Study of Clinico-Pathological Characters of Extremity Soft Tissue Sarcoma

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ABSTRACT

Background: Histological analysis is used to distinguish between benign and malignant tumors, allowing for the definitive diagnosis of soft tissue sarcoma (STS).

Objective: To evaluate the clinicopathological characteristics of extremity soft tissue sarcoma.

Subjects and Methods: The present cross-sectional study included a total sample of 18 participants with soft tissue sarcoma planned for surgery according to their tissue biopsy.

Results: Regarding the characteristics of STS in the present results, the mean size was 20.1± 10.6 cm, ten patients (55.6%) had STS on the right side and 44.4% had STS on the left side. Only five patients (27.8%) had superficial STS and 13 (72.2%) had deep STS. Regarding the stages of STS, 2 (11.1%) were stage IA, 3 (16.7%) were stage IB, 4 (22.2%) were stage IIA, 6 (33.3%) were stage IIB, 1 (5.6%) was stage IIIA and 2 (11.1%) were stage IIIB. Regarding the histopathological diagnosis of STS, 2 (11.1%) had undifferentiated pleomorphic sarcoma, 3 (16.7%) had liposarcoma, 7 (38.9%) had rhabdomyosarcoma, 3 (16.7%) had myxofibrosarcoma, and 3 (16.7%) had leiomyosarcoma. The comparison between males and females regarding characteristics and histopathological types of STS showed that there was no statistically significant difference. **Conclusion**: Males are more likely to be diagnosed with soft tissue sarcoma, while middle-aged people are disproportionately afflicted. The lower extremities are the most prevalent site of involvement, and rhabdomyosarcoma is the most common histologic subtype. The clinicopathological features of soft tissue sarcoma are not influenced by gender distribution.

Keywords: Clinico-pathological characters, Extremity, Soft tissue sarcoma.

INTRODUCTION

Rare connective tissue malignant tumors called sarcomas are characterized by their heterogeneity and the ability to differentiate into several cell types, including those of other connective tissues (lipocytes, fibrous supporting structures, muscle, etc.), visceral tissues, and bone. As much as 40% of all STS develop in the extremities. Lower extremities more often than upper ones (28%) (12 percent). About 44% of all STS involving an extremity occur in the thigh [(1)].

Genetic and environmental variables (such as chemical carcinogens), irradiation, viral infections (especially HHV-8), and immunological weakness have all been linked to an increased risk of STS, although its exact cause remains unknown. Scarred or implanted areas can also experience sporadic occurrences. Symptom-free and big at diagnosis, soft-tissue sarcomas spread hematogenously, most commonly to the lungs [(2)].

Histology is used to provide the definitive diagnosis of STS, ruling out the possibility of a benign growth and, if cancerous, determining the sarcoma's histological grade as well as subtypes [(3)]. When a mass cannot be identified by the use of clinical history, physical examination, laboratory tests, or imaging, a biopsy may be required to make a definitive diagnosis. Biopsies are performed to gather diagnostic tissue while minimizing collateral damage, stopping the spread of cancer, and interfering with future treatment options. Some methods that have been developed to achieve these aims are open surgical biopsy, fine-needle aspiration (FNA) as well as core biopsy [(4)].

Despite the need for drastic or extensive surgical excision as a standard of treatment, the 5-year survival rate for those with localized STS tumors is just 55% to 70%. One of the primary difficulties in STS care is the local relapse of the tumors, which can occur at any time during the course of treatment [(5)].

It was the goal of this study, to evaluate the clinicopathological characteristics of extremity soft tissue sarcoma.

SUBJECTS AND METHODS

Subjects: Our study is a cross-sectional study done on a study sample of 18 cases with soft tissue sarcoma planned for surgery at the General Surgery Department of Zagazig University hospitals.

Inclusion criteria: Patients with STS involving the extremities, all age groups, both sexes, cases during study time, and patients who agreed to sign informed consent.

Exclusion criteria: Patients presenting with local recurrence, patients unfit for surgery, patients who refused to share in the study, and patients who missed the follow-up.

All patients ha ve gone through:

A. Complete history: Each individual will have a thorough clinical history taken, with an emphasis on their current symptoms.

B. Evaluation clinically: Both general and local examinations were performed to every patient.

Operative measures:

The incision was made at the appropriate position and size relative to the tumor based on the information so obtained to determine the extent of the operation.

Biopsy: To properly diagnose STS, a tissue sample should be conducted, ideally by a sarcoma surgeon.

A core needle or Trucut needle biopsy is the quickest and

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most accurate way to obtain tissue samples in an outpatient setting. With either of the biopsy needles, a tiny sample of tissue can be removed for testing with minimal damage to surrounding tissue. Most seasoned pathologists found this amount of tissue sufficient for investigation, and in over 90% of cases, they were able to draw a firm conclusion.

The 'Whoops procedure':

Inadequate margins and a subsequent histological diagnosis of STS after the removal of an undiagnosed soft tissue mass are referred to as a "whoops procedure." Concerns can also pertain to future management, in addition to the psychological discomfort the patient may experience as a result of an unexpected diagnosis. For instance, because of the prior operation, it is now more challenging to comprehend images. It was common for the tumor bed and its immediate surroundings to become scarred and contaminated with tumor cells.

If the initial STS was thin and small, a wide re-excision with a 2 cm margin might be all that's needed to clear it. Roughly a quarter of the STS were found to be 3 centimeters in depth after the whoops. Tumors greater than 5 cm in diameter and located deeper in the body typically required a more extensive excision, complicated reconstruction, and adjuvant radiation.

Classification of surgical margins: Four distinct surgical margins can be taken: intra-lesional, marginal, broad, and radical. The rate of local recurrence is directly proportional to the size of the initial excision, and the Enneking classification of STS tumor margin is generally accepted as the gold standard for such classifications.

- Since local recurrence of sarcoma is so common, intra-lesional excision (also known as the "shell-out") is no longer a viable option for treatment. Only if it were intended to be a palliative measure would it be acceptable.
- In marginal excisions, There was a higher probability of tumor recurrence if the surgical plane contained the pseudo capsule and/or reactive zone. Nonetheless, such gaps may occasionally be inevitable when limb salvage is being performed.
- Wide local excision focused on the tumor and the surrounding reactive zone but did not move out of the tumor's compartment.
- Radical excision was doubted to be attempted if limb salvage was intended.

Post-operative:

The pathologist received the removed tissue and did a thorough analysis.

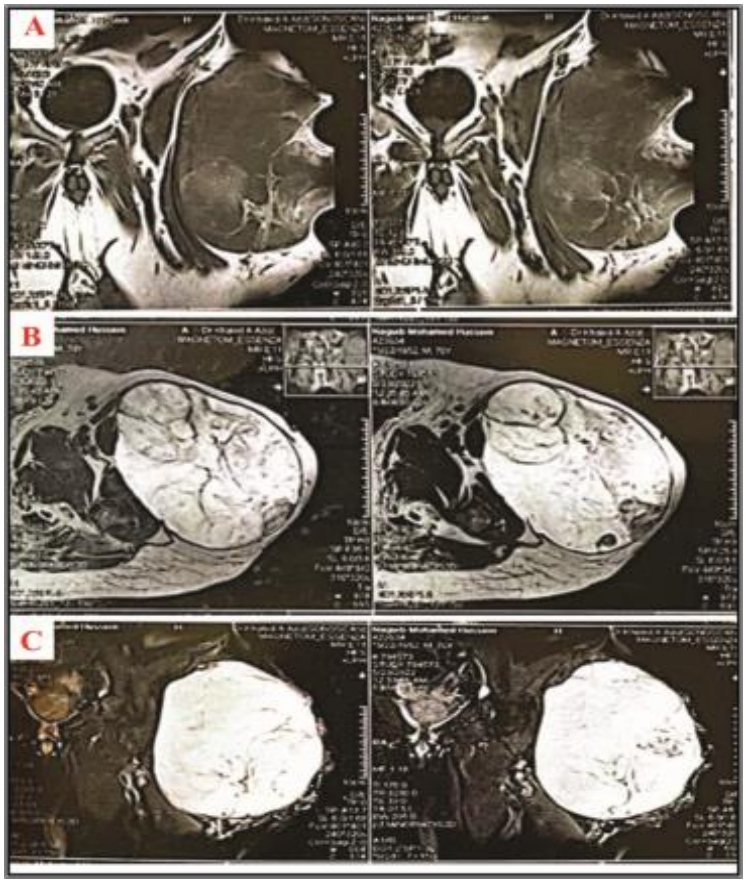

Figure (1. A): Multiplanar multisequence MRI of hip and lower limb without contrast, A- T1, B-T2, C-Stair show large well-defined heterogeneous mass lesion seen involving the lateral aspect of the left thigh (subcutaneous in location) measuring (17×23 cm), and see the low signal intensity in T1 and high signal intensity in T2 and stair.

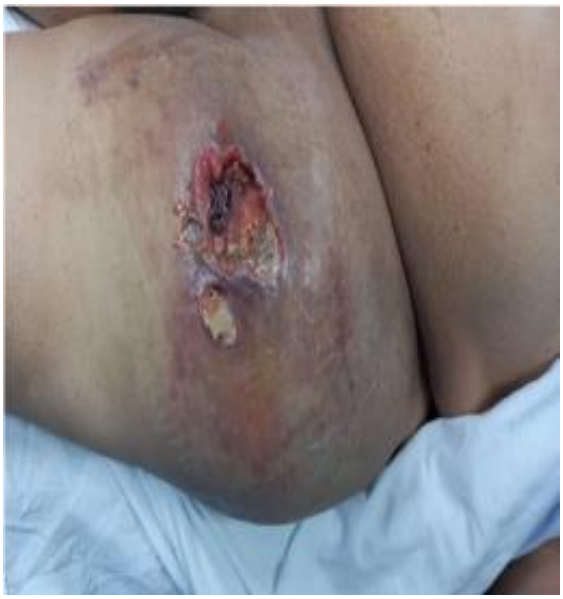

Figure (1. B): Soft tissue sarcoma left upper thigh.

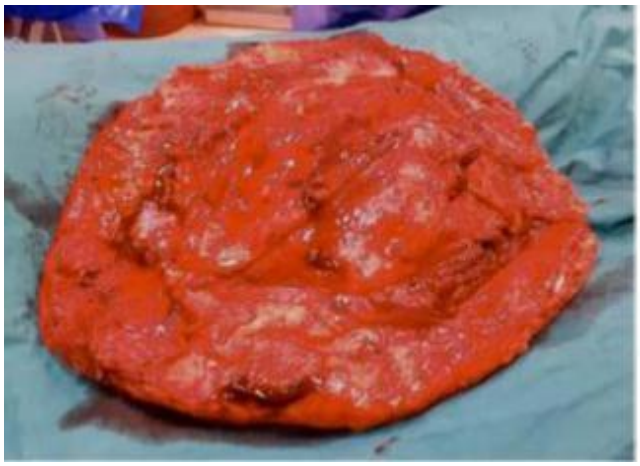

Figure (1. C): Excisional biopsy of STS of the thigh.

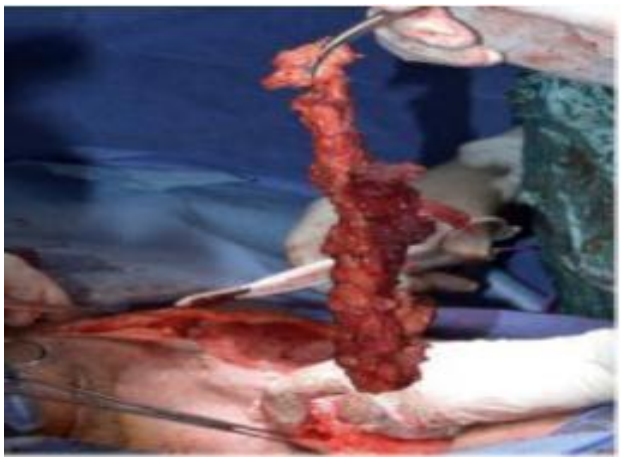

Figure (1.D): Excisional biopsy of STS.

Figure (1): Showing MRI and Images of excisional biopsy of cases.

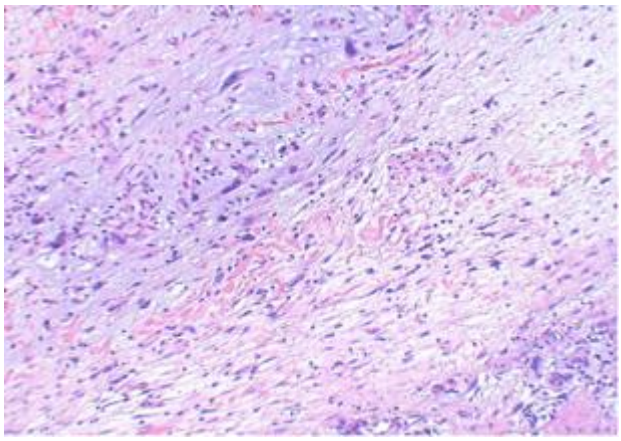

Figure (2. A): Myxofibrosarcoma- Cellular atypia with nuclear pleomorphism and enlarged hyperchromatic nuclei is seen at least focally

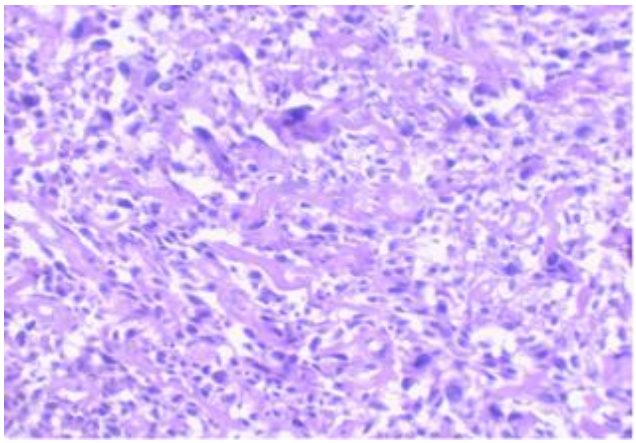

Figure (2. b): Rhabdomyosarcoma; characterized by large pleomorphic cells with cytoplasmic eosinophilia, which stained for myogenin

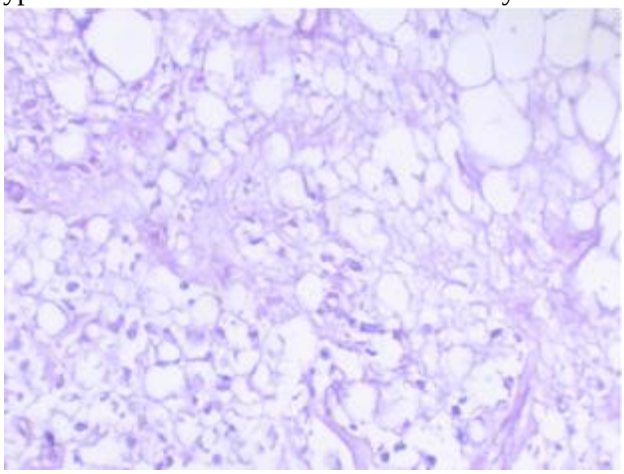

Figure (2. C): Liposarcoma; lipoblasts that have a pleomorphic shape are present.

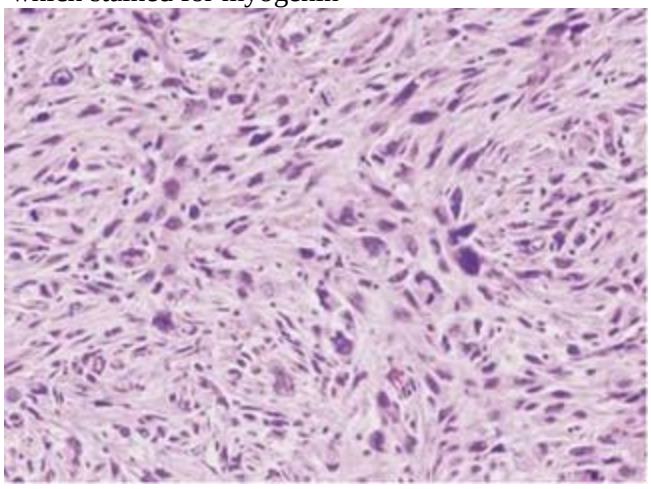

Figure (2.D): Leiomyosarcoma: characterized by eosinophilic cytoplasm and spindle-shaped pleomorphic cells. The smooth muscle actin stain is very visible in these tumors.

Figure (2): Histopathological images of 4 cases.

Ethical approval:

The Research Ethics Committee at Zagazig University approved the research. (IRB number: #9480/20-4-2022) If and only if every person involved signed a waiver acknowledging they had read and understood the risks involved. The Helsinki Declaration, published by the World Medical Association, lays out guidelines for how researchers can safely and ethically interact with patients and other people who volunteer to be studied.

Statistical analysis

The gathered data was analyzed using a computer program called Statistical Package for the Social Services, version 20 (SPSS).

To illustrate the results, charts, and tables were used. Confidence intervals, medians, means, and standard deviations were also provided for the numerical data. Quantitative data like frequency and percentage were used to illustrate the data. With quantitative independent variables, the student's t-test (T) is used to evaluate the data. Both the Pearson Chi-Square and the Chi-Square for Linear Trend (X^2) were used to evaluate the qualitative validity of the collected data. P values of 0.05 or below were deemed statistically significant.

RESULTS

The mean age of 26.9± 10.4 years and the median of 26 ranging from 10 years to 52 years. Ten participants were males and eight were females.

Among the participants, four patients had a positive family history of soft tissue sarcoma while 14 (77.8%) had a negative family history. Three participants had diabetes, four patients had hypertension and only two patients had ischemic heart disease.

Nearly sixty-seven percent of the participants complain of swelling, three patients (16.7%) complain of pain, only two patients complain of ulceration and one participant discovered STS accidentally. The mean systolic blood pressure was 126.8± 9.8 mmHg and the mean diastolic blood pressure was 80.9± 4.6 mmHg. The mean heart rate was 77.1± 5.5 bpm and the mean temperature was 38.2± 0.6 °C.

Table (1): Characteristics of the participated group.

Variable		n= 18
Age (years)	**Mean ± SD**	26.9± 10.4
	Median (Range)	26 (10, 52)
Gender	**Male, n (%)**	10 (55.6)
	Female, n (%)	8 (44.4)
Family history of STS	**Yes, n (%)**	4 (22.2)
	No, n (%)	14 (77.8)
DM	**Yes, n (%)**	3 (16.7)
	No, n (%)	15 (16.7)
HTN	**Yes, n (%)**	4 (22.2)
	No, n (%)	14 (77.8)
IHD	**Yes, n (%)**	2 (11.1)
	No, n (%)	16 (88.9)
Complain	**Swelling, n (%)**	12 (66.7)
	Pain, n (%)	3 (16.7)
	Ulceration, n (%)	2 (11.1)
	Incidental finding, n (%)	1 (5.6)
Systolic blood pressure	**Mean ± SD**	126.8± 9.8
	Median (Range)	127 (110, 140)
Diastolic blood pressure	**Mean ± SD**	80.9± 4.6
	Median (Range)	80 (76, 90)
HR	**Mean ± SD**	77.1± 5.5
	Median (Range)	78 (70, 87)
Temperature	**Mean ± SD**	38.2± 0.6
	Median (Range)	38.4 (37.3, 39.1)

Seven patients (38.9%) had STS located in the thigh or buttock, three patients (16.7%) had STS located in the knee or lower leg, and two patients (11.1%) had STS located in the arm.

Three patients (16.7%) had STS located in the elbow or forearm. Three patients (16.7%) had located in the shoulder. The mean size was 20.1± 10.6 cm, ten patients (55.6%) had STS on the right side and 44.4% had STS on the left side. Only five patients (27.8%) had superficial STS and 13 (72.2%) had deep STS.

Table (2): Site and characteristics of soft tissue sarcoma among the participants.

Variable		n= 18
Site of STS	Thigh or buttock	7 (38.9)
	Knee or lower leg	3 (16.7)
	Arm	2 (11.1)
	Elbow or forearm	3 (16.7)
	Shoulder	3 (16.7)
Size	Mean ± SD	20.1± 10.6
	Median (Range)	18.7 (6.2, 36.0)
Side	Right, n (%)	10 (55.6)
	Left, n (%)	8 (44.4)
Depth	Superficial, n (%)	5 (27.8)
	Deep, n (%)	13 (72.2)

Regarding the histopathology of STS, 2 (11.1%) had undifferentiated pleomorphic sarcoma, 3 (16.7%) had liposarcoma, 7 (38.9%) had rhabdomyosarcoma, 3 (16.7%) had myxofibrosarcoma, and 3 (16.7%) had leiomyosarcoma. Regarding the grades of STS, 5 (27.8%) were grade 1, 9 (50%) were grade 2, and 4 (22.2%) were grade 3.

Table (3): Histopathological and FNCLCC grading data of the soft tissue sarcoma.

Variable		N (%)
Histopathology of STS	Undifferentiated pleomorphic sarcoma	2 (11.1)
	Liposarcoma	3 (16.7)
	Rhabdomyosarcoma	7 (38.9)
	Myxofibrosarcoma	3 (16.7)
	Leiomyosarcoma	3 (16.7)
Grades of STS	Grade 1	5 (27.8)
	Grade 2	9 (50)
	Grade 3	4 (22.2)

Regarding the stages of STS, 2 (11.1%) were stage IA, 3 (16.7%) were stage IB, 4 (22.2%) were stage IIA, 6 (33.3%) were stage IIB, 1 (5.6%) was stage IIIA and 2 (11.1%) were stage IIIB.

Table (4): AJCC Staging of the studied cases (n=18).

Variable		N (%)
Stages of STS	Stage IA	2 (11.1)
	Stage IB	3 (16.7)
	Stage IIA	4 (22.2)
	Stage IIB	6 (33.3)
	Stage IIIA	1 (5.6)
	Stage IIIB	2 (11.1)

No statistically significant difference between the males and females regarding size, side, and depth of STS (p> 0.05).

Table (*2*): Comparison between males and females regarding characteristics of STS.

Variable		Males n= 10	Females n= 8	P-value
Size	**Mean ± SD**	17.9± 9.9	22.9± 11.6	0.337
Side	**Right, n (%)**	7 (70)	3 (37.5)	0.342
	Left, n (%)	3 (30)	5 (62.5)	
Depth	**Superficial, n (%)**	2 (20)	3 (37.5)	0.608
	Deep, n (%)	8 (80)	5 (62.5)	

Mann Whitney U test; Fisher Exact test

No statistically significant difference between the males and females regarding the histopathological types of STS (p> 0.05).

Table (6): Comparison between males and females regarding histopathological types of STS.

Variable		Males n= 10	Females n= 8	P-value
Histo-pathology of STS	**Un-differentiated pleomorphic sarcoma**	1 (10)	1 (12.5)	**>0.999**
	Liposarcoma	2 (20)	1 (12.5)	
	Rhabdomyo-sarcoma	4 (40)	3 (37.5)	
	Myxofibro-sarcoma	2 (20)	1 (12.5)	
	Leiomyo-sarcoma	1 (10)	2 (25)	

DISCUSSION

The present study demonstrated a total sample of 18 participants with soft tissue sarcoma planned for surgery were included in this study with a mean age of 26.9± 10.4 years and a median of 26 ranging from 10 years to 52 years. Ten participants were males and eight were females.

The current study has coincided with **Liang *et al.* [5].** The median age of the 477 patients was 42 (range: 6-85 years); this was reported in a retrospective study aiming to determine the prognostic significance of time to local recurrence (TLR) concerning overall survival (OS) and survival after local recurrence (SAR) in patients with soft tissue sarcoma (STS) of the extremity and abdominothoracic wall. With a male-to-female patient ratio of 1.47:1, there were 284 men and 193

women in the study. The age of cases in their study was higher than ours.

In contrast to the gender distribution in the current study, **Sternheim *et al.*** [6] in A retrospective database study on soft tissue sarcoma found an equal number of female and male patients.

Regarding the basic characteristics in the current study among the participants, four patients had a positive family history of soft tissue sarcoma while 14 (77.8%) had a negative family history.

Aliyu *et al.* [7] stated that fifteen (12.2%) participants were found to have a family history of cancer other than soft tissue sarcoma in either the first or second generation.

Our findings regarding complaints of the participants, nearly sixty-seven percent of the participants complain of swelling, three patients (16.7%) complain of pain, only two patients complain of ulceration and one participant discovered STS accidentally.

The present findings agreed with **Kobayashi *et al.*** [8] **who** found not one of their patients (n=14) had no history of trauma near where the tumor was located. In 14 cases, edema was the main issue, followed by pain (9 cases) and inflammation (2 cases), (7 cases).

Intratumoral hemorrhage and the subsequent fast stretching of surrounding tissues may be the root cause of mass-related pain. Since the lesion swells rapidly, (ii) imaging shows a fluid-filled mass, and (iii) hematomas are more prevalent than sarcomas, the former is often the initial diagnosis [8].

The current findings reported that respecting sites of STS, seven patients (38.9%) had STS located in the thigh or buttock, three patients (16.7%) had STS located in the knee or lower leg, two patients (11.1%) had STS located in Arm. Three patients (16.7%) had STS located in the elbow or forearm. Three patients (16.7%) had located in the shoulder.

The present findings agreed with **Kobayashi *et al.*** [8] results showed that the thigh was the most common site for malignancies (7 cases), followed by the lower thigh (3), buttocks (2), knee (1), and the neck (1) (1 case each).

Also, **Aliyu *et al.*** [7] reported that 53 patients (43%) had primary soft tissue sarcoma in their extremities; of these, 41 (33%) had lesions in their lower extremities and 12 (10%) had involvement of their upper limbs. Twenty-five patients, or 20%, had involvement in their head and neck, followed by seventeen patients, or 14%, in their abdominal region, and ten patients, or 10%, in their thoracic region.

Regarding the characteristics of STS in the present results, the mean size was 20.1± 10.6 cm, ten patients (55.6%) had STS on the right side and 44.4% had STS on the left side. Only five patients (27.8%) had superficial STS and 13 (72.2%) had deep STS.

According to the results of the current study, 54.9% of tumors were smaller than 5 cm and 45.1% were larger than 5 cm, as previously reported by **Liang *et al.* (5)** When broken down by body region, we see that 24.5% of tumors occurred in the upper extremities, 37.3% in the trunk/thoracic/abdominal wall, and 38.2% in the lower extremities. 44.2% were classified as having a surface tumor, whereas 58.8% were classified as having a deep tumor.

Regarding the grades of STS, 5 (27.8%) were grade 1, 9 (50%) were grade 2, and 4 (22.2%) were grade 3. **Ali *et al.*** [9] found that 70.6% of STS students were in the second grade and the rest were in the third A majority of **Carneiro *et al.*** [10] patients also had high-grade neoplasms (90 percent).

Regarding the stages of STS, 2 (11.1%) were stage IA, 3 (16.7%) were stage IB, 4 (22.2%) were stage IIA, 6 (33.3%) were stage IIB, 1 (5.6%) was stage IIIA and 2 (11.1%) were stage IIIB. Also, our findings are similar to what was mentioned by **Nedelcu and his colleagues** [11] as 27.7% had stage IV.

In this study, we found that most of the patients were in stage II (B then A) followed by stage IB, which basically contradicts a study that was carried out by **Morrison *et al.*** [12] that most patients were in stage II followed by III and finally I.

Regarding the histopathological diagnosis of STS, 2 (11.1%) had undifferentiated pleomorphic sarcoma, 3 (16.7%) had liposarcoma, 7 (38.9%) had rhabdomyosarcoma, 3 (16.7%) had myxofibrosarcoma, and 3 (16.7%) had leiomyosarcoma.

The present findings agreed with **Liang *et al.*** [5] **who** found that 28.7% of STS cases were fibrosarcoma, 13.2% were synovial sarcoma, 1.3% were alveolar soft part sarcoma and angiosarcoma, 6.5% were malignant peripheral neve sheath tumors, 2.9% were mesenchymal chondrosarcomas, and 2.5% were leiomyosarcomas. . Our results were in accordance with **Kunhi *et al.*** [13] pleomorphic sarcoma was found to be the most common histologic subtype, accounting for 43% of all cases. Besides synovial sarcoma, liposarcoma (6.5%) and fibrosarcoma (4.7%) were also frequently encountered histologic categories (6.7 percent).

Our study found that the inability to accurately target the small intratumoral nodule contributed to the poor rate of diagnosis by core needle biopsy. Their research found that open biopsies had a perfect diagnostic sensitivity. Excisional biopsies were performed on cancers with tiny, inaccessible nodules. Since the imaging features of hemorrhagic sarcoma and continuously growing hematoma are similar, the latter must be excluded with prompt aspiration, targeted biopsy, or surgical excision if the former is seen [8].

CONCLUSION

Men are more likely to be diagnosed with soft tissue sarcoma than women, and middle-aged people are disproportionately afflicted. Rhabdomyosarcoma is the most prevalent histologic type, and the lower extremities are the most common location of involvement. The clinicopathological features of soft tissue sarcoma are the same regardless of the patient's gender.

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Competing interests: Nil.

REFERENCES

1. **Gamboa A, Gronchi A, Cardona K (2020):** Soft-tissue sarcoma in adults: an update on the current state of histiotype-specific management in an era of personalized medicine. CA: A Cancer Journal for Clinicians, 70(3): 200-229.
2. **Amankwah E, Conley A, Reed D (2013):** Epidemiology and therapies for metastatic sarcoma. Clinical Epidemiology, 5: 147-53.
3. **Dangoor A, Seddon B, Gerrand C *et al.* (2016):** UK guidelines for the management of soft tissue sarcomas. Clinical Sarcoma Research, 6(1): 20. doi: 10.1186/s13569-016-0060-4.
4. **Kasraeian S, Allison D, Ahlmann E *et al.* (2010):** A comparison of fine-needle aspiration, core biopsy, and surgical biopsy in the diagnosis of extremity soft tissue masses. Clinical Orthopaedics and Related Research®, 468(11): 2992-3002.
5. **Liang Y, Guo T, Hong D *et al.* (2020):** Time to local recurrence as a predictor of survival in patients with soft tissue sarcoma of the extremity and abdominothoracic wall. Frontiers in Oncology, 10: 599097. doi: 10.3389/fonc.2020.599097
6. **Sternheim A, Jin X, Shmookler B *et al.* (2008):** "Telangiectatic" transformation in soft tissue sarcomas. A clinicopathology analysis of an aggressive feature of high-grade sarcomas. Annals of Surgical Oncology, 15(1): 345–354.
7. **Aliyu U, Okuofo E, Okwonna C *et al.* (2018):** Clinicopathological pattern of soft tissue sarcoma in a tertiary health institution in North Western Nigeria. International Journal of Research in Medical Sciences, 6(5): 1632–1638.
8. **Kobayashi H, Ae K, Tanizawa T *et al.* (2015):** A Clinicopathological Analysis of Soft Tissue Sarcoma with Telangiectatic Changes. Sarcoma, 15, 740571. doi: 10.1155/2015/740571
9. **Ali A, Sayed A, Sayed D *et al.* (2016):** Pattern of pediatric tumors at the pediatric department in South Egypt Cancer Institute: thirteen years report. Journal of Pediatrics and Child Nutrition, 2(2): 3-5
10. **Carneiro A, Bendahl P, Engellau J *et al.* (2011):** A prognostic model for soft tissue sarcoma of the extremities and trunk wall based on size, vascular invasion, necrosis, and growth pattern. Cancer, 117(6): 1279–1287.
11. **Nedelcu D, Andreescu N, Boeriu E *et al.* (2014):** Retrospective study on osteosarcoma and Ewing sarcoma–our experience. Maedica, 9(2): 151-56.
12. **Morrison B (2003):** Soft tissue sarcomas of the extremities. Proceedings (Baylor University. Medical Center), 16(3): 285–290.
13. **Kunhi M, Pradhan S, Bhattacharyya S *et al.* (2020):** Clinicopathological study of soft tissue sarcoma-retrospective study of tertiary cancer institute in eastern India. International Journal of Research in Medical Sciences, 8(11): 4075–4078.