Alveolar soft-part sarcoma: Analysis of 312 cases

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ABSTRACT

Alveolar soft-part sarcoma (ASPS) is a rare soft tissue malignant tumor. This study aimed to evaluate the epidemiological data of ASPS.

Data on ASPS were obtained from Surveillance, Epidemiology, and End Results (SEER) database. Patients diagnosed with ASPS between 1975 and 2016 were scanned retrospectively. Age, sex, ethnicity, disease prognosis, tumor location, tumor grade, follow-up time, and follow-up results of all patients were evaluated.

A total of 312 patients with ASPS [171 female (54.8%), mean age 27.4 (1–84 years)] were included. The most common tumor location was soft tissues (84.2%). The mean follow-up duration was 86.8 months (range 1–484 months). The most common tumor grade was grade 4, with 30 patients in this category (43.4%). At the time of diagnosis, 104 (48.5%) patients had distant metastasis.

ASPS is a rare soft tissue sarcoma, and approximately half of the patients are metastatic at the time of diagnosis with metastasis to the lungs, most commonly. Despite the high metastasis rate, ASPS has a satisfactory 5-year survival rate.

Key words: Alveolar soft-part sarcoma, epidemiology, soft tissue sarcoma; survival

INTRODUCTION

Alveolar soft part sarcoma (ASPS) is a rare soft tissue malignant tumor. It was first described in 1952 by Christopherson *et al.* [1].

ASPS constituted less than 1% of all soft tissue sarcomas [2]. Besides, these tumors had some interesting features distinctive from other soft tissue sarcomas. One of them was "the frequent occurrence at a young age," and the other one was "metastasis to the brain" [3].

ASPS tends to settle most frequently on the trunk and extremities, but previous studies reported its locations in other body sites. Similar to some other soft tissue sarcomas, the tumor grows slowly and also progresses painlessly. Such cases are often not detected early, and unfortunately, patients are metastatic at the time of diagnosis [1,4].

In the majority of soft tissue sarcomas, the primary treatment is surgical resection. This treatment also applies to ASPS. Adjuvant radiotherapy and chemotherapy are options that can be used to provide local control in the presence of metastasis [2, 5].

This study aimed to define the epidemiology and survival rates of ASPS with information obtained from the Surveillance, Epidemiology, and End Results (SEER) database.

METHODS

In this study, data were obtained from the SEER database. Patients diagnosed with ASPS between 1975 and 2016 were scanned retrospectively.

The SEER database is one of the most comprehensive databases in the United States. This database covers cancer patients. It includes demographic data of patients, cancer incidence, and survival data. This database has been used in many studies, especially in recent years.

The SEER database is a compilation of cancer data in the United States containing the data of approximately 28% of the entire US population [6,7]. One of the most beneficial features of this database is that it provides extensive data from multicenters about rare types of cancers. Thus, studies with high statistical power can be conducted using the SEER database.

The code (ICD-O-3 code 9581/3) in the International Classification of Diseases for Oncology, third edition (ICD-O 3) morphology [8] coding system was used to retrieve patients from the database. The data of patients with ASPS were evaluated in terms of age, sex, ethnicity, marital status, prognosis of the disease, location of the tumor, tumor grade, follow-up time, and follow-up results. The ethnicity of the patients was divided into three groups: white, black, or other (American–Indian or Asian Pacific Islander). The tumor grade was examined in four groups: I, II, III, and IV. Grade I represented well-differentiated tumor, grade II moderately differentiated tumor, grade III less differentiated tumor, and grade IV undifferentiated/anaplastic tumor. The follow-up endpoint was mortality. Patients were categorized into two groups according to the occurrence of death.

Statistical analysis

All statistical analyses were done using IBM SPSS 22.0 statistical software (IBM Corp., NY, USA). Descriptive data were expressed as mean ± standard deviation, frequency, and percentage.

RESULTS

A total of 312 patients, 171 female (54.8%) and 141 male, with ASPS were included in this study. The mean age of the patients was 27.4 (1–84 years). The race/ethnicity of the patients was analyzed; 181 patients were white-skinned (59.5%), 73 were black-skinned, 50 were in the other group, and 8 were not registered in the system.

The lesions were located on the left side in 110 patients and on the right side in 107 patients. In 95 patients, no data on the localization side were found. The most common tumor site was soft tissues (84.2%) (Table 1). The most common location in soft tissues was the lower limb and the hip (58.5%), followed by the upper limb and the shoulder (Table 2).

In histopathological examination, 310 patients had a positive histological diagnosis. Two patients did not have positive histology, but positive exfoliative cytology. While examining the histological gradients of ASPS, the most commonly encountered grade was grade 4 tumors with 30 patients (43.4%), followed by grade 3 tumors with 25 patients. Six patients had grade 1 tumors, and eight patients had grade 2 tumors. The grade of 243 patients was not specified.

Moreover, 104 (48.5%) patients had distant metastases at the time of diagnosis; 110 patients (51.5%) had

Table 1 Tumor localizations

Tumor localization, *n* (%)	
Brain (frontal lobe)	1 (0.3)
Breast	1 (0.3)
Cervix uteri	5 (1.6)
Corpus uteri	7 (2.2)
Cranial nerves	1 (0.3)
Eye and orbid	5 (1.6)
Larynx	1 (0.3)
Liver	1 (0.3)
Lung and bronchus	4 (1.2)
Miscellaneous	3 (0.9)
Nose, nasal cavity and middle ear	1 (0.3)
Other female genital organs	1 (0.3)
Pleura	1 (0.3)
Retroperitoneum	6 (1.8)
Soft tissue	263 (84.2)
Tongue	6 (1.8)
Trachea, mediastinum	1 (0.3)
Uterus	1 (0.3)
Vagina	2 (0.6)

Table 2 Soft tissue localizations

Soft tissue localization, n(%)	
Head, face, and neck	13 (4.9)
Upper limb and shoulder	32 (12.1)
Lower limb and hip	154 (58.5)
Thorax	17 (6.4)
Abdomen	14 (5.3)
Pelvis	23 (8.7)
Trunk	7 (2.6)
Other	3 (1,1)

localized/regional disease. No information was found about other patients regarding whether they had localized or metastatic disease at the time of diagnosis.

The mean follow-up was 86.8 months (between 1 and 484 months) with a survival rate of 50%; 156 (50%) patients are still alive (Table 3). These patients had an average follow-up time of 124.4 months. One-hundred and fifty-six patients were dead. These patients had a follow-up period of 49.3 months.

The 5-year survival was 71.1%, and the average 10-year survival was 63.1%. When the survival rates were evaluated according to the tumor grades, the 5-year average survival was 100% in grade I, 87.5% in grade II, 48% in grade III, and 63.3% in grade IV. The majority of patients were not given grade information. In this group, the 5-year survival was 62.9% (Figure 1).

Table 3 Case processing summary

Grades	Total N	N of deaths	Censored	
			N	Percentage
unspecified	243	120	123	50.6
1.00	6	0	6	100.0
2.00	8	2	6	75.0
3.00	25	18	7	28.0
4.00	30	16	14	46.7
Overall	312	156	156	50.0

DISCUSSION

This study included the scanning of the SEER database for ASPS and analysis of the data of the detected patients. ASPS is a very rare tumor, and studies on this issue are limited. This study represented the analysis of the data of 312 patients. It was found that 50% of the patients in the mean 7-year follow-up period had died. Another conclusion of this study was that the study had partially complicated the analysis as the data of all patients were not fully available. Another result obtained by examining the available data was that approximately 50% of the patients at the time of diagnosis were metastatic. In addition, although ASPS was seen in a broad age range, the mean age of patients was found to be 27 years in this study.

Recent studies indicated that the tumor incidence in Turkey was quite similar to that mentioned in the literature. ASPS was rare and accounted for less than 1% of all soft tissue sarcomas [2]. Therefore, data on ASPA were scarce compared with those on other soft tissue sarcomas. In Turkey, in particular, the ASPS musculo-skeletal system involvement viewed as a single-center case series was seen in a small number of studies [4,9]. Recently, SEER studies examining ASPS have also been conducted. Wang *et al.* investigated the prognostic factors in 2016. In their study, the data between 1972 and 2012 were examined. In their study of 251 patients, they reported that patients had a high rate of metastasis and that their survival was long. They suggested the combination of surgery and radiotherapy in localized patients at the time of diagnosis and surgical treatment in patients with metastatic cancer [10]. In this study, 312 patients were examined and half of the patients were found to have metastatic cancer at the time of diagnosis.

The age range in which ASPS was most common was between 15 and 35 years [5,9]. It commonly occurred in women. In this study, the average age was compatible with the literature data. However, the average was found to be higher in women than in men.

ASPS most commonly occurred on the thigh [11]. As the SEER database grouped the localizations into regions, the most common location was found to be lower extremity and hip in this study.

ASPS had a metastatic rate of 20%–40% at the time of diagnosis. Metastasis to the lung was the most common, as in malignant tumors. Metastasis to the brain and
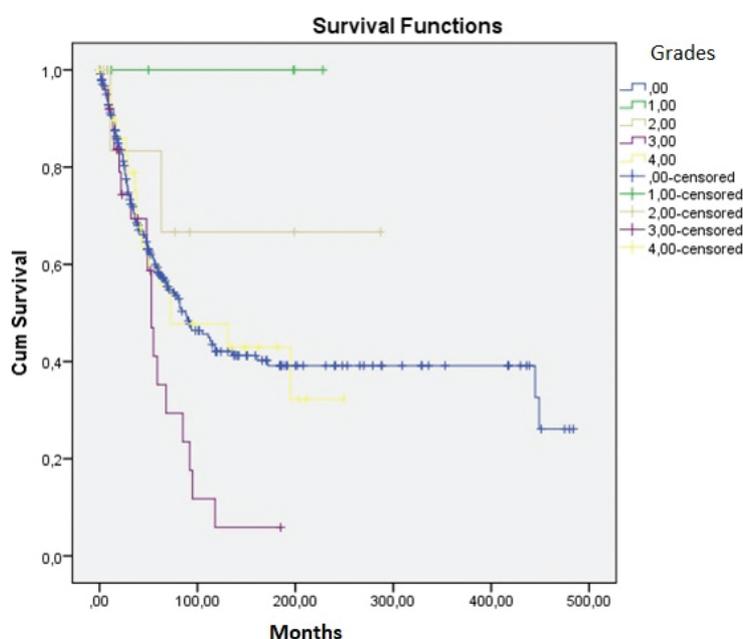

Figure 1 The Kaplan–Meier graph of patients (00: unspecified).

bone was the next most common after the lungs [5,11]. In this study, higher rates of metastasis were found at the time of diagnosis. However, the stages at the time of diagnosis of all patients in the database were not determined. Approximately one-third of the patients had no data on metastasis. Perhaps the clinicians left the metastasis section blank when entering the data of patients without metastasis into the computer.

Previous studies reported on factors affecting the prognosis in ASPS. Some of these factors were stage, surgical margins, and tumor size. In addition, Wang et al. reported that in the presence of metastatic disease at the time of diagnosis, resection of the primary disease was a good prognostic criterion. When the 5-year survival was evaluated according to the tumor stage in this study, grade 1 tumors had the best survival, followed by grade II tumors. Interestingly, the survival of grade IV tumors was slightly better than that of grade III tumors. However, the grade information of most of the patients was not entered. The survival rates of these patients with missing grade information were close to the survival rates of patients with grades III and IV tumors. In addition, the fact that the survival rates of the large group with unknown grades were close to the survival rates of patients with higher grades might mean that the data were not entered in the higher-grade patient group. This might be a reason for the better survival rate of grade IV tumors compared with grade III tumors.

Another interesting point was that, unlike osteosarcoma and Ewing's sarcoma, young patients had better prognosis in ASPS [10,12]. Benign and malign soft tissues were found in the differential diagnosis of ASPS tumors, tumor-like lesions, and metastases. Differential diagnosis was crucial for early diagnosis of the disease [2,9,11,12].

This study had some limitations. First, it was a retrospective analysis. Although it included a period of many years, the number of patients was relatively low as it was a rare disease. Some patients could not be included in the statistical studies because it was a study analyzing database data, and detailed data of all patients could not be found in the database. Hence, some of the demographic data and details on symptoms and treatments for the disease were not mentioned. Besides, detailed data could not be analyzed sufficiently, as some of the data were more general. Large-sample multicenter studies are needed in the future.

CONCLUSIONS

The findings of this study suggested that ASPS is a rare soft tissue sarcoma, and about half of the patients were metastatic at the time of diagnosis. Metastasis to the lung was the most common. It had a relatively indolent clinical course. Despite the high metastasis rates, it had a satisfactory 5-year survival rate.

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