Secondary hematological malignancies in patients with sarcoma: A single-center retrospective study

YOON JUNG JANG[1*], HONG KYU JEONG[1,2*], CHANG-BAE KONG[3], WON SEOK SONG[3], WAN HYEONG CHO[3], DAE GEUN JEON[3], HEYJIN KIM[4], SUNG HYUN YANG[1], IM IL NA[1], HYO-RAK LEE[1] and HYE JIN KANG[1]

[1]Department of Hematology and Oncology, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences, Seoul 01812; [2]Department of Hematology and Oncology, Hallym Hospital, Incheon 21079; Departments of [3]Orthopedic Surgery and [4]Laboratory Medicine, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences, Seoul 01812, Republic of Korea

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Abstract. The present retrospective study investigated the clinical features and prognosis of secondary hematological malignancies (SHMs) in patients with sarcoma at Korea Cancer Center Hospital (Seoul, South Korea). Patients who had been diagnosed with SHMs after having received treatment for sarcoma between January 2000 and May 2023 were enrolled. Clinical data were collected from the patients' medical records. Clinical characteristics were analyzed, including SHM incidence, type and prognosis. Of 2,953 patients with sarcoma, 18 (0.6%) were diagnosed with SHMs. Their median age at the time of sarcoma diagnosis was 39.5 (range, 9-72) years, and 74% (n=14) of these patients were male. The histological features of sarcoma varied, with osteosarcoma diagnosed in nine patients (50%). All patients with sarcoma underwent surgical treatment, and 16 (88.8%) received chemotherapy. The most common type of SHMs was acute myeloid leukemia (n=6; 33.3%), followed by myelodysplastic syndrome (n=5; 27.7%). The median latency period between the sarcoma diagnosis and SHM identification was 30 (range, 11-121) months. A total of 13 (72.2%) patients received treatment for the SHM. The median overall survival after SHM diagnosis was 15.7 (range, 0.4-154.9) months. The incidence of SHMs in sarcoma in the present study was consistent with that reported previously. The presence of SHMs was associated with a poor patient prognosis, especially if treatment for SHMs was not administered.

Correspondence to: Dr Hye Jin Kang, Department of Hematology and Oncology, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences, 75 Nowon-ro, Nowon, Seoul 01812, Republic of Korea
E-mail: hyejin@kirams.re.kr

*Contributed equally

Abbreviations: SHM, secondary hematological malignancy; IRB, Institutional Review Board; RT, radiotherapy; AML, acute myeloid leukemia; AA, aplastic anemia; OS, overall survival; NED, no evidence of disease; t-MNs, therapy-related myeloid neoplasms

Key words: RT, latency, sarcoma, SHM, secondary malignancies

Introduction

Sarcoma is a mesenchymal-derived tumor that accounts for ~1% of all cancers and has a particularly high incidence in children, accounting for ~20% of pediatric solid cancers (1,2). The World Health Organization classifies sarcomas into soft tissue and bone tumors, and numerous subtypes have been identified (3). Sarcomas can occur in various locations, including the abdominal cavity, arms, legs, and head and neck. The prognoses of sarcomas vary depending on their location and subtype. The 5-year survival rate for sarcomas is >50% (4,5).

The number of cancer survivors is increasing, leading to an increased occurrence of secondary malignancies (6,7). Secondary malignancy is defined as the development of a new primary tumor unrelated to the recurrence or metastasis of the initial tumor (8). Owing to the growing interest in secondary malignancies, their incidence, risk factors and screening have been studied (9-11). Previous studies suggested that age and treatment dose as well as the well-known chemotherapy and radiotherapy (RT) were associated with the development of secondary hematological malignancies (SHMs) (12-15).

Regarding the epidemiology of sarcoma, young adults and adolescents comprise 30-50% of the patient population, in which long-term survival has been reported (1). However, the common treatment methods, cytotoxic chemotherapy and radiation therapy, can increase the risk of secondary malignancies; thus, the incidence of these malignancies in patients with sarcoma is expected to increase (16-19). Nevertheless, research on SHMs in sarcoma, including the clinical characteristics, SHM types, and prognosis of affected patients, is scarce (20-22). Furthermore, previous studies have focused only on specific subgroups including young patients, subtypes

of sarcoma, or therapy-related acute myeloid leukemia (t-AML) alone (20,22,23).

Therefore, the present retrospective study investigated the clinical characteristics and prognoses of all SHMs in patients with sarcoma.

Materials and methods

Study design and patients. A retrospective analysis of the data of patients diagnosed with SHMs after receiving treatment for sarcoma was performed at the Korea Cancer Center Hospital (Seoul, South Korea) between January 2000 and May 2023 (Seoul, Korea). The inclusion criteria were: (i) Pathological diagnosis of sarcoma, ii) sarcoma treatment history, and iii) SHMs diagnosis after sarcoma treatment. The exclusion criterion was sarcoma, identified as a secondary malignancy that developed after a primary cancer diagnosis. The present study was approved (approval no. 2023-05-004) by the Institutional Review Board of Korea Cancer Center Hospital. Due to the retrospective nature of the current analysis, informed consent was not required for the present study, which was conducted in accordance with the tenets of the 2013 Declaration of Helsinki.

Data collection. Clinical characteristics were obtained from the patients' medical records. The following variables were analyzed: Age, sex, date of diagnosis of sarcoma, pathological diagnosis of the sarcoma, stage of the sarcoma, primary site of the sarcoma, whether treatment was performed, chemotherapy regimen, number of chemotherapy cycles, whether radiation therapy was performed, date of SHM diagnosis, SHM type, sarcoma status at the time of its diagnosis, latency between the dates of sarcoma and SHM diagnoses, SHM treatment, and date of patient's death.

Statistical analysis. Categorical variables are presented as numbers and proportions, while continuous variables are described as medians (ranges). Latency was defined as the time interval between the diagnosis of sarcoma and the occurrence of SHMs. Overall survival (OS) indicated the period from SHM diagnosis to death, regardless of the cause. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp.).

Results

From January 2020 to May 2023, 2,953 patients were diagnosed with sarcoma and received treatment, including chemotherapy, in 1,658 patients. Among the patients diagnosed with sarcoma, 18 who developed SHMs were ultimately enrolled in the present study. The patient details are summarized in Fig. 1.

Patient characteristics. The clinical features of the 18 patients included in the present study are included in Table I. Their median age was 39.5 (range, 9-72) years, with a predominance of men (n=14, 77.7%). Osteosarcoma accounted for half of the cases (n=9, 50%), followed by undifferentiated pleomorphic sarcoma (n=4, 22.2%) and Ewing's sarcoma (n=2, 11.1%). Regarding the initial disease stage, most patients had localized

Table I. Baseline patient characteristics (n=18).

Characteristic	Value
Sex, n (%)	
Male	14 (77.7)
Female	4 (22.3)
Median age at diagnosis of sarcoma (range), years	39.5 (9-72)
Sarcoma histology, n (%)	
Osteosarcoma	9 (50.0)
Ewing sarcoma	2 (11.1)
Chondrosarcoma	1 (5.5)
Liposarcoma	1 (5.5)
Undifferentiated pleomorphic sarcoma	4 (22.2)
Synovial sarcoma	1 (5.5)
Stage of sarcoma at initial diagnosis, n (%)	
Localized	14 (77.7)
Metastatic	4 (22.2)
Primary site of tumor, n (%)	
Femur	6 (33.3)
Thigh	6 (33.3)
Tibia	3 (16.6)
Buttock	1 (5.5)
Chest wall	1 (5.5)
Axilla	1 (5.5)
Sarcoma treatment, n (%)	
Surgery[a]	
Yes	18 (100.0)
No	0 (0.0)
Chemotherapy[a]	
Yes	16 (88.8)
No	2 (11.1)
Radiotherapy	
Yes	0 (0.0)
No	18 (100.0)
SHM type, n (%)	
Myelodysplastic syndrome	5 (27.7)
Acute myelogenous leukemia	6 (33.3)
Acute lymphocytic leukemia	3 (16.6)
Aplastic anemia	1 (5.5)
Chronic myeloid leukemia	1 (5.5)
Follicular lymphoma	1 (5.5)
Multiple myeloma	1 (5.5)
Median age at SHM diagnosis (range), years	44 (10-77)
Median time from sarcoma diagnosis to SHM diagnosis (range), months	30 (11-121)
SHM treatment, n (%)	
Yes	13 (72.2)
No	5 (27.7)
Sarcoma status at SHM diagnosis, n (%)	
NED	9 (50.0)
Local recurrence	1 (5.5)
Distant recurrence	8 (44.4)

SHM, secondary hematological malignancy; NED, no evidence of disease; [a], 16 patients received surgery and chemotherapy.

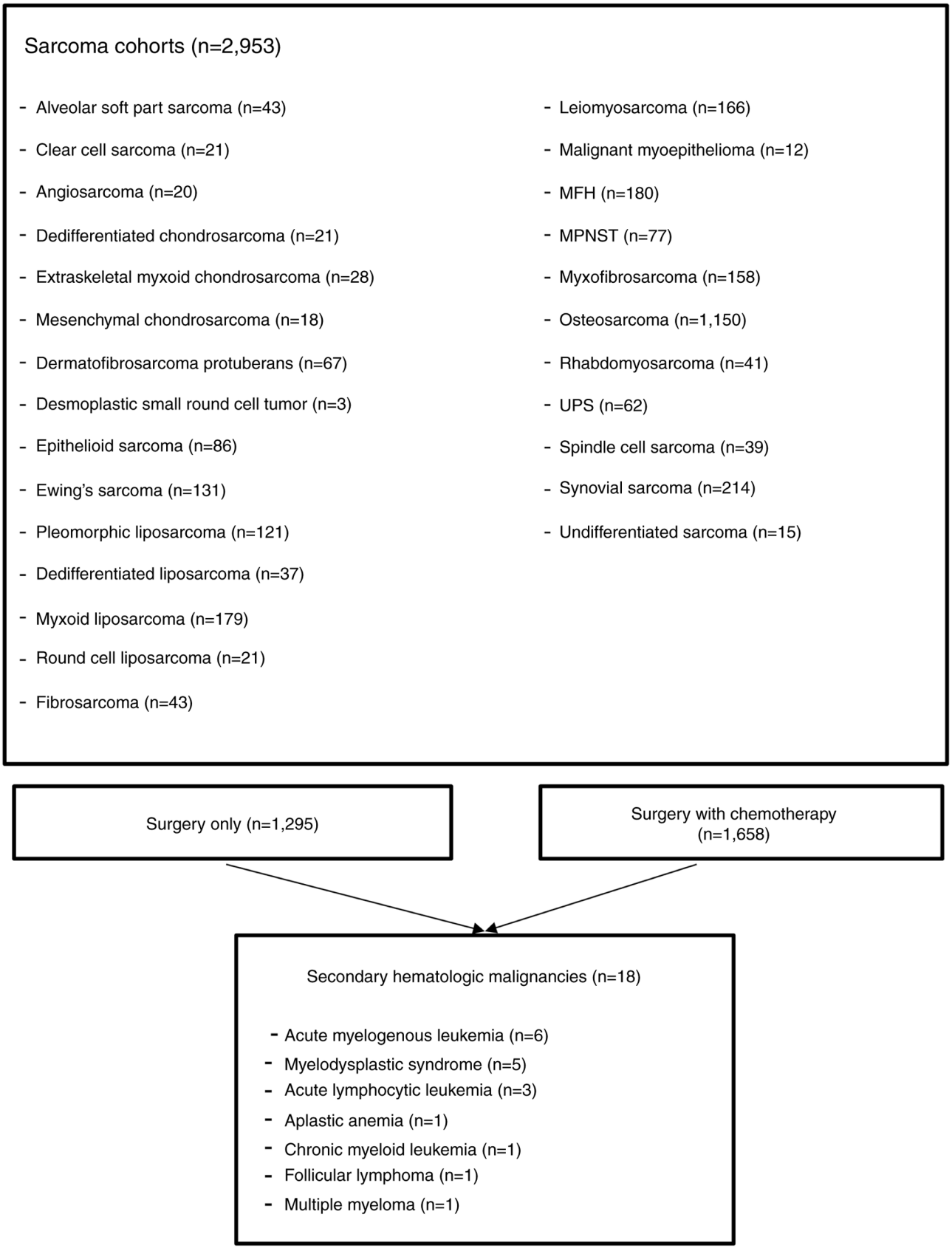

Figure. 1. Flowchart of patient inclusion. MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; UPS, undifferentiated pleomorphic sarcoma.

disease (n=14, 77.7%), whereas a small proportion had metastatic disease (n=4, 22.2%). The most frequent primary tumor sites were the femur and thigh (n=6; 33.3%), followed by the tibia (n=3; 16.5%) and buttocks (n=1; 5.5%). All patients (n=18,

Table II. Clinical and therapeutic details and outcomes of the study patients.

Patient no.	Age at sarcoma diagnosis (years)	Sex	Histology	Chemotherapy regimen	Sarcoma status at the time of SHM diagnosis	SHM	Cytogenetics		Latency (months)	SHM treatment	Treatment regimen	Current status	Median OS time after SHM diagnosis (months)
							Chromosome	FISH					
1	24	M	Osteosarcoma	MMCA (6 cycles) MMIB (6 cycles)	Distant recurrence	MDS		del (7q)	59.3	N	Not treated	Dead	3.3
2	57	F	Synovial sarcoma	MAID (1 cycle) IA (6 cycles) VIP (2 cycles)	Distant recurrence	MDS		del (7q)	14.6	N	Not treated	Dead	3.2
3	68	M	Osteosarcoma	Not treated	NED	MDS	46, XY, del (20) (q11,2) [13]/46, idem, der (Y) t (Y;1) (q12: q12), del (11) (q14) [7]		112.4	N	Not treated	Alive	29.7+
4	59	F	UPS	MMCA (6 cycles)	NED	AML	-7[13]		21.0	N	Not treated	Dead	6.2
5	47	M	Chondrosarcoma	MAID (2 cycles) ICE (2 cycles) CYVADIC (4 cycles)	NED	FL	Not tested		11.2	Y	IFRT	Alive	38.7+
6	18	F	Ewing sarcoma	IA (6 cycles)	NED	AML	Not tested		31.2	Y	HDAC induction-HSCT	Alive	154.9+
7	16	F	Osteosarcoma	(MM)CA (2 cycles) (M)ICE (4 cycles) CA (6 cycles)	Distant recurrence	AML	inv(11)(p15q22) [17]/46,ide m,del(13)(q12q14)[3]		25.7	Y	AD induction-f/u loss	Dead	13.9
8	44	M	UPS	MAID (2 cycles) MMCA (2 cycles) IP (2 cycles) ICE (8 cycles)	Distant recurrence	ALL	t(4;11)(q21;q23)[20]		49.5	Y	CTX+PD	Dead	0.9
9	21	M	Osteosarcoma	MMCA (6 cycles)	NED	AML	inv(16)(p13.1q22) [9]/46,X Y[6]		18.5	Y	AD induction + HDAC consolidation	Alive	88.3+

Table II. Continued.

Patient no.	Age at sarcoma diagnosis (years)	Sex	Histology	Chemotherapy regimen	Sarcoma status at the time of SHM diagnosis	Cytogenetics			Latency (months)	SHM treatment	Treatment regimen	Current status	Median OS time after SHM diagnosis (months)
						SHM	Chromosome	FISH					
10	50	M	UPS	ICE (5 cycles) MAID (6 cycles)	Distant recurrence	AML	t(8;16)(p11.2;p13.3)[16]/4 6,XY[4]		24.9	Y	AD induction + HDAC consolidation	Alive	27.8+
11	68	M	UPS		Distant recurrence	MM		Trisomy 1q	18.6	Y	Rd	Alive	17.6+
12	21	M	Osteosarcoma	(MM)CA (6 cycles) ICE (10 cycles) Gemcitabine + docetaxel (4 cycles) ICE (1 cycle)	Distant recurrence	AML	der(2)t(2;11)(q31;p15),der(11)add(11)(p15)t(2;11)[19]/46,XY[1]		45	N	Not treated	Dead	0.4
13	45	M	Osteosarcoma	MMCA (4 cycles)	NED	CML	t(9,22)(q34;q11.2)[19]/4 6, XY[1]	BCR/A BL1 rearrangement	110.6	Y	Imatinib	Alive	131.1+
14	9	F	Osteosarcoma	CA (3 cycles) IB (1 cycle) CA (2 cycles) IB (1 cycle) CA (2 cycles) IB (1 cycle)	NED	ALL	68~72,XXY,+1,-2,-3,der(4)t(4;5)(q25;q13),-5,-7,+8,-9,+10,+11,add(13)(p11.2),-15,-16,-17,-18,+19,+20,+21,+5~7mar/46,XY[17]		48.3	Y	VPDL-6MP-MTX	Dead	11.2
15	35	M	Osteosarcoma	CA (5 cycles)	NED	MDS	Not tested		65.8	Y	NA	Dead	12.6
16	20	M	Osteosarcoma	CA (7 cycles) ICE (6 cycles)	Distant recurrence	MDS		del(5q31) del(7q) del(20q32)	123.7	Y	Azacitidine	Alive	9.4+

Table II. Continued.

Patient no.	Age at sarcoma diagnosis (years)	Sex	Histology	Chemotherapy regimen	Sarcoma status at the time of SHM diagnosis	SHM	Cytogenetics		Latency (months)	SHM treatment	Treatment regimen	Current status	Median OS time after SHM diagnosis (months)
							Chromosome	FISH					
17	9	M	Ewing sarcoma	IA (6 cycles)	NED	ALL	Not tested		12.8	Y	HSCT	Dead	36.3
18	72	M	Liposarcoma	ICE (3 cycles)	Local recurrence	AA	46, XY		30.9	Y	CsA + Eltrombopag	Dead	0.8

SHM, secondary hematological malignancy; OS, overall survival; FISH, fluorescence *in situ* hybridization; MMCA, high-dose methotrexate, cisplatin, MMIB, high-dose methotrexate; MDS, myelodysplastic syndrome doxorubicin/adriamycin; MAID, mesna, doxorubicin/adriamycin ifosfamide, dacarbazine; IA, ifosfamide, doxorubicin/adriamycin; VIP, etoposide, ifosfamide, cisplatin; NED, no evidence of disease; UPS, undifferentiated pleomorphic sarcoma; AML, acute myeloid leukemia; ICE, ifosfamide doxorubicin/adriamycin, carboplatin, etoposide; CYVADIC, cyclophosphamide vincristine, dacarbazine; FL, follicular lymphoma; IFRT, involved field radiation therapy; HDAC, high-dose cytarabine; HSCT, hematopoietic stem cell transplantation; CA, cisplatin, doxorubicin/adriamycin; AD, daunorubicin, cytarabine; IP, ifosfamide, cisplatin; ALL, acute lymphoblastic leukemia; CTX, cyclophosphamide; PD, prednisolone; MM, multiple myeloma; CML, chronic myeloid leukemia; IB, ifosfamide, bleomycin; VPDL, vincristine, prednisolone, L-asparaginase, daunorubicin; 6MP, 6-mercaptopurine; MTX, methotrexate; AA, aplastic anemia; CsA, cyclosporine.

100%) underwent surgery as part of their treatment and did not receive RT. Most patients (n=16, 88.8%) received chemotherapy.

Chemotherapy. The data of the 16 patients who received chemotherapy for sarcoma treatment are presented in Table II. A median of 8.5 chemotherapy cycles was administered (range, 3-21 cycles). Among these patients, six received more than third-line chemotherapy. Each patient received a median of five chemotherapy agents (range, 2-8). The most commonly used chemotherapeutic agent was doxorubicin/adriamycin (15 patients, 83.3%), followed by ifosfamide and cisplatin [13 (72.2%) and 11 (61.1%) patients, respectively]. Among topoisomerase II inhibitors, doxorubicin/adriamycin (15 patients, 83.3%) and etoposide (eight patients, 44.4%) were commonly administered. Among alkylating agents, ifosfamide, cisplatin, carboplatin and dacarbazine were administered to 13 (72.2%), 11 (61.1%), eight (44.4%), and four (22.2%) patients, respectively. Additionally, seven (38.8%) and one (5.5%) patients received methotrexate and gemcitabine, respectively. A detailed list of the chemotherapeutic agents administered is provided in Table SI.

SHMs. Among the 2,953 patients with sarcoma included in the present study, 18 developed SHMs. The most prevalent SHMs were AML (n=6, 33.3%) and myelodysplastic syndrome (n=5, 27.7%). Additionally, three patients (n=3, 16.6%) developed acute lymphoblastic leukemia, whereas one each (n=1, 5.5%) developed aplastic anemia (AA), chronic myeloid leukemia, follicular lymphoma and multiple myeloma. Regarding the SHMs incidence according to the type of treatments, two of 1,295 patients (0.15%) who had a history of surgery alone developed SHMs, while 16 of 1,658 patients (0.96%) who underwent both surgery and chemotherapy developed SHMs. The incidence of SHMs differed significantly between the two groups (P<0.001) (Table SII). The SHMs occurred at a median patient age of 44 (range, 10-77) years. The latency from sarcoma diagnosis to SHM occurrence was 30 (range, 11-121) months. A total of 10 out of 18 patients (55.5%) succumbed to SHM. The median OS period after SHM diagnosis was 15.7 (range, 0.4-154.9) months. A summary of the clinical history of the 18 patients who were diagnosed with SHMs following sarcoma is provided in Fig. 2.

Of these 18 patients, 14 had available data from cytogenetic studies. Among these 14, four patients (22.2%) had monosomy 7 or 7q/5q deletions. Additional information regarding the cytogenetic study data for each of these patients is provided in Table II.

A total of five patients (n=5, 27.8%) did not receive treatment for SHMs. Among them, three patients did not receive treatment due to metastatic sarcoma, poor performance status and the risk of cytopenia-related infection. The other patients had no evidence of sarcoma disease (NED) at the time of SHMs diagnosis but had pancytopenia with pneumonia; thus, the patient refused further treatment. The last patient who already had NED for sarcoma did not need further treatment for SHMs because of low-risk myelodysplastic syndrome. All patients succumbed except for one patient who did not require chemotherapy (Table SIII).

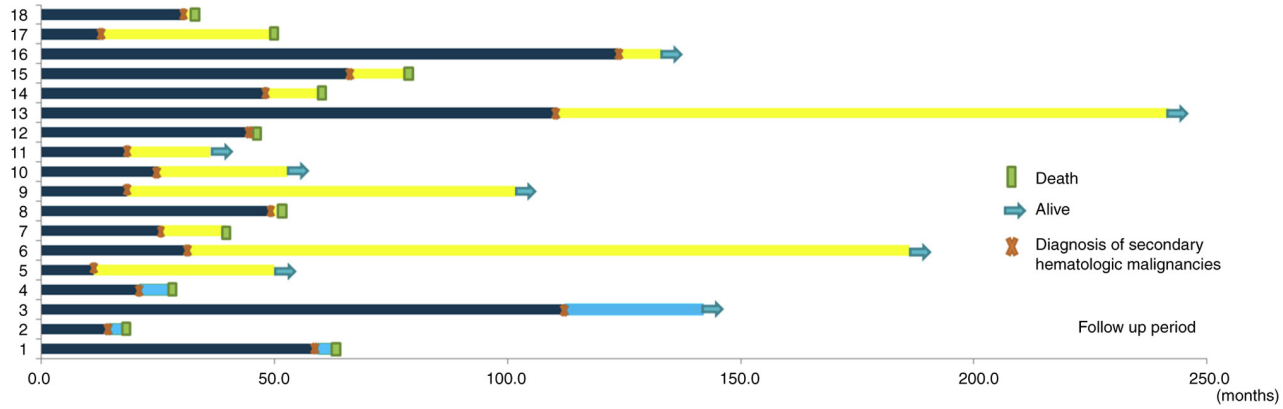

Figure. 2. Timeline-based clinical history of 18 patients diagnosed with SHMs after sarcoma diagnosis. Yellow line, patients who received SHM treatment; light blue line, patients who did not receive SHM treatment; orange X, diagnosis of a SHM; yellow-green square, death; blue arrow, survival. SHM, secondary hematological malignancy.

Discussion

In the present single-center retrospective study, the analysis of SHM occurrence in patients treated for sarcoma revealed that SHMs occurred rarely. Among the patients included in the present study, osteosarcoma was the most common sarcoma, while therapy-related myeloid neoplasms (t-MNs) were the most common among the SHMs. The prognosis of patients who developed SHMs was poor. Although they rarely occur, the risk of SHMs in patients who have received treatment for sarcoma, especially chemotherapy, and who have shown long-term survival, should be considered.

The incidence rate of SHM after sarcoma treatment was 0.6%, similar to the incidence rate of 0.79% reported previously (23). There is a complex mechanism involving multiple factors regarding the occurrence of SHM. According to a previous study, DNA damage and mutations caused by chemotherapy and radiation therapy were reported to be the causes of SHMs (15). Chemotherapy, or RT, does not just focus on tumor cells; it also impacts normal cells. Critically, prolonged exposure can interfere with the genes that regulate the growth and specialization of hematopoietic stem and precursor cells, potentially leading to the emergence of a neoplastic myeloid clone (16). Since the degree of occurrence of DNA damage and mutation varies depending on multiple factors that each patient has, SHMs may have occurred only in some patients who received chemotherapy. Previous studies have also identified factors associated with SHMs, such as patient age, the sensitivity of the organs, and RT treatment dose (12).

The analysis of the present study revealed a significant difference of the incidence of SHMs according to previous treatment history, consistent with those of other studies. Considering this result, chemotherapy may be associated with the occurrence of SHMs though there is a potential bias in the present results. Multivariate analysis would have been useful in the present study to identify other risk factors, but due to the nature of the data, the analysis was unable to be performed. A larger-scale study in the future is necessary to identify factors associated with SHM occurrence.

Among the patients in the present study, 16 (88.8%) received chemotherapy. Among these patients, doxorubicin/adriamycin was the most frequently administered chemotherapy agent (93%), followed by ifosfamide (81%) and cisplatin (68%). Additionally, methotrexate, carboplatin and etoposide, which correspond to similar real-world practices, were used. A study conducted across four European countries, including patients with soft tissue sarcoma, reported that 68.4 and 40.2% of patients were administered doxorubicin/adriamycin and ifosfamide, respectively (24). Furthermore, an investigation of patients with bone sarcoma in Korea revealed that high-dose of methotrexate, doxorubicin/adriamycin, and cisplatin and also vincristine, doxorubicin/adriamycin, cyclophosphamide, etoposide, and ifosfamide were used as first-line chemotherapy in most patients, similar to the findings of the present study (25).

Alkylating agents and topoisomerase II inhibitors are chemotherapeutic agents commonly known to cause t-MNs. Alkylating agents modify DNA, resulting in DNA cross-linking, double-stranded breaks, mutations and cytotoxicity. In particular, t-MN is commonly characterized by chromosomal abnormalities involving chromosome 5 and/or 7, complex karyotypes and TP53 aberrations (26). Conversely, topoisomerase II inhibitors hinder the rejoining of DNA strands cleaved during replication, thereby inducing double-stranded DNA breaks. The two prevalent mutations are t(11q23.3) and t(21q22.1) (27). In the present cohort study, ten patients were diagnosed with t-MN after chemotherapy. A total of eight out of ten underwent cytogenetic testing, five of whom exhibited cytogenetic abnormalities commonly associated with t-MN. The latency period for developing t-MN is typically 5-7 years for alkylating agents and 2-3 years for topoisomerase II inhibitors (28). In the patient group of the present study, the median latency period for developing t-MN following chemotherapy was relatively short, at 28.5 (range, 14.6-123.7) months. Recent studies have reported varying latency periods for t-MN appearance, ranging from 1 to 10 years; therefore, the results of the present study do not differ considerably from previously reported results (26). Considering the well-known risk factors of chemotherapy or radiation therapy for AA (29), it is reasonable to suspect that the patients in the present study who underwent chemotherapy had a high risk of developing therapy-related AA. The results of the present study were

consistent with those of previous studies on SHMs, suggesting that prior treatment for the primary tumor is a considerable risk factor.

After the SHM diagnosis, 10 patients succumbed. Among these patients, at the time of SHM diagnosis, four, one, and five had no evidence of sarcoma, local recurrence, or distant recurrence, respectively. Regarding the five patients who did not receive treatment for SHMs, four succumbed. Among the patients, three had refractory metastatic sarcoma. A previous study suggested that metastatic soft tissue sarcoma has a poor prognosis (30). Their attending physicians determined that the risks associated with SHM treatment, such as the risk of infection, outweighed the potential benefits of chemotherapy for these patients. On the other hand, the other two patients who did not received chemotherapy showed no evidence of sarcoma disease. Although one of them was considered for SHM treatment, it was not pursued due to complications of pancytopenia with pneumonia caused by SHMs. The last one did not require chemotherapy because of the presence of low-risk myelodysplastic syndrome. These findings may suggest that physicians managing SHM patients consider the status of sarcoma during their decision-making process about the treatment of SHMs in real-world practice.

The present study had several limitations. First, this was a retrospective study, and because of insufficient data, multivariate analysis was not possible to be performed due to factors contributing to the occurrence of SHMs. Secondly, soft tissue and bone sarcomas analyses were not within the capacity of the present study to be conducted separately. Thirdly, most of the patients who were diagnosed with SHMs had been treated for sarcoma before the implementation of NGS at Korea Cancer Center Hospital. Consequently, no NGS data were available for any of patients diagnosed with SHMs. Finally, the prevalence of SHMs may have diminished owing to the loss of follow-up after a sarcoma diagnosis. Despite these limitations, to the best of the authors' knowledge, this is the first study focusing on the incidence of SHMs in all patients with bone and soft tissue sarcoma across all age groups. Future nationwide studies should identify the risk factors associated with the development of SHMs.

In conclusion, this is the first study on the overall incidence and characteristics of SHMs in patients with all types of sarcoma. As in the case of previous studies, SHMs occurred infrequently among the patients in the present study diagnosed with sarcoma. However, patients who received chemotherapy for sarcoma were more prone to develop SHMs than those who did not. Additionally, the presence of SHMs was associated with a poor prognosis. Therefore, caution is needed regarding SHM occurrence in patients with long-term survival after a diagnosis of sarcoma, especially in pediatric patients who have received chemotherapy.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

YJJ and HKJ conceived and designed the analysis. YJJ, HKJ, CBK, WSS, WHC, DGJ, HK, SHY, IIN, HRL and HJK contributed data and analysis tools. YJJ and HKJ confirm the authenticity of all the raw data. YJJ and HJK wrote the first draft of the manuscript. YJJ, HKJ, CBK, WSS, WHC, DGJ, HK, SHY, IIN, HRL and HJK performed data interpretation, and reviewed and commented on the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved (approval no. 2023-05-004) by the Institutional Review Board of Korea Cancer Center Hospital (Seoul, South Korea) and was conducted in accordance with the tenets of the Declaration of Helsinki. Due to the retrospective nature of the current analysis, informed consent was not required for the present study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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