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Abstract

We conducted a clinicopathological analysis of chondrosarcomas in 17 patients treated in our institute. The 5- and 10-year overall survival rates of the patients were 72.3% and 61.9%, respectively. The significant prognostic factors were size and histologic grade of the tumor. Sex, age, location of the primary tumor, or the presence of a preceding exostosis did not affect the treatment results significantly. Chondrosarcomas of histologic grades I and II did not metastasize, while all grade III and dedifferentiated chondrosarcomas metastasized to the lung. The local recurrence rate depended on the surgical margin. Wide excision with an adequate surgical margin is important to achieve local control of the chondrosarcoma.

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Clinicopathology of Chondrosarcoma

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We conducted a clinicopathological analysis of chondrosarcomas in 17 patients treated in our institute. The 5- and 10-year overall survival rates of the patients were 72.3% and 61.9%, respectively. The significant prognostic factors were size and histologic grade of the tumor. Sex, age, location of the primary tumor, or the presence of a preceding exostosis did not affect the treatment results significantly. Chondrosarcomas of histologic grades I and II did not metastasize, while all grade III and dedifferentiated chondrosarcomas metastasized to the lung. The local recurrence rate depended on the surgical margin. Wide excision with an adequate surgical margin is important to achieve local control of the chondrosarcoma.

Key words: chondrosarcoma, pathological grading, prognostic factors

Chondrosarcoma is a relatively rare neoplasm which originates mainly in the skeletal system. According to the bone tumor registry in Japan, the number of chondrosarcomas registered annually is under 50, and it accounts for 2.3% of bone tumors and 17% of bone sarcomas (1). As the histological findings and clinical course of the disease are varied, it is important to understand the factors which affect the treatment results before treating patients with chondrosarcoma. Previous clinicopathological evaluations of the disease have shown that tumors of higher histologic grade are associated with shorter survival (2-5). However, because of its rarity, there have been a few reports about the clinicopathological features of the disease. In this paper, we review the treatment outcomes of 17 chondrosarcomas in our institute and investigated the factors which affect the rate of local recurrence, metastasis, and survival of the patients.

Patients and Methods

From July 1967 to June 1995, we treated 17 patients with chondrosarcoma in our institute. Seven of the patients were men and 10 were women. Their ages ranged from 16 to 60 years with an average of 41.8 years (Fig. 1). The patients were divided into two age groups in 40 years. The location of the primary tumors and their average size are shown in Table 1. Chondrosarcoma which developed in preexisting exostosis were defined as secondary chondrosarcoma. There were three patients with secondary chondrosarcoma. Their ages were 18, 19 and 43 with an average of 26.7 years. Surgical treatments were performed in all patients and the surgical margin of the original operative procedures were evaluated in 14 patients. The numbers of patients treated by intralesional, marginal, and wide excisions were 2, 4, and 8, respectively. In this series, none of the patients was given adjuvant chemotherapy. The follow-up period was 7.3 years on the average (0.4-22.5 years).

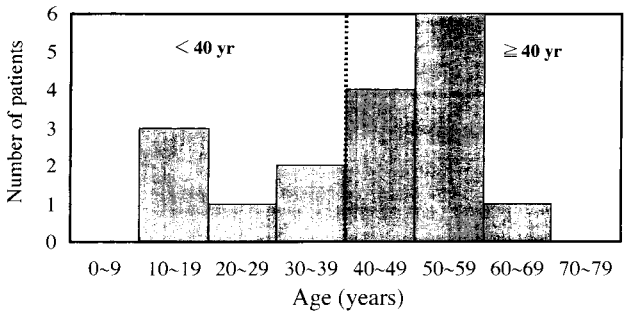

Fig. 1 Distribution of 17 patients of chondrosarcoma by age.

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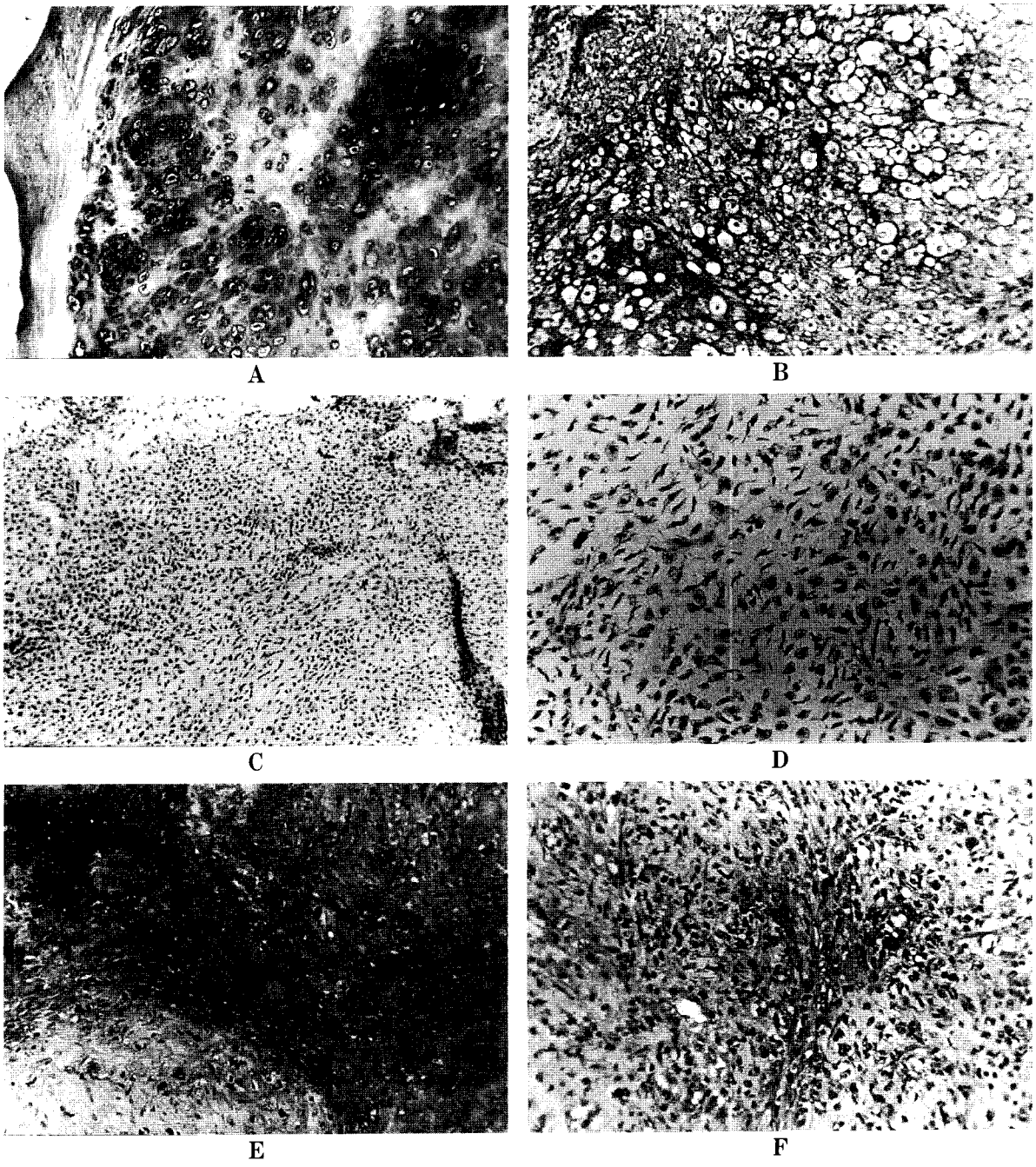

Fig. 2 Histological findings of the tumors.

A: Chondrosarcoma, grade I. Chondrocytes with mild atypia produce a well-developed chondroid matrix and infiltrate into muscle. One or more tumor cells including binucleated or multinucleated cells occupy one lacuna. H.E. × 80

B: Chondrosarcoma, grade II. Note the hypercellularity with moderate pleomorphism. Myxomatous change is seen. H.E. × 200

C: Chondrosarcoma, grade III. Marked hypercellularity with nuclear enlargement and pleomorphism is seen. The lobular pattern is lost. H.E. × 80

D: Higher magnification of (**C**). H.E. × 200

E: Dedifferentiated chondrosarcoma. Fibrosarcoma-like spindle cell sarcoma is seen in the periphery of the cartilaginous component. H.E. × 200

F: Dedifferentiated chondrosarcoma showing the histological feature of malignant fibrous histiocytoma-like pleomorphic sarcoma. HE. × 200

Table 1 Location and size of the tumors

Site	No. of patients	Size of tumors (cm)
Extremities		
Femur	6	6.1
Tibia	2	4.5
Humerus	2	8.5
Radius	1	3.5
Trunk		
Pelvis	3	11.0
Spine	1	7.0
Scapula	1	10.0
Rib	1	5.0

Histologic sections were available and reviewed in 14 patients. Histologically, they were classified as classical chondrosarcoma (grades I, II, and III) and as dedifferentiated chondrosarcomas (5–7) (Fig. 2). The numbers of patients with grades I, II, and III, and with dedifferentiated chondrosarcomas were 8, 2, 2, and 2, respectively. When the histological grade of original tumors progressed to a higher grade after recurrence, the higher grade was taken as the grading.

The survival rates were calculated by the Kaplan-Meier method, and the statistical significance of differences between curves was determined by the generalized Wilcoxon test.

Results

The overall 5- and 10-year survival rates were 72.3 % and 61.9 %, respectively (Fig. 3). At the time of the last follow-up, nine patients (52.9 %) remained tumor-free, three (17.6 %) had no evidence of tumor in spite of recurrence, one was alive with inoperable pulmonary metastasis, and four (23.5 %) had died of the tumor. The difference in survival between patients with tumors less than and more than 5 cm was statistically significant ($P < 0.05$) (Fig. 4). Patients with tumors in the trunk tended to have a lower survival rate than those having tumors in an extremity; however, the difference was not significant ($P = 0.13$) (Table 2). The differences in survival between genders and ages were not significant, nor was the difference in survival between patients with secondary chondrosarcomas and those without the preceding disease.

Survival curves for patients according to histologic grade are shown in Fig. 5. The 5-year survival rates for patients with grades I, II, and III, and with dedifferentiated chondrosarcomas were 80 %, 100 %, 50 %, and 0 %, respectively. The difference in survival between patients with grade I chondrosarcomas and those with dedifferentiated chondrosarcoma was significant ($P < 0.05$). Although patients with grade III chondrosarcomas tended to have a poorer survival than those with grade I tumors, the difference was not significant ($P = 0.14$). The rates of local recurrence and pulmonary metastasis for each histologic grade are shown in Table 3. The rates of local recurrence were not related to the histologic grades. In contrast, the difference in the incidence of distant metastasis by histologic grade was striking. The rates of metastasis of grade I and II chondrosarcomas were 0 %, while those of grade III and dedifferentiated tumors were 100 %.

The effect of the type of initial surgery on local

Table 2 Prognostic factors

	Factors	No. of patients	5-year survival (%)	*P*-value
Sex	Male	7	50.0	N.S.
	Female	8	87.4	
Age	< 40	6	83.3	N.S.
	≧ 40	9	58.3	
Site	Trunk	5	40.0	N.S.
	Extremity	10	85.7	
Size	< 5 cm	6	100	$P < 0.05$
	≧ 5 cm	9	43.8	
Exostosis	+	3	50.0	N.S.
	−	12	77.9	
Histology	Grade I	8	80.0	$P < 0.05$
	Grade II	2	100	
	Grade III	2	50.0	
	Dedifferentiated	2	0	

N.S.: Not significance.

Table 3 Rate of recurrence and metastasis classified by histologic grade

	Recurrence (%)	Metastasis (%)
Grade I	3/8 (37.5)	0/8 (0)
Grade II	1/2 (50.0)	0/2 (0)
Grade III	1/2 (50.0)	2/2 (100)
Dedifferentiated	0/2 (0)	2/2 (100)

recurrence and pulmonary metastasis is shown in Table 4. Local recurrence did not develop in the patients who were treated by wide excision. The rate of local recurrence was related to the local surgical margin.

The clinical course of the five patients who experienced local recurrences is shown in Table 5. The four patients with grade I or II chondrosarcoma experienced a total of 9 local recurrences; however, none of the recurrent tumors metastasized. In spite of repeated local recurrences, tumors of grades I and II did not metastasize. In

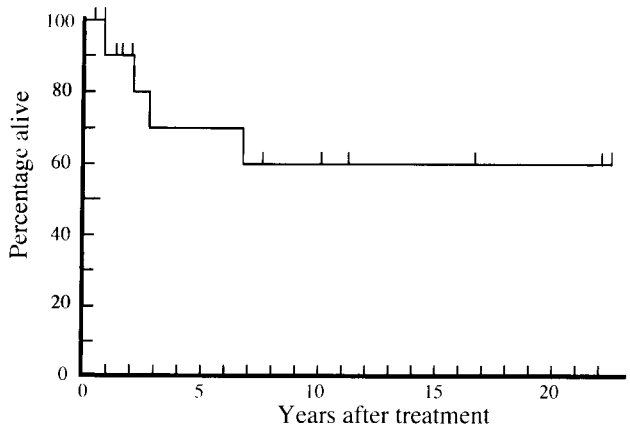

Fig. 3 Overall survival of the 17 patients. (Kaplan-Meier method)

Table 4 Rate of recurrence and metastasis classified by surgical margin

Surgical margin	Recurrence (%)	Metastasis (%)
Intralesional	2/2 (100)	0/2 (0)
Marginal	3/4 (75)	2/4 (50)
Wide	0/8 (0)	2/8 (25)
Unknown	0/3 (0)	0/3 (0)

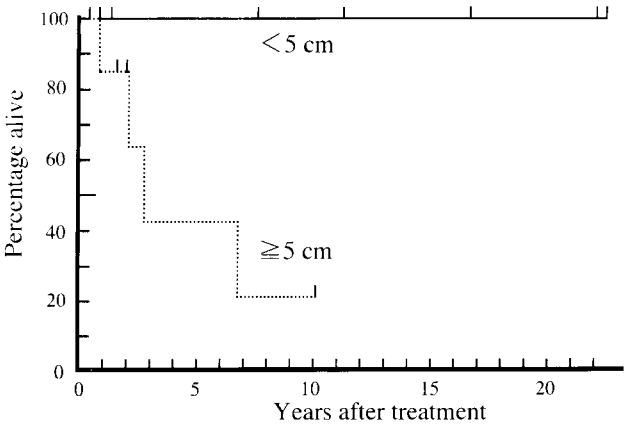

Fig. 4 Survival of the 15 patients by tumor size. (Kaplan-Meier method)

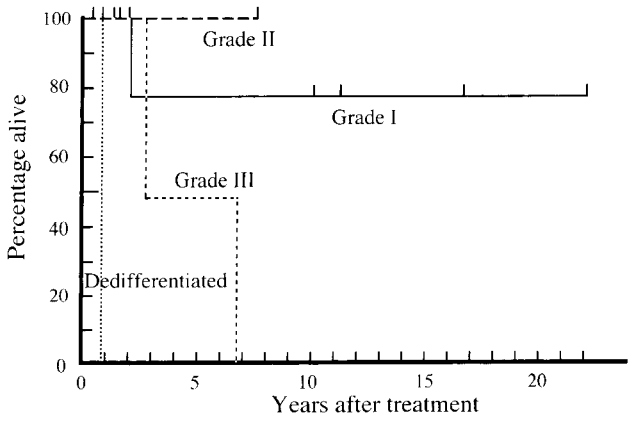

Fig. 5 Survival of the 14 patients by histologic grade. (Kaplan-Meier method)

Table 5 Clinical course of the patients with local recurrences

Patient	Age/Sex	Location	Therapy/Histologic grade of tumors							Outcome
			Orig.	Rec. (1st	2nd	3rd	4th	5th	6th)	
1	38/f	Tibia	C/I	W/I						NED
2	18/m	Pelvis	M/I	M/I						DOD
3	19/f	Scapula	M/I	M/I	M/I	M/I	M/I	M/I	M/I	NED
4	54/f	Tibia	C/I	Amp/II						NED
5	60/f	Humerus	W/III	W/III	M/III					DOD

Orig.: Original tumor, Rec.: Recurrent tumor, C: Curettage, M: Marginal resection, W: Wide resection, Amp: Amputation, I: Grade I, II: Grade II, III: Grade III, NED: No evidence of disease, DOD: Died of the disease

contrast, tumors of all four of the patients with grade III and dedifferentiated chondrosarcomas metastasized. Three of these patients died of the tumor and one of them is still alive with metastatic tumor.

Discussion

Chondrosarcoma is defined as a malignant tumor whose cells produce a chondroid matrix. Although it is thought that chondrosarcoma has a better prognosis than osteosarcoma, which is one of the most common primary bone tumors, some patients suffer repeated local recurrences and/or distant metastasis. The prognosis of patients with chondrosarcoma may be variable.

The overall survival rate in the present series (72.3 % at 5 years, 61.9 % at 10 years) is identical with those found in earlier studies (5, 8–11). The significant prognostic factors were size and histologic grade of the tumor. Location of the primary tumor, age, and presence of a preceding exostosis, which were proposed as prognostic factors in several papers (5, 11–13), did not affect the overall survival significantly. However, because of our small-scale study, we can not rule out the possibility that these factors affect the prognosis of patients with chondrosarcoma. The present results show that the histologic grade of the tumor was related to the rate of distant metastasis but not to the rate of local recurrence.

The histologic interpretation of chondrosarcoma is often very difficult. Especially, distinction between a benign chondroid lesion and a borderline or well-differentiated chondrosarcoma may be nearly impossible (6–7). In this series, there were two cases which were diagnosed as chondroma at first and there was local recurrence after intralesional excision. Mirra *et al.* reported a new histologic approach to the differentiation of enchondroma from chondrosarcoma (14, 15). They described the valuable histologic findings of enchondromatous islands of a cartilage pattern, and enchondroma encasement pattern and a chondrosarcoma permeation pattern. In the future, a study of oncogene expression may provide useful information about the distinction between benign tumors and low-grade sarcomas.

It is important to avoid local recurrence of chondrosarcoma. The recurring chondrosarcoma may exhibit a higher grade of malignancy than the original tumor (1, 2, 16). Several studies have shown that adequate surgical treatment results in a lessened risk of local recurrence (4, 5, 8, 11, 17–19). We agree with the authors of those reports that wide excision of the primary tumor with an adequate surgical margin is important to achieve local control of chondrosarcoma.

In general, chondrosarcoma is resistant to radiotherapy and chemotherapy (4, 10, 11, 19). In this series, none of the patients was given adjuvant treatment. However, the patients with high-grade tumors, who appropriately received radical operations, died of the metastatic tumor early (5, 12). In dedifferentiated chondrosarcoma, the dedifferentiated component usually metastasize (16). We suppose that high-grade tumors had micrometastasis at an early stage. Capanna *et al.* stated that it seems theoretically correct to employ chemotherapy with the aim of controlling micrometastases from dedifferentiated component (16). There seems to be some possibility that poorly differentiated cells respond to chemotherapy.

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