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Extremity Soft Tissue Sarcomas of Uncertain Differentiation: Presentation, Treatment and Outcomes in a Clinical Series of 60 Patients

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ABSTRACT

Objectives: The purpose of this study is to assess the clinical characteristics and treatment modalities of 60 patients diagnosed with extremity soft tissue sarcomas of uncertain differentiation.

Methods: Clinical findings, treatments, outcomes and treatment failures in a case series of 59 patients, who were diagnosed with localized or metastatic extremity soft tissue sarcomas of uncertain differentiation between 2002 and 2015, were examined retrospectively.

Results: Out of 59 cases, 40 had synovial sarcoma, 7 had ASPS, 6 had extra-skeletal Ewing's sarcoma, 3 had clear cell sarcoma, 2 had epithelioid sarcoma and 1 had extra-skeletal myxoid chondrosarcoma. Metastases were developed in 18 patients, whereas 42 patients had localized tumors at diagnosis. While 5-year overall survival rate was 36% in all patients, it was 46% in patients with localized tumor and 18% in patients who had metastasis at diagnosis. 23 patients died in 40.7 months on average (12-130). The mean diameter of the mass in all patients was 108±87 mm. The mean follow-up duration was 49.4±41.5 months (12-176).

Conclusions: Uncertainly differentiated soft tissue sarcomas are a group of diseases that are similar to benign tumors and some are very rare and have a very poor long-term prognosis. Wide surgical margin and early diagnosis are especially important.

Keywords: Sarcoma of uncertain differentiation, synovial sarcoma of the extremities, soft tissue sarcoma of the extremities, treatment outcome, prognosis

ÖZ

Belirsiz diferansiasyonlu ekstremite yumuşak doku sarkomları: 60 hastalık seride klinik prezentasyon, tedavi ve sonuçları

Amaç: Bu çalışma, belirsiz diferansiasyonlu ekstremite yumuşak doku sarkomu olan 60 hastanın klinik karakteristikleri ve tedavi modalitelerini değerlendirmeyi amaçlamaktadır.

Yöntem: 2002-2016 yılları arası, lokalize ya da metastatik, belirsiz diferansiasyonlu ekstremite yumuşak doku sarkomu olan hasta serisinde klinik bulgular, tedavi, sonuçlar, tedavi başarısızlıklarını retrospektif inceledik.

Bulgular: Toplam 60 hastanın 35'i erkek, 25'i kadındı. Ortalama yaş 33.8 (7-68 arası) hesaplandı. 41 hasta sinovial sarkomlu, 7 hasta asps li, 6 hasta extraskeletal Ewing sarkomlu, 3 hasta clear cell sarkomlu, 2 hasta epiteloid sarkomlu ve 1 hasta ekstraskeletal mixoid kondrosarkomlu idi. 18 hasta tanı anında metastaza sahipken, 42 hasta tanı anında lokalize tümöre sahipti. Tüm hastalarda 5 yıllık sağkalım genel grupta %28, lokalize tümörü olan hastalarda %34, tanı anında metastaza sahip hastalarda 11% idi. 20 hasta ortalama 42.6 ayda (10-125 ay) hayatını kaybetti. En sık primer tümör lokalizasyonu uyluktu. Ortalama kitle çapı 96 mm idi. 30 hastada tam (R0) rezeksiyon yapıldı. 7 vakada preoperatif, 43 vakada postoperatif sistemik kemoterapi uygulandı. 2 vakada neoadjuvan, 24 vakada adjuvan radyoterapi uygulandı. Toplam 37 vakada, tanı anında ya da ileri dönemde metastaz gelişti. ortalama takip süresi 45.2 ay (10-136 ay) idi. Cerrahi komplikasyonları tartışıldı.

Sonuç: Belirsiz diferansiasyonlu ekstremite yumuşak doku sarkomları, benign tümörlerle karıştırılabilen ve bazı türleri çok nadir görülen ve uzun dönem prognozu çok kötü olan hastalık grubundadır. Geniş cerrahi sınır ve erken evrede tanı koyma, özellikle önemlidir.

Anahtar kelimeler: Belirsiz diferansiasyonlu sarkomlar, sinoviyal sarkom, ekstremite yumuşak doku sarkomları, tedavi sonuçları, prognoz

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INTRODUCTION

The prevalence of soft tissue sarcomas within all malign tumors is around 0.8% (1). Soft tissue sarcomas are usually categorized on the basis of histogenesis and/or cytomorphological findings. Some malign tumors are defined as the uncertain differentiate tumors according to World Health Organisation criteria and grouped (2). Subtypes of uncertain differentiate extremity soft tissue sarcomas of are; synovial sarcoma(SS) (~10%), extra-skeletal Ewing's sarcoma(EES) (~2%), alveolar soft part sarcoma (ASPS)(~1%), clear cell sarcoma (CCS)(~1%), epithelioid sarcoma (ES)(~1%), and extraskeletal myxoid chondrosarcoma (EMC)(~1%) (3).

Over 80% of synovial sarcoma are presented patients aged 40 years or younger. Epitheloid sarcoma tends to affect adolescents and young adults, although any age group may be affected, clear-cell sarcoma tends to occur in young adults with a peak incidence between 20 and 40 years of age. ASPS tends to arise in young adults and adolescents (mean age 22-27 years), although it may affect younger children and older adults (2). Ewing's sarcoma occurs most often in children and adolescents (4). Mean age at diagnosis for EMC is 52 (5).

It is rather difficult to differentiate these tumors from each other since they frequently appear as painless, sizeable masses, and lead to various histological and MRI imaging findings. Even so, sub-differentiation is important as different subtypes have different prognoses and require different treatment strategies (6,7).

Synovial sarcoma is nearly always misdiagnosed as a benign tumor since they are characterized by slow-growth and small size. Because of these characteristics, all soft tissue masses developing insidiously should be considered as malign until proven otherwise (8). ASPS is observed as a slow-growing soft tissue mass and is usually late-diagnosed with symptoms and signs due to lung or brain metastases (9). The major clinical symptom of extraskeletal Ewing's sarcoma is deep soft tissue sarcoma. Although local pain might be seen in some of the cases, rash, swelling or other inflammatory signs are not observed usually (4). Clear cell sarcomas are typically stiff, slow-growing, painless tumors in almost half of the cases. Doubts of malignancy rarely raise (10). Epitheloid sarcomas, in turn, often emerge as firm, painless, subcutaneous or dermal nodules and dermal involvement often cause ulcerations on the skin (11). EMC often emerges as a slow-growing mass on extremities in adults (12).

Synovial sarcoma, extra-skeletal Ewing's sarcoma and clear cell sarcoma have relatively bad prognosis, with possible relapse and metastasis after tumor resection (4,10,13). Epitheloid tumor, ASPS and extra-skeletal myxoid chondrosarcoma are slow-growing tumors, but they are characterised by a high potential of metastasis, and hence they are considered to have bad prognosis (12,14,15). In all extremity soft tissue sarcomas of uncertain differentiation, tumor size and surgical margin are common prognostic factors (4,10,12-15). The most frequent metastases of these tumors are seen in lungs, which may cause lymph node metastases (4,9,12,14,16,17).

In this study, we report a retrospective analysis of 60 patients. Total of 35 were male and 25 were female with the mean age 33 and postoperative follow-up duration was 45 months. The purpose of this study was to evaluate the clinical outcomes of patients diagnosed with extremity soft tissue sarcoma of uncertain differentiation followed up at our hospital, and to define prognostic factors related with these outcomes.

MATERIALS AND METHODS

Patients who were diagnosed with extremity soft tissue sarcoma of uncertain differentiation at the Department of Tumor Orthopedics of our hospital between 2002 and 2015 were evaluated retrospectively.

The exclusion criteria of the study were the lack of data (missing radiological examination), length of follow-up shorter than 5 years, and first application with a relapsing mass. 3 cases with synovial sarcoma, one case with extra-skeletal Ewing's sarcoma, one case with epitheloid sarcoma, and one case with clear cell sarcoma were excluded from the study.

The patient files were reviewed for PA chest X-ray, pulmonary computed tomography and MRI of the affected extremity.

All patients were assessed in terms of age, sex, primary tumor localization (upper extremities, shoulder joint-proximal part of the arm and further distal, and hip joint-

proximal part of the femur and further distal), regional lymph node involvement, time elapsed until diagnosis, symptoms and findings, grade and size of the tumor, previous treatments, histological subtype of the tumor, type of surgical procedure (marginal resection, wide resection or amputation), microscopic surgical margins (inadequate surgical margin was defined as the tumor being 2 mm or closer to the marked margin), chemotherapy, radiotherapy, post-surgery complications, and post-treatment conditions of patients (Table 1).

Table 1: Baseline and tumor characteristics for the 60 patients with Extremity soft tissue sarcomas of uncertain differentiation (n, %)

Kolej	Localized Disease (n=42)	Metastasis at first diagnosis (n=18)
Sex		
Male	23 (55)	12 (67)
Female	19 (45)	6 (33)
Age (years)		
Median	30 (7-68)	40 (24-66)
Site		
Upper extremities		
Proximal	1 (2)	1 (6)
Distal	9 (21)	1 (6)
Lower extremities		
Proximal	6 (14)	4 (22)
Distal	26 (62)	12 (67)
Size		
< 5 cm.	8 (19)	1 (6)
≥ 5 cm.	34 (81)	17 (94)
Histologic subtype		
Monophasic	12 (46)	5 (71)
Biphasic	14 (54)	2 (29)
Initial surgical resection from other hospitals		
Yes	6 (14)	2 (11)
No	36 (86)	16 (89)
Type of definite surgery		
Wide excision	18 (43)	7 (39)
Radical (amputation)	3 (7)	2 (11)
Marginal excision	21 (50)	9 (50)
Chemotherapy		
Neoadjuvant	4 (10)	3 (14)
Adjuvant	27 (61)	16 (76)
None	13 (29)	2 (10)
Radiation		
Yes	20 (48)	6 (33)
No	22 (52)	12 (67)

Furthermore, patients were divided into two groups as those who had localized tumors and those who had metastases at diagnosis. We aimed to determine the effect of metastas on prognosis. Moreover, both groups were evaluated among themselves in terms of age, sex, primary tumor localization (proximal or distal of the extremity), size (maximum diameter <5 cm or ≥5cm), histological subtype of the tumor, previous treatments, type of surgical procedure (marginal resection, wide resection or amputation), chemotherapy, radiotherapy, and whether bone resection was performed, and their effect on prognosis was evaluated statistically (Table 1).

Statistical Analysis

Overall survival time was calculated from the time of admission to our hospital to death or last follow-up visit. Disease-free survival time was calculated from the time of admission to the occurrence of a local recurrence, distant metastasis or death. The survival analysis was performed by the Kaplan–Meier method. In patients with localized tumor, the following parameters were analyzed by the log–rank test for prognostic value: age, sex, primary tumor site and size, previous treatment, histological subtype, microscopic surgical margins, chemotherapy and radiotherapy.

All statistical analyses were performed by IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp. Armonk, NY). Statistically significant p level was chosen as <0.05, in the study.

Patients' Characteristics

The demographic characteristics of patients were as follows: the mean age was 33.8±14.9 (range: 7-68); 35 (58%) were male and 25 (42%) were female.

18 (30.0%) patients had the metastatic tumor at time of diagnosis. Out of 11 cases with synovial sarcoma, 10 had lung metastases and one had vertebral metastasis. One of 4 ASPS patients had unilateral lung, one had bilateral lung and vertebral, one had lung, vertebral and bone, and one had lung, liver and brain metastasis. One epitheloid sarcoma, one clear cell sarcoma, and one extra-skeletal myxoid sarcoma patients had diffuse lung metastasis.

42 patients (70.0%) had localized disease without any sign of metastasis. 30 patients had synovial sarcoma, 3 had ASPS, 6 had extra-skeletal Ewing's sarcoma, 2 had clear cell

Table 2: Management of problems and failures

Problem	Threatment	N
Preoperative tumor seconder problems		
Deep peroneal nevre palsy (drop foot)	PAFO	4
Post. interosseoz nevre palsy (drop hand)	static wrist splint	1
Wound complications		
Delayed wound healing (i.e. seperation)	Antibiotics, debridgement, suturation	3
Major hematoma/seroma	Antibiotics, debridgement,	1
Wound infection	Antibiotics, debridgement,	4
Wound necrosis	Antibiotics, debridgement, suturation	4
Rt induced complications		
Radyoterapi induced fracture	ORIF	2
Radiodermatitis	Clean, dry dressing, Antibiotics	1
Contracture in the fingers	Physical Therapy and Rehabilitation	1
Extremity edema	Compression socks, mobilization	1

sarcoma and 1 had epitheloid sarcoma (Table 1). The most frequent localization of tumor was in femoral region (24 patients, 40.0%), while tumors localized in lower legs and feet (22, 36.7%), forearms and hands (6, 10.0%), elbows (4, 6.7%), proximal arm (1, 1.7%), sacrum (1, 1.7%), tibia shaft (1, 1.7%) and proximal humerus (1, 1.7%) were also observed.

The mean tumor size was 9.6 ± 5.54 cm (range: 2-25 cm) in all patients (95% CI, 8.1-11.0). While 9 patients (15%) had tumors with a diameter of <5 cm, 51 patients had tumors with a diameter of ≥5cm. 11 patients had low grade, 20 patients had high grade tumors, whereas tumor grades of 29 patients were not specified. Among patients with synovial sarcoma, 18 had monophasic (42.9%), 16 had biphasic (38.0%) sarcomas, while the subtypes of 8 patients (19.0%) were not specified. Even though pre-surgery symptom durations could not be obtained for all patients, it was 26.0 months (range: 1-204 months) for 30 patients. According to the data we obtained, the most frequent symptoms for the admittance of patients were palpable mass and pain, and symptoms and findings related with metastases. Lymph node involvement was present in 11 patients (in 8 patients with synovial sarcoma, 1 patient with epitheloid sarcoma, 1 patient with extra-skeletal Ewing's sarcoma, 1 patient with extra-skeletal myxoid sarcoma).

Only 8 of 60 patients (13.3%) were have been operated by orthopedics or general surgery clinics of different centers with a benign tumor pre-diagnosis and were have been referred to our hospital for definitive diagnosis. Three of the patients who have been operated at different clinics had synovial sarcoma, 2 had ASPS, 1 had clear cell sarcoma, 1 had extraskeletal Ewing's sarcoma and 1 had epitheloid sarcoma. 3 patients were re-excised and 5 patients underwent radical surgery. 1 hip disarticulation and 2 below-knee amputations were performed. 2 patients did not accept amputation; in these patients, tumors were excised instead of performing an amputation, but microsurgery margins remained positive.

Among 52 of 60 patients in total (86.7%), other than 8 patients referred to our hospital for definitive diagnose, 38 had synovial sarcoma, 5 had ASPS, 5 had extra-skeletal Ewing's sarcoma, 2 had clear cell sarcoma, 1 had epitheloid sarcoma and 1 had extraskeletal myxoid chondrosarcoma.

While resection was performed in 34 of 38 patients diagnosed with synovial sarcoma, below-knee amputation was performed in 2 patients, above-knee amputation was performed in 1 patient and ray amputation was performed in 1 patient.

Post-operative adjuvant radiotherapy was administered to patients. 5 patients were excluded from radiotherapy because of the inadequate vascular calibration, lesions or disapproval of treatment.

Bone resection was performed in 19 patients (31.7%) in total (the reasons of bone resection were local invasion to the bone in several of the cases, the necessity of bone resection in order to create a surgical margin due to the proximity of the mass to the bone, proximity/invasion of the mass to important neurovascular structures or bone resection in amputation surgery performed as functional results after extremity-sparing surgery were not expected).

18 patients were metastatic at the time of diagnosis. In

10 of 11 patients with synovial sarcoma had lung metastases and one had vertebral metastasis; one of 4 patients with ASPS had lung metastasis, one had lung and vertebral metastasis, one had lung, vertebral and bone metastasis, one had lung, liver and brain metastasis; 1 patient with clear cell sarcoma had lung metastasis, and 1 patient with extra-skeletal myxoid chondrosarcoma had lung metastasis.

42 patients (70.0%) had localized disease (30 had synovial sarcoma, 3 had ASPS, 6 had extra-skeletal Ewing's sarcoma, 2 had clear cell sarcoma, and 1 had epitheloid sarcoma).

Complications

Four patients had preoperative peroneal damage (drop foot) due to tumoral involvement of deep peroneal nerve, 1 patient had preoperative radial nerve damage (wrist drop) due to posterior interosseous nerve involvement, and 1 patient had impotence due to sacral lesion. PAFO (plastic ankle foot orthosis) for drop foot and static wrist splint for wrist drop were used. All patients tolerated the use of orthoses well.

Twelwe patients (20.0%) had lesion complications. Latency in the epithelization of the lesion was observed in 3 cases, haematoma was observed in 1 case, wound site infections were observed in 4 cases, and necrosis was observed on wound margins in 4 cases. All patients were treated with debridement and antibiotherapy. Radiation-induced complications developed in 5 patients (8.3%). Open reduction internal fixation was performed in 2 patients with secondary fracture development in radiotherapy; 1 patient with radiodermatitis was treated with clean dry dressing and antibiotics; 1 patient developed finger contracture, which was treated with physical therapy and rehabilitation; and 1 patient had edema in extremities, which was treated with compression socks and mobilization (Table 2).

Outcomes

The mean duration of follow-up was 45.2±SD 34.1 months (range:10-136) (95% CI, 36.3-54.0). 5-year overall survival rates of all patients, patients with localized tumors and patients who had metastases at diagnosis were 28%, 34% and 11%, respectively (Figure 1). 20 patients (33.3%) died in 42.6 months on average (between 10 and 125 months) because of disease or chemotherapy. The follow-up and treatment of 22 patients are still ongoing.

21 patients (35.0%) were followed up with disease-free status for 50.6±SD 35.0 months (between 12 and 136 months) on average (95% CI, 36.3-37.8). 19 patients (31.7%) were followed up with disease activity for 42.0±29.6 months (between 12 and 116 months) on average (95% CI, 27.7-56.2).

In 14 patients (23.3%) local recurrence occurred in 33.9 months (between 7 and 95 months) on average after the

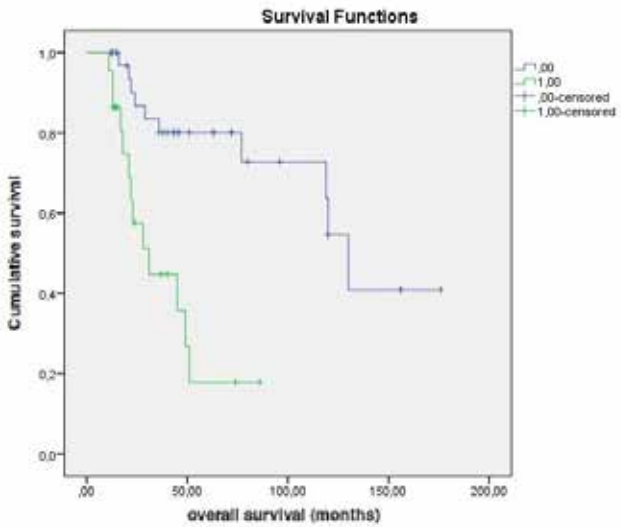

Figure 1: Kaplan-Meier curve comparing survival in soft tissue sarcomas of uncertain differentiation patients with 1.00, metastasis at first diagnosis and those with a 0.00, localised tumor (p≤0.01).

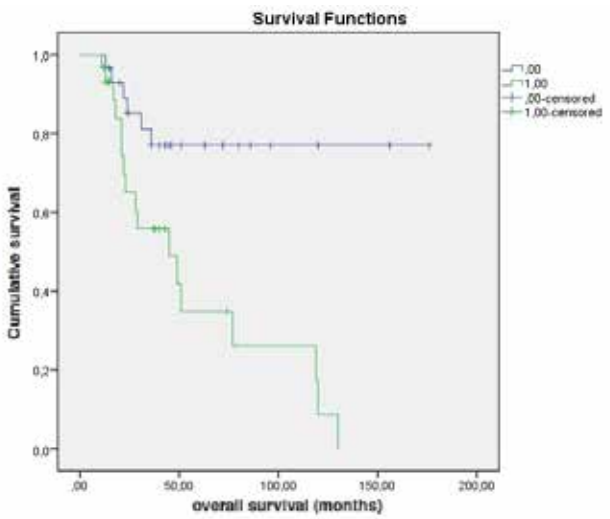

Figure 2: Kaplan-Meier curve comparing survival between soft tissue sarcomas of uncertain differentiation patients with 0.00 , adequate versus 1.00, inadequate surgical margins (p≤0.01).

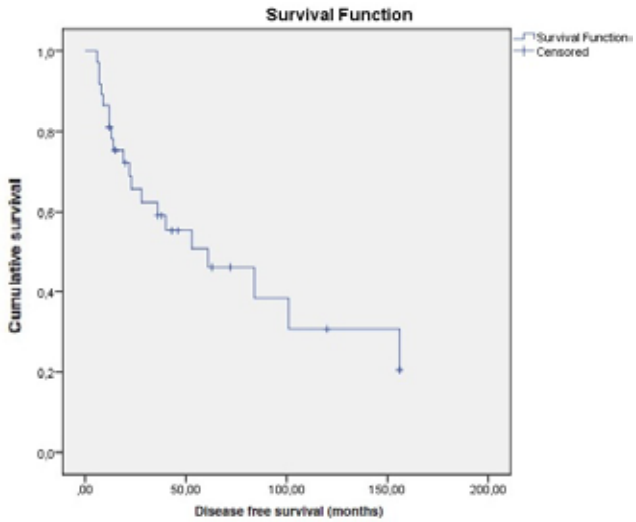

Figure 3: Kaplan–Meier curve showing time from diagnosis to local recurrence or distant metastasis in patients with only localised tumor at diagnosis (n=37).

treatment. 9 of these 14 patients had localized and 5 had metastatic tumors at the time of diagnosis, and lung metastasis developed in 6, and lung, femur and cruris metastases developed in one of these 9 patients with localized disease.

5-year disease-free survival rate was 21% (Figure 2). Metastases developed in 19 patients (31.7%) in 29.7 months (between 4 and 96 months) on average after the treatment.

The presence of metastasis at the time diagnosis affects cumulative survival negatively ($p \leq 0.01$) (Figure 1). Negative surgical margin, on the other hand, affects cumulative survival positively ($p \leq 0.01$) (Figure 2). Prognostic factors which affect the survival time of patients with localized disease at diagnosis are given in Table 2. According to this univariate analysis, statistically significant factors that affect prognosis were tumor size smaller than 5 cm ($0.05<p<0.10$), and the presence of negative surgical margin in definitive surgery ($p \leq 0.01$).

DISCUSSION

The ratio of soft tissue sarcomas within all malign tumors is around 0.8%, and almost 75% of soft tissue sarcomas occur in extremities (1,6). There are a few studies about the distribution of bone and soft tissue tumors in Turkey (18).

It is rather difficult to differentiate these tumors from each other since they frequently appear as painless, sizeable masses, and lead to various histological and MRI imaging findings (6,7).

What should be considered for the first diagnosis of soft tissue malignant sarcomas? Is early diagnosis possible? In the evaluation of soft tissue tumors, potential malignancy should be considered and just follow-up and observation are not enough to even if the lesion is small and painless. If there is a pain in the lesion of the subject, characteristic of the pain should be evaluated well. While the mechanical pain is exacerbated by trauma, a neoplasm originated pain is dull and continuous. Resting pain and night pain should remind malignancy (7).

Another factor that must be evaluated well is age. Because most soft tissue sarcomas are seen frequently in certain age intervals (7). In this study, the most frequent interval was 20-40.

The growth rate of the tumor should also be evaluated. Even if rapid growth leads us to malignancy, malignancy can not be excluded in a soft tissue tumor with a long time history and slow growth (7).

Extremity soft tissue sarcomas of uncertain differentiation include synovial sarcoma (~10%), extra-skeletal Ewing's sarcoma (~2%), %), alveolar soft part sarcoma (~1%), clear cell sarcoma (~1%), epitheloid sarcoma (~1%) and extra-skeletal myxoid chondrosarcoma (~1%) (3). These lesions are typically observed in younger patients (between 20 and 40 years of age) (19). The mean age in our study was 34.0.

In this study, even if the time elapsed from the first symptom to diagnosis cannot be detected in all patients, for the 30 patients, this time was 26 months (1-204). We could not find the common preoperative symptom duration of these tumors in the literature review. The fact that the mean duration is 26 months and duration may be prolonged to 204 months reminds us a question of whether Turkish society is indifferent to soft tissue tumors.

All of these sarcomas may cause lymph node involvement (2). Lymph node involvement was observed in 11 of our cases.

Synovial sarcomas usually develop around joints, and as distinct from other soft tissue sarcomas, they frequently emerge at the distal parts of extremities (most frequently at knees, ankles, and feet) (7). ASPS usually emerge in the

skeletal system, particularly at lower extremities (2), EES paravertebral region and lower extremities (4). Clear cell sarcomas of the soft tissue have a tendency to localize at the lower extremities (20). Epitheloid sarcomas, on the other hand, emerge at distal extremities and have a tendency to localize at forearm and hands (21). Extraskeletal chondrosarcomas typically appear as a sizeable mass of extremities in adults (5).

In literature, 5-year survival rates of synovial sarcoma, ASPS, EES, CCS, ES and EMC range from 57 to 88%, from 46 to 72%, from 32 to 69%, from 48 to 68%, from 40 to 80% and from 82 to 90%, respectively (4,10,13,14,21-23). In this study, 5-year-survival rate for all patient groups was 28%. With respect to other studies, high frequency of microsurgery margin positivity, high frequency of patients with metastasis at the time of diagnosis, patient noncompliance (patients' disapproval of radical surgery and/or re-excision and/or adjuvant treatments or dropping out of follow-up), and failure to administer adjuvant treatments due to surgical complications were suggested as the reasons of relatively worse prognoses.

The main treatment method of synovial sarcoma is surgery (7,13). While the purpose is to achieve surgical margin, the status of chemotherapy and radiotherapy are equivocal (13). There are no reports published so far indicating that radiotherapy administration affected prognosis positively in ASPS treatment, while many publications point out that ASPS is resistant to conventional cytotoxic chemotherapy, indicating that complete excision of the tumor is the only viable treatment (24). Rud examined 42 patients diagnosed with EES retrospectively, and his results revealed that radiotherapy was effective in increasing local control rate in patients who do not have a clear surgical margin and that chemotherapy may eliminate micrometastases in all patients (25). The treatment recommended in 2009 NCCN bone tumor guideline was chemotherapy plus local treatment (surgery and/or radiotherapy) and chemotherapy (4). The treatment option in clear cell sarcoma is surgical wide excision. Radiotherapy is indicated for local control at proximal surgical margins. In case the lesion could not be resected with secure margins or resection would cause vascular or neural damage in the extremity, radical surgery should be planned. Since it is a rarely observed tumor, there are very few publications in the literature on clear cell sarcomas; hence, the benefit of chemotherapy could not be recognized yet (10). Surgical wide excision is the treatment option in epitheloid sarcomas, as well. Although chemotherapy and radiotherapy are standard treatments for recurrent, metastatic or inoperable tumors, their success rates are low (26).

The treatment option in EMC is also surgical wide excision; chemotherapeutic agents or combinations are ineffective, whereas radiotherapy can be administered curatively only if surgical margins are not clear or palliatively when the patient is inoperable (22).

In a study covering 256 patients, Synopsis retrospectively examined the risk factors for postoperative, major wound complications after soft tissue sarcoma resection. Achieving negative surgical margin or sparing the extremity does not always lead to acceptable functional outcomes, which represents approximately 10% of all cases.

Wound complications include dehiscence, cellulitis, abscess, seromas, hematomas, and wound necrosis. These complications are observed in 16-56% of all cases. Available data suggest that the timing of radiotherapy, rather than surgery, leads to significant differences in wound complications, indicating that preoperative and postoperative radiotherapy are associated with wound complication rates of 35% and 17%, respectively (27).

In our study, 12 patients (28.6%) had wound complications; none of them received neo-adjuvant radiotherapy.

Radiotherapy-induced complications were previously defined in the literature as fractures (6-25%), delayed bone healing (45%), osteonecrosis (15%), wound-healing complications (10-28%), and in cases of the skeletally immature, growth plate arrest (60%) (28). 5 patients had secondary radiotherapy complications in our study.

Bone involvement in soft tissue sarcomas is correlated with high patient-related mortality rates. Success of the surgical method in soft tissue sarcomas is defined as the excision of the tumor with wide margins, and soft tissue, bone, and neurovascular structures might be reconstructed if necessary. If wide surgical margins can be achieved without sacrificing critical structures for sufficient functional results such as major nerves, vessels and bones, surgery is

the only treatment option (29). In our study, bone resection was applied to 19 patients (31.7%).

Considering all the bone and soft tissue tumor operations, one of the most catastrophic complications of reconstruction after bone resection is the infection and these cases may present from simple forms that could be treated just with antibiotherapy to heavy forms that may need amputation (30). In this study, wound complications were seen in 12 patients.

The present study had several limitations. Various surgeons participated in the study. It was designed as a retrospective study, and the number of patients was low due to the fact that the evaluated diseases are observed rarely. The same problem occurred in other studies, as well. It may be necessary to conduct a multicenter study in order to obtain a larger population.

Ethics Committee Approval: Ethics committee approval was not received for this study from the local ethics committee.

Informed Consent: Informed consent was obtained.

Author contributions: Development of study - R.O., S.M.A., B.S.G.; Methodological design of the study - R.O., M.A., S.M.A., B.S.G.; Data acquisition and process - M.A.S., E.T.; Data analysis and interpretation - R.O., M.A.S., E.T.; Literature review - R.O., M.A.S., E.T.; Manuscript writing - R.O., M.A., S.M.A.; Manuscript review and revision - R.O., M.A., S.M.A., B.S.G.

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