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Original Article

Clinical outcomes of extremity synovial sarcoma

Ekstremite sinovyal sarkomunun klinik sonuçları

Halil Sezgin SEMİS[1]*, Aliekber YAPAR [2], Fener CELEBI[3], Guray TOGRAL[4], Bedii Safak GUNGOR[4]

[1]Erzurum Buhara Hospital, Department of Orthopaedics and Traumatology, Erzurum/TURKEY
[2]Antalya Training and Research Hospital, Department of Orthopaedics and Traumatology, Antalya/TURKEY
[3]İzmir Bozyaka Training and Research Hospital, Department of Orthopaedics and Traumatology, Izmir/TURKEY
[4]Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Department of Orthopaedics and Traumatology, Ankara/TURKEY

Abstract

Aim: The aim of this study is to emphasize the demographic data, follow-up results and the importance of approach to these tumors of synovial sarcoma, which is a rare tumor in the extremities.

Material and Methods: In this study, twenty patients who were operated on for extremity synovial sarcoma between 2008 and 2018 at Dr. Abdurrahman Yurtaslan Oncology Hospital were retrospectively analyzed. Demographic information, surgical treatments, follow-up periods, recurrence and metastases of the patients were recorded.

Results: Twenty patients with a diagnosis of synovial sarcoma with a mean age of 32.7 (range, 13 to 66) years were included in this study. According to the localization, it was observed that the tumors were mostly located in the thigh (25%), cruris (25%) and ankle (25%). It was observed that the tumor size was 5 cm or more in 70% of the patients. While 55% (n=11) of the patients had metastases at the time of diagnosis (lung), recurrence developed in 25% of the patients during follow-up. Wide resection was performed as the primary surgical treatment in 85% of the patients, while 75% received RT, only 30% received CT. 25% of patients died during follow-up. The mean survival time of the patients was 109.4±8.9 months. While the 3-year survival rate was 90%, the 5-year survival rate decreased to 80%. There was no significant difference in survival times according to gender, age, side, grade, tumor size, metastasis, RT, KT and recurrence status.

Conclusion: In conclusion, synovial sarcoma is a rare malignant soft tissue sarcoma with high grade and high metastasis capacity. For understanding the characteristics of synovial sarcoma, multicenter studies with a larger number of patients are needed.

Keywords: Synovial Sarcoma, Outcome, Extremity

Corresponding author*: Halil Sezgin Semis, Erzurum Buhara Hospital, Department of Orthopaedics and Traumatology, Erzurum/TURKEY
E-mail: hsezginsemis@gmail.com
ORCİD: 0000-0001-9912-174X
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Öz

Amaç: Bu çalışmanın amacı ekstremitelerde nadir görülen bir tümör olan sinoviyal sarkomun demografik verilerini, takip sonuçlarını ve bu tümörlere yaklaşımın önemini vurgulamaktır.

Gereç ve Yöntemler: Bu çalışmada Dr. Abdurrahman Yurtaslan Onkoloji Hastanesi'nde 2008-2018 yılları arasında ekstremite sinoviyal sarkomu nedeniyle ameliyat edilen 20 hasta retrospektif olarak incelendi. Hastaların demografik bilgileri, cerrahi tedavileri, takip süreleri, nüks ve metastazları kaydedildi.

Bulgular: Ortalama yaşı 32.7 (dağılım, 13-66) yıl olan sinoviyal sarkom tanısı alan 20 hasta bu çalışmaya dahil edildi. Lokalizasyona göre tümörlerin en çok uyluk (%25), kruris (%25) ve ayak bileği (%25) yerleşimli olduğu görüldü. Hastaların %70'inde tümör boyutunun 5 cm ve üzerinde olduğu görüldü. Hastaların %55'inde (n=11) tanı anında (akciğer) metastaz varken, %25'inde takip sırasında nüks gelişti. Hastaların %85'inde primer cerrahi tedavi olarak geniş rezeksiyon yapılırken, %75'ine RT, sadece %30'una BT uygulandı. Hastaların %25'i takip sırasında öldü. Hastaların ortalama sağkalım süresi 109.4±8.9 ay idi. 3 yıllık sağkalım oranı %90 iken, 5 yıllık sağ kalım oranı %80'e düşmüştür. Cinsiyet, yaş, taraf, derece, tümör boyutu, metastaz, RT, KT ve nüks durumuna göre sağkalım süreleri arasında anlamlı fark yoktu.

Sonuç: Sonuç olarak, sinoviyal sarkom, yüksek dereceli ve yüksek metastaz kapasiteli, nadir görülen bir malign yumuşak doku sarkomudur. Sinoviyal sarkomun özelliklerini anlamak için daha fazla hasta sayısı ile çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Sinovyal Sarkom, Sonuç, Ekstremite

Introduction

Soft tissue sarcomas are a rare and heterogeneous group of tumors that seen less than 1% of all adult malignancies. 60 percent of soft tissue sarcomas occur in the extremities which is the most common localization. Synovial sarcoma is a rare subgroup (10%) of soft tissue sarcomas [1].

Synovial sarcoma, occuring for approximately 10% of soft tissue sarcomas, most commonly develops in the extremities of young adults, is considered high-grade, and contains a characteristic translocation (X;18;p11;q11). While surgery and radiation therapy have excellent local control, distant metastasis remains the main problem limiting survival. Although ifosfamide-based chemotherapy has been associated with better survival in patients with synovial sarcoma, the search for less toxic and more targeted systemic therapy continues [2-6].

We, as an oncology center, tried to emphasize the demographic data of synovial sarcoma, a rare tumor in the extremities, the results of follow-up and the importance of the approach to these tumors, based on the results of the patients we operated with the diagnosis of synovial sarcoma.

Material and Methods

In this study, twenty patients who were operated on for extremity synovial sarcoma between 2008 and 2018 at Dr. Abdurrahman Yurtaslan Oncology Hospital were retrospectively analyzed. Demographic information, surgical treatments, follow-up periods, recurrence and metastases of the patients were recorded. Patients whose diagnosis was not confirmed pathologically were excluded at the study.

The study protocol was approved by the local institutional review board. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analyses were done using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics are presented as numbers and percentages for categorical variables and mean ± standard deviation, median (minimum value – maximum value) for continuous variables. Normal distribution for continuous variables were assessed with visual (histograms and probability graphics) and analytic methods (Kolmogorov-Smirnov and Shapiro-Wilk's test). In the data that do not fit the normal distribution, Mann-Whitney U test was used for comparison analysis between the two independent groups and the independent sample t test was used for the data that fit the normal distribution. Comparison analyses for categorical variables between independent groups were done by chi-square test. Survival analyses were performed by Kaplan-Meier methods and Log-rank test. $P < 0.05$ was considered to be statistically significant.

Results

Twenty patients with a diagnosis of synovial sarcoma with a mean age of 32.7 (range, 13 to 66) years were included in this study. 55% (n=11) of the patients were male. According to

the localization, it was observed that the tumors were mostly located in the femur (25%), cruris (25%) and ankle (25%). Grade 3 (65%) tumors were detected in 13 patients. It was observed that the tumor size was 5 cm or more in 70% of the patients. While 55% (n=11) of the patients had metastases at the time of diagnosis (lung), recurrence developed in 25% of the patients during follow-up. Wide resection was applied to 85% of the patients as the primary surgical treatment, while 75% received RT, only 30% received LT. 25% of the patients died (Table 1).

Table 1. Basal Demografics of Patients

Characteristic	Total N=20
Gender, n (%)	
Female	9 (45)
Male	11 (55)
Age, years	
Mean±sd	32.7±15.6
Median(min-max)	28.5 (13-66)
Side, n (%)	
Right	10 (50)
Left	10 (50)
Localization, n (%)	
Thigh	5 (25)
Ankle	5 (25)
Cruris	5 (25)
Knee	3 (15)
Shoulder	2 (10)
Grade, n (%)	
Grade 1	-
Grade 2	7 (35)
Grade 3	13 (65)
Grade 4	-
Tumor size, n (%)	
< 5cm	6 (30)
≥ 5cm	14 (70)
Metastasis, n (%)	
No	9 (45)
Yes (Lung met)	11 (55)
Exitus, n (%)	
No	15 (75)
Yes	5 (25)
Surgical treatment, n (%)	
Below-the-knee amputation	1 (5)
Above-knee amputation	1 (5)
Femur Disarticulation	1 (5)
Wide Resection	17 (85)
RT	
No	5 (25)
Yes	15 (75)
CT	
No	14 (70)
Yes	6 (30)
Recurrence, n (%)	
No	15 (75)
Yes*	5 (25)

* Recurrence surgery: Wide resection was applied to 5 patients.

When the patients are compared according to their exitus status; 60% of surviving patients and 40% of deceased patients are male. The median age of the surviving patients was 26 (13-66) and the deceased was 29 (15-42). There was no significant difference between the groups in terms of age (p=0.617) and gender distribution (p=0.965). Side, localization and grade distributions were similar between the groups (p=0.303, p=0.569 and p=0.613, respectively). The tumor size of 80% of the patients who died and 66.7% of the patients who survived was 5 cm or more, and this difference was not statistically significant (p=1.000). The distribution of metastasis, surgical treatment, RT, LT, and recurrence were also similar between the groups (p>0.05) (Table 2).

Table 2. Evaluation of patients according to exitus status

Characteristic	Alive n=15	Died n=5	p value
Gender, n (%)			
Female	6 (40)	3 (60)	0.617*
Male	9 (60)	2 (40)	
Age, years			
Mean±sd	33.5±17.2	30±10.1	0.965**
Median(min-max)	26 (13-66)	29 (15-42)	
Side, n (%)			
Right	9 (60)	1 (20)	0.303
Left	6 (40)	4 (80)	
Localization, n (%)			
Thigh	3 (20)	2 (40)	
Ankle	3 (20)	2 (40)	0.569
Cruris	4 (26.7)	1 (20)	
Knee	3 (20)	-	
Shoulder	2 (13.3)	-	
Grade, n (%)			
Grade 1	-	-	
Grade 2	9 (60)	4 (80)	0.613
Grade 3	6 (40)	1 (20)	
Grade 4	-	-	
Tumor size, n (%)			
< 5cm	5 (33.3)	1 (20)	1.000
≥ 5cm	10 (66.7)	4 (80)	
Metastasis, n (%)			
No	7 (46.7)	2 (40)	1.000
Yes (Lung met)	8 (53.3)	3 (60)	
Surgical treatment, n (%)			
Below-the-knee amputation	-	1 (20)	
Above-knee amputation	1 (6.7)	-	0.297
Femur Disarticulation	1 (6.7)	-	
Wide Resection	13 (86.7)	4 (80)	
RT			
No	3 (20)	2 (40)	0.560
Yes	12 (80)	3 (60)	
CT			
No	11 (73.3)	3 (60)	0.613
Yes	4 (26.7)	2 (40)	
Recurrence, n (%)			
No	11 (73.3)	4 (80)	1.000
Yes	4 (26.7)	1 (20)	

*Chi-square test **Mann-Whitney U test

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Median survival time could not be reached in this study, therefore, average survival times are presented. The mean survival time of the patients in the study was 109.4±8.9 months. While the 3-year survival rate was 90%, the 5-year survival rate decreased to 80% (Figure 1). There was no significant difference in survival times according to gender, age, side, grade, tumor size, metastasis, RT, KT and recurrence status (log rank test p>0.05). (Table 3).

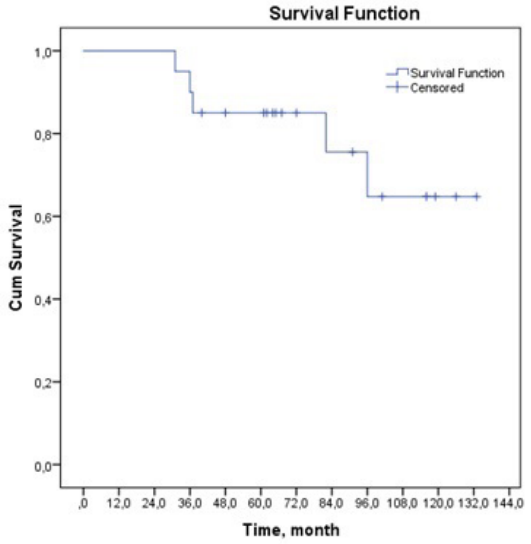

Figure 1. Kaplan Meier Plot of overall survival rate

Discussion

Although synovial sarcoma has traditionally been viewed as a high-grade, deep-seated sarcoma with a poor prognosis, it has become increasingly clear that not all synovial sarcomas actually share this outcome. It was found to be in low-grade variants and also that there are many factors that can affect prognosis [2,3]. The main finding of this study is that synovial sarcoma is a rare malignant soft tissue sarcoma with high grade and high metastasis capacity.

Synovial sarcoma (SS) is a malignant mesenchymal neoplasm with variable epithelial differentiation that tends to occur in young adults and can occur in almost any region. There is a slight male preference (M:F ratio of 1.13) [4]. 55% of the patients in this study (11 patients) were male. Hussaini et al. [7] they showed that in 102 synovial sarcoma patients followed for 5.7 years, the most common location was the lower extremity (57%), and tumors of ≥5 cm were 64% more. Similarly, 90% of the tumors in this study were located in the lower extremities and 70% of the tumors were ≥5 cm.

Some authors believe that histological grade is not a prognostic factor for synovial sarcoma [8], but there are publications in the literature that claim otherwise [9]. Guillou et al. [9] showed that FNCLCC grade 3 patients had a much worse prognosis in their study, also found no effect of histological grade on survival in this study. In order to resolve this contradiction in the literature, studies with a larger number of patients are needed.

Table 3. Overall Survival Rates according to factors

Total N=13	Log Rank Test p	Overall Survival, months mean±se*	3-year Survival Rate, %	5-year Survival Rate, %
All Patients		109.4±8.9	90	85
Gender	0.401			
Female		101.4±14.3	88.9	77.8
Male		111.2±9.4	91	91
Age	0.720			
<28.5 (Median age)		111.8±12.7	90	90
≥28.5		97.4±10.8	90	80
Side	0.151			
Right		123.8±8.1	100	90
Left		92.4±13.2	100	80
Grade, n (%)	0.635			
Grade 2		107.3±10.8	100	85.7
Grade 3		107.1±10.8	84.6	84.6
Tumor size, n (%)	0.725			
< 5cm		116±15.5	83.3	83.3
≥ 5cm		103.4±9.4	92.9	85.7
Metatasis, n (%)	0.660			
No		111±13.7	88.9	77.8
Yes (Lung met)		108.8±8.9	90.9	90.9
RT	0.852			
No		102.2±15.5	100	80
Yes		110.9±11.1	93.3	86.7
CT	0.550			
No		113.1±9.7	92.9	92.9
Yes		96.2±17.2	83.3	66.7
Recurrence, n (%)	0.623			
No		105.8±10.8	93.3	86.7
Yes		108±16.1	80	80

* Since the median survival time could not be reached, the mean±standard error is presented

70% of cases are located in the extremities and the most common form of metastatic spread is to the lung [2]. The natural course of the disease is such that many patients experience recurrence of the primary tumor and/or metastatic disease. Metastatic disease occurs in approximately 50% of patients. The lungs, the most common site of metastasis, are seen in 74-81% of patients with metastatic disease [9,10]. In this study, only extremity synovial sarcomas were considered and 55% of the patients had lung metastases at the time of diagnosis.

The mainstay of treatment in synovial sarcoma is wide surgical excision with adjuvant or neoadjuvant radiotherapy, which provides a good chance of cure for the localized disease [2]. Al-Hussaini et al. The rate of radiotherapy and chemotherapy in patients were 82% and 24%, respectively [7]. In the literature, daxorubicin and ifosfamide-based chemotherapies are the most common in synovial sarcoma [10]. In their retrospective analysis of 171 synovial sarcoma cases, Zhang et al.[11] reported that post-surgical chemoradiotherapy improved the prognosis. In our study, all patients using cometapic agents used daxorubicin and ifosfamide-based chemotherapy regimens. In this study, the rates of radiotherapy and chemotherapy were 75% and 30%, respectively.

Although it can be graded according to the mitotic index, percentage of necrosis, and tumor differentiation, Synovial sarcoma should always be considered as a high-grade sarcoma characterized by local invasiveness and a tendency to metastasis. 5-year disease-free survival remains in the order of 70%. Hussaini et al. [7] reported a 5-year survival of 69% in 102 synovial sarcoma patients they followed. Five-year survival has improved from the reported 75-81% figures in the 1960s [8]. The reason for this is the increase in early diagnosis and effective treatment methods thanks to increasing medical and technological developments. In this study, while the three-year survival rate was 90%, it was observed that the 5-year survival rate decreased to 80% and was higher than the literature. We think that the reason for this is that more complicated and metastatic patients are sent to us from an external center, since we are an oncology center.

In the literature, there is no consensus among prognostic factors affecting survival. Mackenzie et al. Prognostic factors associated with survival include tumor size, tumor invasiveness, stage, tumor location, histological subtype, and grade [10]. In this study, the effects of gender, age, side, grade, tumor size, metastasis, RT, CT and relapse on survival were not found. We attribute this to the small number of patients, which is one of the most important limitations of this study. Studies with larger numbers of patients are needed. Another limitation of this study is the retrospective features of the study. However, this study is important as we share our experience with synovial sarcoma, a rare soft tissue sarcoma, as an oncology center.

Conclusion

In conclusion, synovial sarcoma is a rare malignant soft tissue sarcoma with high grade and high metastasis capacity. In order to understand the characteristics of synovial sarcoma, multicenter studies with a larger number of patients are needed.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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