6. Findings of the Study:

6.1 Findings of Case Study No-1: it was case of biphasic synovial sarcoma with no area of necrosis

6.2 Findings of Case Study No-2: it was case of benign fibrous histiocytoma

6.3 Findings of Case Study No-3: it was case of dermatofibrosarcoma protuberans with low mitotic activity

[31] https://www.mayoclinic.org/diseases-conditions/emphysema/symptoms-causes/syc-20355555

6.4 Findings of Case Study No-4: it was case of low-grade fibro myxoid sarcoma

6.5 Findings of Case Study No-5: it was case of carcinoid tumor

7. Discussion:

Soft tissue sarcomas can have a diverse range of presentation while some tumors, albeit looking like a soft tissue sarcoma on initial examination, can turn out to be something quite different. The age of presentation, sites as well as the chief complaints are varied.

While a core needle biopsy is the recommended confirmatory diagnosis before surgery, we opted for a cytology report for these patients. This allowed us to decrease the chances of seeding along the biopsy tract and also easily include the site of aspiration in our final operative specimen. Thus, this decreased the chances of local recurrence.

Another point of bewilderment for us was whether pregnancy and childbirth in synovial sarcoma cause any decrease in recurrence for the patient. But there have not been any reported studies which provide such results. Patient was cured in all probability because of prompt surgery, adjuvant full course of chemotherapy, since Synovial Sarcoma is one of the few STS which respond readily to systemic treatment with chemotherapy. Also, synovial sarcoma has a reportedly better prognosis in females.

8. Conclusion:

STS present in a wide spectrum of patients independent of sex or age. These patients have no classical symptoms on presentation hence it should always be included in our differential. Although STS is relatively chemo resistant, certain histopathological variants like Synovial Sarcoma show excellent response to systemic therapy with chemotherapeutic drugs and hence included in the treatment protocol of such cases. A core needle or true cut biopsy is the recommended norm prior to surgery however, in certain patients where the clinical as well as initial cytological report make a preoperative diagnosis clear, we can proceed without a biopsy. This decreases the chances of local seeding of tumor cells and thus decreases chances of local recurrence.

9. Suggestions for Further Study:

This study aimed at highlighting a series of sarcomas and lesions presenting as sarcomas over a period of fourteen years. The confirmatory diagnosis of each such case was cytopathological in order to decrease the chances of local recurrence after which they were managed accordingly. On follow up of four out of these five patients, there has been no local recurrence till date.
But further study could help one evaluate long term effect of the treatment as well as recurrence.

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