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CLINICOPATHOLOGICAL SPECTRUM OF SYNOVIAL SARCOMA AT ARMED FORCES INSTITUTE OF PATHOLOGY, RAWALPINDI, PAKISTAN

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ABSTRACT

Objective: To analyse the clinicopathological spectrum of synovial sarcoma cases presenting in our institution.
Study Design: Descriptive case series.
Place and Duration of study: Armed Forces Institute of Pathology (AFIP) Rawalpindi, from Jan 2010 to Jan 2015.
Material and Methods: All cases of synovial sarcoma diagnosed on histopathological examination were recovered from the Armed Forces Institute of Pathology (AFIP) laboratory information management system. The inclusion criteria consisted of optimally processed Haematoxylin and Eosin stained slides. Positive immunohistochemistry for epithelial membrane antigen/cytokeratin and CD99. Both genders were included. Patients' gender, age, tumour size, site, histological subtype, grade, microscopic margin status, depth and stage were noted. The data were analysed using SPSS Version 21. Frequencies and percentages were calculated for qualitative data and the standard deviation and mean for quantitative data.
Results: Sixty-seven cases of synovial sarcoma (SS) were included in this study. The mean age of the patients was 35.1 years, with males at 55.2%. The most common site was the lower extremity 41.8%. The average size was 8.5 cm. The most common stage was pT2b (64.2%). Monophasic histological subtype was more common at 58.2%. Grade 2 tumours were 77.6%. Microscopic positive margins were 30.0%. Specimens that were fragmented or not oriented properly were 33.3%.
Conclusion: The clinicopathological spectrum of synovial sarcoma in our institution is similar to that of other parts of the world. This study has highlighted that a significant proportion (33.3%) of resection specimens were fragmented or unmarked; therefore surgical margins could not be evaluated in these cases, increasing the chances of inadequate surgeries.

Keywords: Clinicopathological spectrum, Synovial sarcoma.

INTRODUCTION

Synovial sarcoma (SS) is a mesenchymal neoplasm showing epithelial differentiation. It bears a chromosomal translocation t(X; 18) (p11; q11) that results in the SS18-SSX fusion gene[1]. It was first described by Simon in 1865 and later named by Knox[2]. The World Health Organization classifies it as a tumour of uncertain differentiation[1]. Soft tissue sarcomas represent 1% of cancers worldwide, out of which 10-15% are SS[3]. It is the second most common soft tissue tumour in children and adolescents[4]. Thirty per cent arise in people younger than 20 years of age[5]. Seventy per cent of tumours occur in the lower extremity and 3% of tumours occur in the head and neck region[6]. Histologically, biphasic and monophasic patterns are seen. Some tumours exhibit poorly differentiated areas. Monophasic SS shows either spindle cells or epithelial cells. Biphasic SS contains areas of glandular differentiation[4]. Poorly differentiated tumours show increased cellularity, high grade nuclear features and a high mitotic count of more than 15 per 10 High Power Field (HPF), with areas of necrosis[1]. The diagnosis of SS is made on histology, supplemented by ancillary techniques such as immunohistochemistry, electron microscopy and the gold standard cytogenetic analysis[6]. Histological features associated with a worse prognosis are a high mitotic rate[7] tumour necrosis, grade 3[8] and a positive microscopic surgical margin, especially in relevance to local tumour recurrence[9]. Clinical features associated with an adverse outcome are a size of >5 cm, a

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truncal location[8] and intralesional or marginal surgery[4]. It is an aggressive tumour with a tendency to reoccur locally and late distant metastases[4]. Common sites of metastases are the lungs and the skeleton[3]. Lymph node metastasis, although rare in other sarcomas, is more frequent in SS[3]. The 5-year disease-specific survival is 83% in children and adolescents (age <19 years), and 62% in adults[1]. The standard treatment is wide surgical excision[4,10] followed by chemotherapy[4]. SS is chemo-sensitive; survival in advanced disease has improved due to better chemo-therapy[3,11]. SS is a second common soft tissue tumour in Pakistan's young population. The purpose of this study was to analyse the clinicopathological spectrum of SS cases presenting in our institution.

MATERIAL AND METHOD

This descriptive case series was conducted at the Histopathology Department of Armed Forces Institute of Pathology (AFIP), Rawalpindi. Records of histopathology laboratory reports were retrieved from the laboratory information management software (LIMS) from Jan 2010 to Jan 2015. The sample size is 67 cases. The sampling technique was non-probability pur-posive sampling. The inclusion criteria consisted of optimally processed and Haematoxylin and Eosin stained sides with a diagnosis of SS, positive immunohistochemistry for epithelial membrane antigen/cytokeratin and CD99. Both genders were included. Broken slides, improperly fixed or stained slides were excluded from the study. Patients' gender, age, tumour size, site, depth and stage were noted along with tumour histological subtype, grade and microscopic margin status. The data were analysed using SPSS Version 21. Frequencies and percentages were calculated for qualitative data such as gender, histological subtype and stage. Mean and SD were calculated for quantitative data such as age and tumour size.

RESULTS

A total of 67 cases of SS were included in the study. The mean age of presentation was 35.1 ± 14.4 years, with an age range of 13-75 years. The study showed male preponderance at 55.2% (37) while females were 44.8% (30). The male to female ratio was 1.24:1. The most common tumour site was the lower extremity 41.8% (28), followed by the upper extremity at 19.4% (13), non-limb based tumours (shoulder, gluteal region, inguinal region and axilla) were 11.9% (8) and the head and neck constituted 7.5% (5) cases. There was one each from breast, abdomen, perineum and lung. Large specimens including wide local excision, radical neck dissection, amputation and resection were 30, whereas trucut biopsies and review cases were 37. The average size of the largest dimension of the tumour was 8.5 cm, with a size range of 2.5-23 ± 5.3 cm (details are in table). The most common stage at presentation was pT2b 64.2% (18) cases. The most common histological subtype was monophasic 58.2% (39) cases, with biphasic 26.9% (18), monophasic with poorly differentiated areas 10.4% (7), biphasic with poorly differentiated areas were 4.5% (3) as shown in fig-1,2 & 3. Grade 2 tumours were 77.6% (52) and grade 3 tumours were 22.4% (15). The margin involve-ment was noted in the large specimens, with 33.3% (10) specimens being fragmented or not oriented

Table: Clinicopathological Features of Synovial Sarcoma.

Characteristics	Mean	Frequency	Percentage (%)
Size of Tumour (30 cases)			
≤5.0 cm	8.5 cm	11	36.6
>5.0 cm		19	63.3
Most Common Tumour Site (n=67)			
Lower extremity		28	41.8
Most Common Tumour Stage (28 cases)			
pT2b		18	64.2

properly. In the remaining 20 cases, margin clearance was noted: tumours with microscopic positive margins were 30% (6) and with negative margins were 70% (14). In the remaining 55.2% of the cases, margin review was not applicable.

DISCUSSION

This study showed male preponderance. Similar trend was observed in a local study of soft tissue sarcomas at Aga Khan University Hospital (AKUH) by Qadir et al[12], a Turkish study by Tarkan et al[13] and in a Chinese study by Alimujiang et al[6]. Gender distribution was found to be equal in a study conducted by Spurrell et al at the Royal Marsden Hospital[3]. A European study, Guillou et al, had 48.5% (80) males and 51.5% (85) females[14]. A Swiss study by Krieg et al, reported 42% (26) males and 58% (36) females[4]. The gender difference in Asia as compared to that of Europe should be further analysed. It could be due to the fact that males have better access to health facilities than females in Asia. The average age at diagnosis was 35.1 years. A local study of soft tissue sarcoma at AKUH showed 41.8 ± 21.9 years, with 56% of patients <45 years and 44% being >45 years. An age of >45 years is associated with a poor prognosis[12]. A median age of 34.5 years is reported by Tarkan et al, with the age range being from 14 to 68 years[13]. Alimujiang et al also described the age of 32.1 years at the time of diagnosis with an age range of 4 to 76 years[6]. Krieg et al reported the average age to be 35.4 years[4]. Spurrell et al put the average age of a patient with advanced SS as 33 years[3]. Guillou et al also reported the mean age to be 35 years with an age range of 4 to 82 years[14]. The most common histological subtype is monophasic. Ladanyi et al reported 74.6% (180) cases with a monophasic pattern and 25.3% (61) cases with a biphasic pattern[7]. Guillou et al reported 72.1% (119) monophasic and 27.9% (46) biphasic cases. All except one of the 38 poorly differentiated cases exhibited a monophasic pattern[14]. Krieg et al put the monophasic at 56% and biphasic at 44%[4]. Tarkan et al studied 69 cases with monophasic 47.8% (33) cases, biphasic 40.6% (28) cases and poorly differentiated 11.6%(8) cases[13]. Spurrell et al showed an equal distribution of monophasic and biphasic histologic subtypes with 9 out of 104 tumours (8.65%) being poorly differentiated[3]. The tumours were graded according to the French Federation of Cancer Centers Sarcoma Group system. The differentiation score of SS is 3 by definition. Therefore SS are either grade 2 or 3 based on mitotic count in 10 HPF and extent of necrosis (<50%, >50%). Grade 2 is more common.

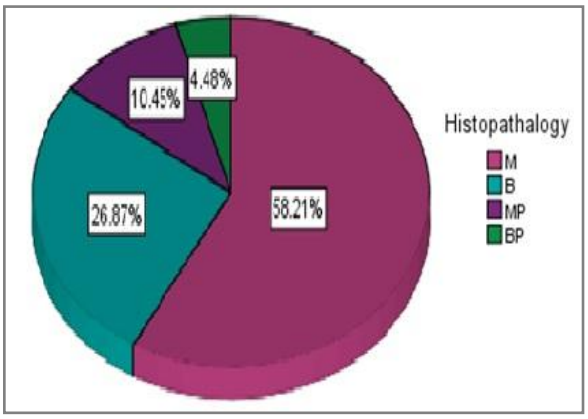

Figure-1: Histological Subtypes of Synovial Sarcoma (n=67).

M – monophasic. B – biphasic. MP – monophasic poorly differentiated. BP – biphasic poorly differentiated.

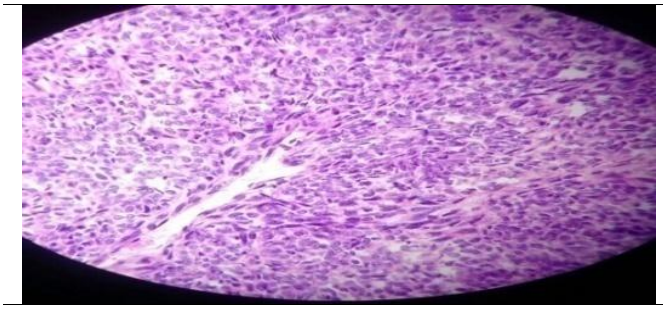

Figure-2: Monophasic Synovial Sarcoma.

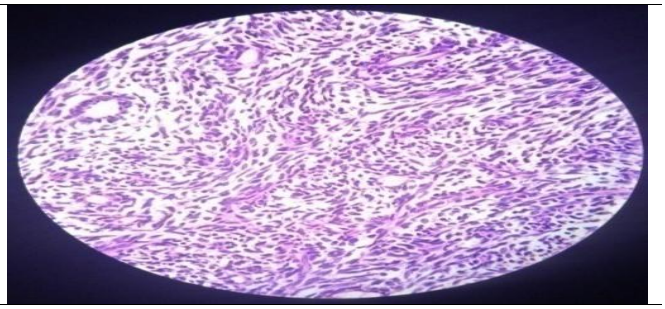

Figure-3: Biphasic Synovial Sarcoma.

A similar trend is reported by Krieg et al with grade 2 tumours constituting 74% (32) and grade 3 tumours 26% (11)[4]. Tarkan et al reported grade 1 tumours and grade 2 tumours constituting 50.7% (35) and grade 3 tumours 49.3% (34)[13].

Spurrell et al reported an equal number of grade 2 and grade 3 tumours[3]. Guillou et al reported 51.5% (84) tumours in grade 3 and 48.5% (79) in grade 2[14]. This study included 37 cases of tru-cut biopsies and review cases; therefore the tumours in these cases could be upgraded from grade 2 to grade 3 in a larger resection specimen.

The most common tumour site were the lower extremities. The site of tumour was unspecified in 4 cases (6.0%). Most of the studies showed the extremities to be the commonest site, such as AKUH[12], Tarkan et al[13] Guillou et al[14] and Krieg et al[4]. Spurrell et al conducted a study on advanced SS that also demonstrated the lower limb to harbour the majority of the tumours[3]. Alimujiang et al reported the majority of head and neck tumours to be in the upper aero-digestive tract[6]. This study showed 7.5% of tumours in the head and neck region; a similar trend was observed by Tarkan et al[13]. In this study, five cases were of the head and neck, and one each was from the nasopharynx, para-pharyngeal space, cervical region, mandible and the parotid gland. The first three were tru-cut biopsies and the last two were resection specimens. Squamous cell carcinoma is an important differential to consider in spindle cell neoplasms of the head and neck region[6]. The average size of the tumour was calculated for the 30 large resection specimens. The average size of the largest dimension of the tumours was 8.5 cm. The tumour size was stratified into ≤5cm and >5cm. The majority of the tumours were >5cm. Qadir et al has also stratified tumours into 5 cm cut-offs with 34 (40.5%) ≤5cm and 50 (59.5%) >5cm[12]. Tarkan et al reports 20 (29%) <5cm and 49 (71.0%) >5cm tumours[13] Krieg et al reported an almost equal number of tumours that are >5 cm and <5 cm[4]. In another large study by Guillou et al, the mean size of the tumour was 7cm with 35.5% (54) cases measuring ≤5cm and 78.3% (119) measuring ≤10 cm[14]. The tumour size is a major prognostic factor as illustrated by Krieg et al,[4] Alimujiang et al[6] and Qadir et al[12]. For staging purposes, the tumours are stratified into ≤ or >5cm. The large specimens included wide local excision, lobectomy, mandibulectomy, amputation and radical neck dissection. Six specimens were fragmented while four were not properly oriented, therefore margins could not be commented upon in these 10 cases (33.3%). Tumours with microscopic positive margins were 30% (6) while 70% (14) tumours had negative margins. In 37 cases (55.2%) margin review was not applicable. Of the six tumours with positive margins, three were extremity-based, of which two were grade 3 and one tumour was very large, measuring 23cm in its largest dimension. Two tumours were in the foot and one was in the perineum. The anatomical complexity most likely contributed to the inadequacy of margins. Tarkan et al reported 21.7% of tumours with positive margins and 78.3% with negative margins[13]. Alimujiang et al observed 93 cases of SS of the head and neck where, on follow-up, only one of the patients with no recurrence had a tumour with a positive margin[6]. Guillou reported 36.3% (49) tumours with microscopically positive margins, 63.7% (86) tumours with micro-scopically negative margins[14]. Ladanyi et al reported 124 tumours with microscopically negative margins, 25 with microscopically positive margins and 7 with macroscopically positive margins[7]. The importance of negative margins cannot be over-emphasised, as illustrated by Alimujiang et al,[6] Qadir et al,[12] and Guillou et al[14]. Qadir et al stated a negative margin for soft tissue sarcomas of more than 10 mm associated with enhanced survival[12]. The pT stage of the tumour was calculated for 28 cases because in two of the 30 large specimen cases, the site of tumour was not mentioned. Therefore, the depth of location could not be established. A total of 39 cases formed 58.2% where tumour stage was not calculated.

The tumours were staged according to the 7th edition of the American Joint Committee on

Cancer Staging manual[15]. The most common tumour stage presentation was pT2b. This was followed by pT1b at 32.1% (9), pT2a at 3.5% (1) and none in pT1a. Tarkan et al reported 53.6% of SS in stage 2 (pT1a, pT1b, pT2a) followed by 37.7% in stage 3 (pT2b) and 8.7% tumours in stage 1 (pT1a, pT1b)[13]. Spurrell et al also reported a majority of the tumours to be in stage 2 at the time of diagnosis[3] Guillou et al reported 30.5% tumours in stage 3 corresponding to pT2b[14]. Data from Qadir et al (56% superficial tumours, 59.5% >5cm tumours) places the majority of tumours in pT2a[12].

CONCLUSION

The clinicopathological spectrum of synovial sarcoma in our institution is similar to that of other parts of the world. The average age of diagnosis is 35 years, with the lower extremity being the most common tumour site. The majority of tumours were >5cm in the largest diameter. The monophasic histological subtype is more common than biphasic. The majority of tumours present in pT2b. This study has highlighted that a significant proportion (33.3%) of resection specimens were fragmented or unmarked; surgical margins could not be evaluated in these cases, increasing the chances of inadequate surgeries.

RECOMMENDATION

The adequacy of the first surgery is of the utmost importance especially in a resource-poor country like Pakistan because patients usually do not present themselves for a follow-up. Therefore a multidisciplinary approach between pathologists and clinicians should be encouraged to ensure a better outcome.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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