ORIGINAL ARTICLE

Spectrum of Soft Tissue Sarcomas - A Retrospective Analysis in a Tertiary Care Centre

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ABSTRACT

Introduction: Soft tissue tumors represent a diverse group of neoplasms that originate from the soft tissues of the body. There are more benign than malignant soft tissue tumors with an annual incidence of malignant soft-tissue tumors (sarcomas) being 50 cases per 1 million population. Sarcomas exhibit a broad range of histological subtypes and are undergoing rapid changes, particularly due to the rise in molecular pathology. **Materials and methods:** This study employed a retrospective approach and analyzed both biopsy and resected specimens received between January 2019 and December 2022 (four years). The specimens that were histomorphologically and immunohistochemically diagnosed as sarcomas were included in the study. Clinical data of the patients and the corresponding histomorphological findings were retrieved from the Hospital database and the Histopathology Register, respectively. **Results:** A total of 38 sarcoma cases were evaluated in this study. The median age of patients at presentation was 46 ± 15 years with a balanced distribution between males and females. The majority of diagnoses (52%) fell within the fourth and fifth decades of life. The most frequent anatomical site of involvement was the extremities (47.3%), followed by the retroperitoneum (15.7%) and abdomen (13.1%). Malignant peripheral nerve sheath tumors emerged as the most prevalent subtype (28%), while leiomyosarcoma and liposarcoma each constituted 20% of the cases examined. **Conclusion:** Extremities remain the primary location, aligning with past research. However, our data hints at a possible increase in the incidence of sarcomas in females, warranting further studies.

Malaysian Journal of Medicine and Health Sciences (2024) 20(SUPP13): 11-15. doi:10.47836/mjmhs20.s13.3

Keywords: soft tissue tumors, sarcoma, morphology, IHC, location

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INTRODUCTION

Soft tissue tumors stand as a challenge in cancer research and treatment. These are rare and diverse malignancies, arising from the mesenchymal tissue with an annual incidence of 50 cases per 1 million population [1]. There are more benign than malignant soft tissue tumors. They encompass many histological subtypes, each presenting with unique clinical features and therapeutic considerations. The rate of sarcomas in all malignancy-related death ranges from 1.5% to 2% [2]. Soft tissue sarcomas can emerge in various anatomical locations, including muscles, tendons, nerves, and connective tissues, presenting a diagnostic and therapeutic dilemma. The rarity of these tumors, coupled with their heterogeneity, often leads to delayed or misdiagnosis, contributing to the challenges in developing effective treatment strategies.

Our analysis aims to highlight the histomorphological spectrum of malignant soft tissue tumors in different age groups and genders.

MATERIALS AND METHODS

Study design and samples

This is a retrospective study conducted in our Department of Pathology at Saveetha Medical College and Hospital, Chennai for four years from January 2019 to December 2022. Our study analyzed the histomorphological patterns of malignant soft tissue tumors. The sections for H & E stain and Immunohistochemistry (IHC) were prepared from formalin-fixed, paraffin-embedded tissue blocks of all malignant sarcoma cases received at our center.

Inclusion criteria

All cases of sarcomas irrespective of age and gender.

Exclusion criteria

All benign soft tissue tumors, blocks received for opinion, and insufficient or unavailable data.

Data collection

The resected and biopsy specimens encompassing the entire spectrum of sarcomas during the timeframe of the study were included. Details of the patient were retrieved from the hospital database and request forms that were received in our department. The histopathological findings were accessed from the histopathological registers in our department.

RESULTS

A total of 1,709 specimens were identified as malignant during the study period. Among these, malignant cases, soft tissue sarcomas comprised only 38 cases (2.2%). It included both excised (28 cases) and trucut biopsy (10 cases) specimens. Patient ages at diagnosis ranged from 4 to 77 years, with a median age of 46 ± 15 years. Notably, the gender distribution was equal (19 males,19 females). Most diagnoses (20 cases,52.6%) clustered within the 41- 60 age range, suggesting a peak prevalence within this demographic. Furthermore, within this specific age range, a female predilection was observed (12 cases,60%) (Fig.1). Analysis revealed a slight difference in average age at diagnosis by gender. Females had an average diagnosis age of 45.5 ± 16.3 years, while males averaged 46.4 ± 14 years.

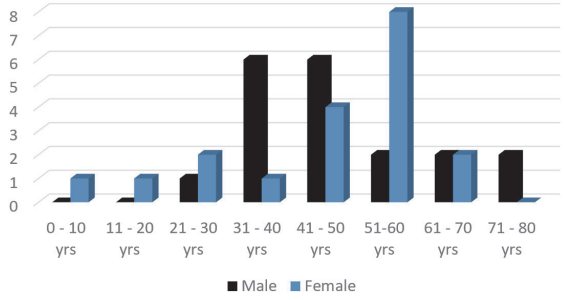

Fig. 1: Gender-specific distribution of sarcomas among different age groups.

Of the 38 identified malignant soft tissue tumors,13 cases (34.2%) were unclassified which included 7 trucut biopsies and 6 excised specimens. Gender distribution among the unclassified cases was nearly equal, with 7 males and 6 females. Among the classified tumors (25 cases), 3 cases represented trucut biopsies, while the remaining 22 cases were excised specimens. The Malignant Peripheral Nerve Sheath Tumor (MPNST) was most frequently identified (7 cases, 28%), followed by Leiomyosarcoma and Liposarcoma (5 cases each, 20%), Myxofibrosarcoma (4 cases,16%), and other less common subtypes (4 cases,16%) (Table I).

Concerning age and gender, Liposarcoma was most encountered in males (80%) with a median age of 56.2 ± 14 years, followed by MPNST (71.4%), with an average presentation age of 45.2 ± 7.9 years. Leiomyosarcoma predominantly occurred in females (80%) with an average age of presentation being 43.4 years ± 13.8 years followed by Myxofibrosarcoma (75%) with 48.25 ± 12.9 years average presentation (Fig.2).

Table I: Frequency of various subtypes of soft tissue sarcomas

Tumor type	Frequency	Percentage
Liposarcoma	5	13.1%
Myxofibrosarcoma	4	10.5%
Angiosarcoma	1	2.6%
Leiomyosarcoma	5	13.1%
Embryonal Rhabdomyosarcoma	1	2.6%
MPNST	7	18.4%
Synovial sarcoma	2	5.26%
Unclassified	13	34.2%

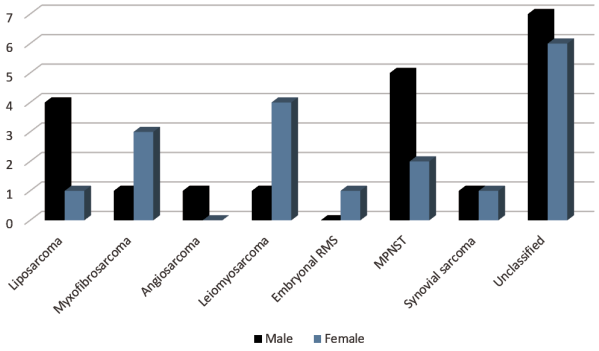

Fig. 2: Gender-specific distribution among various subtypes of sarcomas. RMS- Rhabdomyosarcoma MPNST- Malignant Peripheral Nerve Sheath Tumor

In our observation, Extremities (18 cases, 47.3%) were the most encountered sites followed by the retroperitoneum (6 cases,15.7%), abdomen (5 cases,13.1%), and head&neck (3 cases,7.8%). Sarcomas were encountered more in the lower extremities (16 cases, 88.8%) than in the upper extremities (2 cases,11.1%) (Fig.3). MPNST (26%), Myxofibrosarcoma (26%), and synovial sarcoma (13.3%) were commonly encountered in the lower extremities. Synovial sarcoma was exclusively involved in the lower extremities. The retroperitoneum showed more liposarcoma (50%). Leiomyosarcoma was encountered more in abdominal lesions (75%).

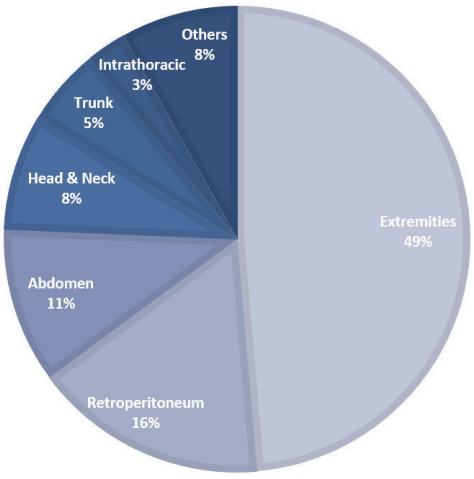

Fig. 3. Location-specific distribution of sarcomas.

DISCUSSION

Soft tissue sarcomas have remarkably low annual incidence, constituting less than 1% of all malignant tumors [3]. Among the 1,709 malignant tumors analyzed, only 38 cases were soft tissue sarcomas supporting their relative rarity. However, despite their lower incidence, soft tissue sarcomas hold a disproportionate impact on mortality and are responsible for a significant portion of cancer-related deaths, contributing between 1.5% and 2% [2]. This disparity between their relative rarity and substantial mortality rate emphasizes the critical need for further research and improved treatment strategies in this area. Given the significant public health burden associated with malignant soft tissue tumors, our study exclusively focuses on malignant soft tissue tumors (sarcomas).

Our study identified a mean patient presentation age of 46 years ± 15 years. This finding aligns closely with previous research by Bansal et.al and Almas et al, who reported average presentation ages of 48 and 45.32 years, respectively [4,5]. This consistency across studies suggests a potential central tendency in the age of presentation for malignant soft tissue tumors. Furthermore, our data demonstrated an equal distribution of diagnoses between males and females, mirroring the observations of Almas et al [5]. This finding suggests that sarcoma may not exhibit a significant gender bias, although further investigation with larger sample sizes may be warranted.

In terms of tumor location, our study aligns with previous work by Bansal et al and Pratti SD et al by demonstrating a higher prevalence of sarcomas in the lower extremities compared to the upper extremities and other sites respectively [4,6]. This anatomical distribution pattern could be due to several factors, including inherent differences in soft tissue composition and vascularity between the upper and lower limbs. Delays in diagnosing soft tissue tumors of the extremities are common. Research has identified potential predictive features, including swelling exceeding 5 cm, rapid growth, pain, and deep location [4]. These features warrant prompt histopathological examination for definitive diagnosis.

A significant portion of the tumors could not be definitively classified (34.2 %) mainly due to non-compliance of patients following biopsy and limited availability of IHC at our facility. The most encountered sarcoma in our study was MPNST. All these cases were confirmed immunohistochemically by S100. It typically affects the trunk and extremities, our study predominantly observed cases within the extremities as observed by Singh HP et al and Stucky CC et al [7,8]. Interestingly, our investigation also identified two rare presentations of MPNST. One case involved a 31-year-old male presenting with an MPNST as an intradural space-occupying lesion. Another unique case involved a 47-year-old woman with a presacral MPNST, further demonstrating the potential for atypical presentations. Furthermore, one case within the more typical lower extremity location (thigh) in a 56-year-old female displayed rhabdomyoblastic differentiation, characteristic of a Malignant Triton Tumor (MTT). Studies by Hsieh MC et al. and GY Hung et al. in the USA and Taiwan indicate regional and racial differences in the incidence rates of certain soft tissue sarcoma subtypes [9,10]. While MPNST is generally considered rare [11], our study revealed a higher incidence than reported by Pratti SD et al and Singh HP et al [6,7]. More nationwide studies are needed to confirm this finding to facilitate tumor-specific effective diagnostic and management strategies.

Our study identified several noteworthy observations regarding the presentation of specific soft tissue sarcoma subtypes, deviating from established expectations. The distribution of myxofibrosarcoma cases differed from the expected male predominance and elderly presentation [12,13]. Our findings revealed a contrasting distribution, with a female predominance and a young male patient diagnosed at just 29 years. This highlights the potential for this tumor to occur outside the expected demographic range. A case of each angiosarcoma and embryonal rhabdomyosarcoma confirmed by Myo D1 (Fig.4) were identified in the chest wall of a 41-year-old male and the left external auditory canal of a 4-year-old girl child respectively.

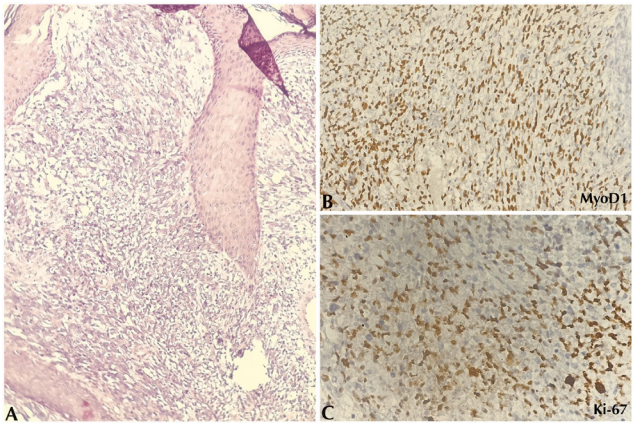

Fig. 4: Embryonal Rhabdomyosarcoma A. Pleomorphic cells showing varying stages of rhabdomyoblastic differentiation. B. Myo D1 showing strong nuclear positivity C. Ki 67 showing strong nuclear positivity.

Liposarcoma in our study predominately involved the retroperitoneum which was in concordance with the study by Singh HP et al but contrasted with findings by Khan N et al where most cases of liposarcoma were noted in the lower extremity [7,14]. Pleomorphic liposarcoma was also identified in two cases. Beyond the established prevalence of liposarcomas, in general, involving the extremities and retroperitoneum, our study identified a particularly uncommon presentation in a case of myxoid liposarcoma within the para-testicular region (Fig.5). Leiomyosarcoma constituted the second most commonly

presenting sarcoma along with liposarcoma in our study which was in concordance with the study done by Singh HP et al where leiomyosarcoma was noticed to be the second most common [7]. It is most often seen to involve the abdomen, retroperitoneum, and uterus [15]. Leiomyosarcoma in general is rarely known to affect the head and neck region [16]. Intriguingly, our study documented two cases that deviated from this pattern. One case involved a 35-year-old male presenting with leiomyosarcoma of the scalp (occipital region), while the other case involved a 26-year-old female with a leiomyosarcoma manifesting as cheek swelling. This emphasizes the importance of maintaining a broad clinical suspicion for sarcomas, even in less typical anatomical locations. Synovial sarcomas constituted only 2 cases in our study and were seen to be involved in the lower extremities as observed by Singh HP et al [7] (Fig.6).

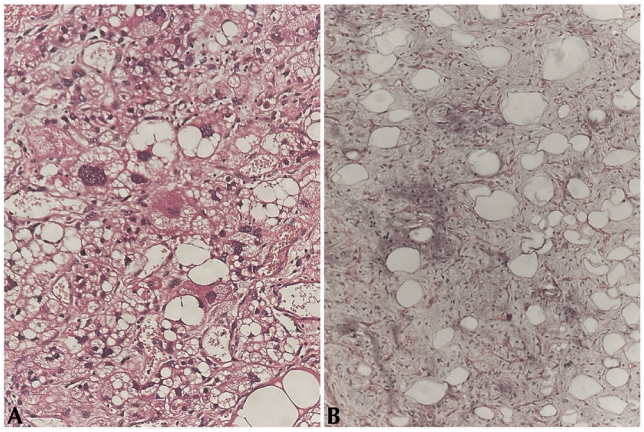

Fig. 5: Liposarcoma (H&E) A. Pleomorphic liposarcoma of retroperitoneum B. Myxoid liposarcoma of paratestis.

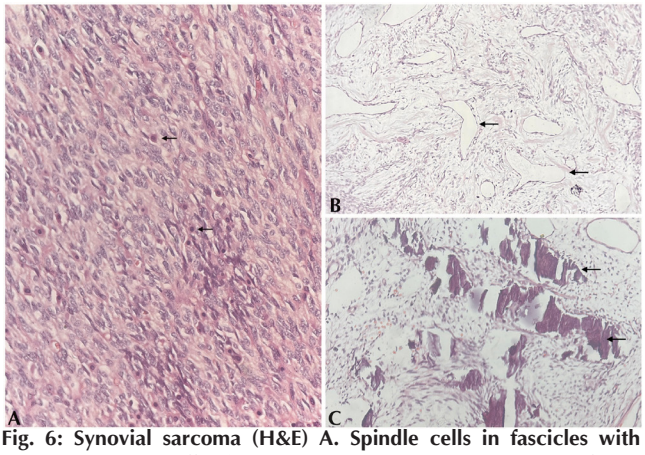

Fig. 6: Synovial sarcoma (H&E) A. Spindle cells in fascicles with numerous mast cells (arrows) B. Hemangiopericytic vessels C. Intratumoral calcifications.

CONCLUSION

Our study reveals an increasing trend of MPNST, which differs from other studies. To substantiate this observation, a nationwide study with participation from multiple centers over longer periods may be required to understand sarcoma trends, ultimately facilitating targeted clinical trials for more effective diagnosis and treatment. Our findings also confirm extremities as the predominant site consistent with prior studies. However, it suggests a potential rise in sarcomas among females warranting more studies with a larger population. Given the frequent misidentification of extremity soft tissue lesions as benign by the public, increased awareness is crucial. Meticulous history-taking, examination, and histopathological evaluation for early and accurate detection ultimately improve patient outcomes despite molecular diagnostics and therapeutic advancements.

ACKNOWLEDGEMENT

We extend our gratitude to our technical team for their constant support throughout this study.

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