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Limb-Salvage Operations in Primary Malignant Tumors of the Bone

— Interim Report —

Soo-Yong Lee, M.D. and Goo Hyun Baek, M.D.

Department of Orthopedic Surgery Korea Cancer Center Hospital

Between June 1985 and March 1990, 25 patients with primary malignant bone tumors, including 15 cases of osteogenic sarcoma, two cases of periosteal osteogenic sarcoma, six cases of chondrosarcoma, and two cases of malignant fibrous histiocytoma, were treated with limb-salvage procedures.

Fourteen patients underwent limb salvage operations with tumor prosthesis arthroplasty, 6 with resection-arthrodesis, 4 with wide resection, and 1 with autoclaved autograft.

Pre- and/or post-operative chemotherapy with or without radiotherapy was combined with these limb salvage operations. The average follow-up period was 25.2 months (6 to 52 months) since diagnosis. The estimated 3.5-year survival rate of the total 25 patients was 39.5% based on the Kaplan-Meier survival plot. In the 15 cases of osteogenic sarcoma, the estimated Kaplan-Meier 34-month survival rate was 46.2%. Seventeen patients who were followed up for more than 1 year were grouped by functional grading: 11 (65%) were excellent; 3 (18%) good; 2 fair (12%); and 1 poor. Complications occurred in 4 patients, 1 had a local recurrence, 2 had superficial wound infections, and 1 a loosening of the femoral stem. Metastases were shown in 15 case, and the most common location was the lung.

Key Words: *Bone tumor, Primary malignant, Limb salvage operation, Functional grading, Survival rate, Chemotherapy*

INTRODUCTION

For primary malignant bone tumor of the extremities, amputation was the treatment of choice until successful chemotherapy was introduced around 1975.

Systemic chemotherapy using properly combined multiple drugs can control distant metastasis and reduce the reactive zone of the tumor. In addition to the surgical staging system proposed by Enneking (1986), the improvement of diagnostic techniques such as computed tomography and magnetic resonance imaging allowed more accurate preoperative assessment of the tumor extent (Sundaram et al., 1986). With the development of chemotherapy and anatomical staging, the limb-salvage operation has recently become more popular, and it is often chosen for patients who have sarcomas (Eilber et al., 1987; Jaffe et al., 1981; Marcove, 1987).

Furthermore, some authors (Simon et al., 1986; Springfield et al., 1988) reported that the patients' survival as well as recurrence rates were similar between those who were treated with either a limb salvage procedure or amputation in osteosarcoma.

Since June 1985, we have done 25 cases of the limb-salvage operation for primary malignant bone tumors.

The purpose of this study was to obtain the interim

Address correspondence to: *Soo-Yong Lee, M.D. Department of Orthopedic Surgery, Korea Cancer Center Hospital, Gongneung-dong 215-4, Nowon-Ku, Seoul 139-240, Korea. Tel: (02) 974-2501 (Ext. 219,246)*

results of the survival rate and the functional assessment of the limb.

MATERIALS

From June 1985 to March 1990, 25 cases of primary malignant bone tumors, such as osteogenic sarcoma, periosteal osteogenic sarcoma, chodrosarcoma, and malignant fibrous histiocytoma, were treated with limb-sparing procedures in the Orthopedic Department of Korea Cancer Center Hospital. The minimum follow-up period was 6 months. Demographic pictures of each case are illustrated in Table 1.

Table. 1. Details of 25 patients

Case Number	Age/Sex	Pathologic Dx and Stage	Location	Preoperative Chemotherapy	Type of Operation	Postop. Chemo/RT	Duration Since Dx (months)	Duration After Op (months)	Functional Evaluation	Complication	Metastasis	Current Status
1	26/M	OS/IIB	P Humerus	+	Tumor prosthesis	+/−	30	25	E	—	—	CDF
2*	14/F	OS/IIB	P Humerus	+	Tumor prosthesis	+/−	20	8	—	—	—	CDF
3*	16/M	OS/IIB	D Femur	+	Tumor prosthesis	+/−	12	9	—	Local recurrence	Lung	Dead
4	19/F	OS/IIA	P Fibula	+	Tumor prosthesis	+/−	34	31	E	Superficial infection	—	CDF
5	17/M	OS/IIB	D Femur	+	Tumor prosthesis	+/−	22	17	F	—	Lung, spine	Alive with metastasis
6*	15/M	OS/IIB	D Femur	+	Tumor prosthesis	+/−	17	11	—	—	Spine	Alive with metastasis
7	19/M	OS/IIB	D Femur	-	Resection and arthrodesis	+/+	21	19	E	—	Lung	Dead
8*	16/F	OS/IIB	D Femur	+	Tumor prosthesis	+/−	15	11	—	—	Lung	Dead
9	16/M	OS/IIB	P Femur	+	Tumor prosthesis	+/−	28	24	E	—	—	CDF
10*	20/M	OS/IIB	P Tibia	+	Tumor prosthesis	+/−	10	5	—	—	Lung, scapula	Dead
11	13/F	OS/IIB	D Femur	+	Resection and arthrodesis	+/−	21	16	E	—	Lung	Dead
12	34/M	OS/IIA	D Femur	+	Resection and arthrodesis	+/−	20	18	E	—	Lung	Dead
13	29/M	OS/IIB	D Femur	+	Tumor prosthesis	−/−	34	30	E	—	—	CDF
14*	15/F	OS/IIB	P Humerus	+	Resection and arthrodesis	+/−	19	9	—	—	Lung	Dead
15	14/M	OS/IIB	P Humerus	+	Tumor prosthesis	+/−	19	15	F	Superficial infection	Spine,rib & skull	Alive with metastasis
16	18/F	Periosteal OS/IA	P Tibia	-	Resection & gastrocnemius flap	+/−	52	51	E	—	—	CDF
17	34/M	Periosteal OS/IA	Shaft of femur	-	Resection and autoclaved autograft	−/−	42	41	E	—	—	CDF
18*	49/M	CS/IIB	Pubis	+	Tumor prosthesis	−/−	6	3	—	—	—	CDF
19	26/M	CS/IIB	Ilium	-	Iliectomy Enneking Type	−/+	34	33	E	—	—	CDF
20	41/F	CS/IIB	Scapula	-	Subtotal scapulectomy	+/+	36	34	G	—	Lung	Dead
21*	24/M	CS/IIB	D Femur	+	Tumor prosthesis	−/−	20	11	—	Screw failure	—	CDF
22	41/F	CS/IIB	Scapula	-	Subtotal scapulectomy	−/+	52	51	G	—	Lung	Dead
23	55/M	CS/IIB	P Femur	-	Tumor prosthesis	+/−	30	13	G	—	Lung	Dead
24	65/M	MFH/IIA	D Femur	-	Resection and arthrodesis	−/+	18	18	E	—	Lung	Dead
25	61/F	MFH/IIA	D Femur	-	Resection and arthrodesis	−/+	17	16	P*	—	Lung	Dead

*These cases were excluded in the functional grading because the duration of the follow-up period was less than one year, postoperatively.

Abbreviations: Dx, diagnosis; RT, radiotherapy; Op, operation; OS, osteogenic sarcoma; CS, chondrosarcoma; MFH, malignant fibrous histiocytoma; P, proximal; D, distal; E, excellent; G, good; F, fair; P*, poor; CDF, continuously disease-free.

1) Age and sex

Sixteen cases were males and 9 were females.

The age range was from 13 to 65 years (average 27.6 years).

2) Classification

Fifteen cases were osteogenic sarcoma: 2 of them were stage IIA; 13 were stage IIB by Enneking's criteria (1986).

Two cases were stage IA periosteal osteogenic sarcoma; 6 cases were stage IIB chondrosarcoma; and 2 cases were stage IIA malignant fibrous histiocytoma.

3) Location

The most frequent site in fifteen cases of osteogenic sarcoma was the distal femur (8 cases). Other sites were the proximal humerus (4), proximal femur (1), proximal tibia (1), and proximal fibula (1). In the two cases of periosteal osteogenic sarcoma, one was in proximal tibia, and the other was in femur shaft. In the six cases of chondrosarcoma, 2 were in scapula, 2 were in pelvis, 1 was in proximal femur, and 1 was in distal femur. Two cases of malignant fibrous histiocytoma were in distal femur.

4) Preoperative chemotherapy

All of the 15 cases of osteogenic sarcoma except one (Case No. 7) were preoperatively treated with intraarterial or intravenous cisplatin for 3 to 7 cycles and intravenous adriamycin for 2 to 4 cycles.

Two cases of chondrosarcoma (Case No.18 and 21) received chemotherapy; one with 2 cycles of high dose methotrexate combined with cisplatin and adriamycin and the other with 6 cycles of cytoxan, vincristine, adriamycin, and actinomycin-D.

5) Surgery

The level of bone dissection was determined by examining the roentgenograms, bone scans, and computed tomograms in all cases, except in some cases where magnetic resonance imaging was additionally used.

We tried to remove the lesion as widely or radically as possible. The margin was at least 7cm above or below the limit of increased activity of the bone scan in osteogenic sarcoma.

Arthroplasty using tumor prosthesis was done in 14 cases: the Kotz modular reconstruction system was used (Kotz, 1988; Ritschl et al., 1987) in 10 cases (8 cases of osteogenic sarcoma and 2 cases of chondrosarcoma); custom-made prostheses were used in 2 cases (Case No.15 and 18) (Fig. 4); and 2 cases (Case No. 1 and 2) who had osteogenic sarcoma in the proximal humerus were treated with a wide resec-

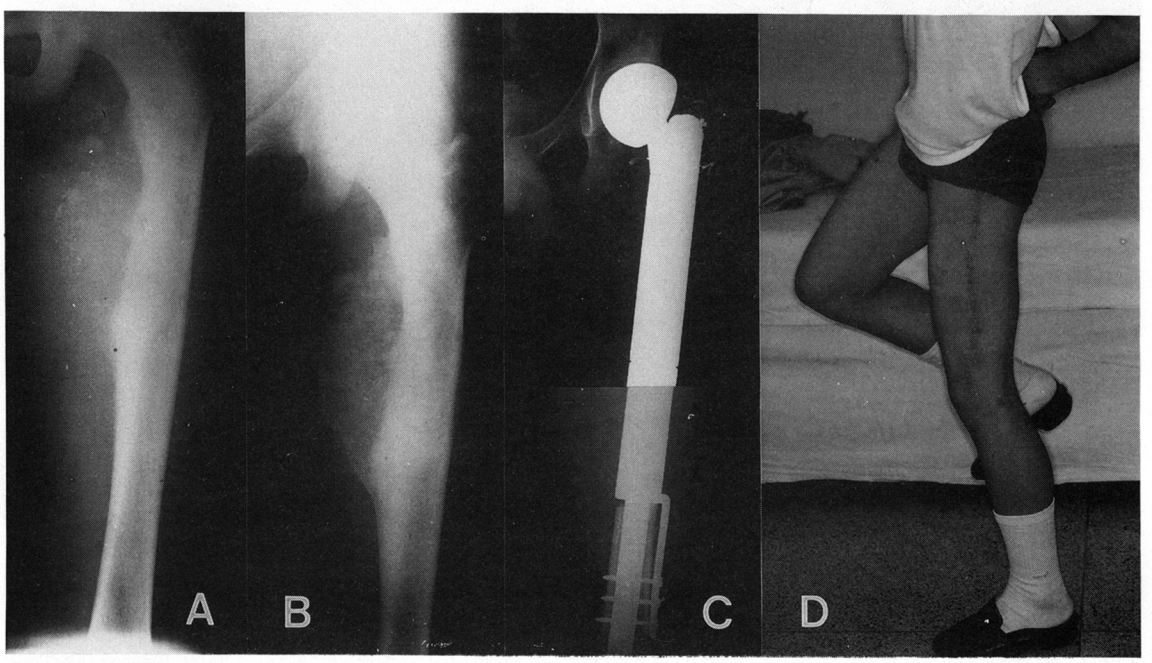

Fig. 1. Initial film of a 16-year-old boy with a IIB osteosarcoma (A). After preoperative chemotherapy, the lesion showed good margination and calcification (B). The function was excellent at postoperative 2 years follow-up (C, D). (Case No.16).

tion of the proximal humerus, along with reconstruction, using an autoclaved autograft and a Neer prosthesis (Fig. 2).

Resection and arthrodesis were done in 6 cases (4 cases of osteogenic sarcoma and 2 cases of malignant fibrous histiocytoma): five of them were stabilized with a Huckstep intramedullary nail and bone cement; and in Case No.14, a nonvascularized fibula graft was used for the arthrodesis.

In Case No.17, who had periosteal osteogenic sarcoma of the femoral shaft, the widely resected femoral shaft was autoclaved and reinserted with a Huckstep intramedullary nail.

Wide resections were made in 4 cases: 2 of them who had chondrosarcoma of the scapula (Case No.20 and 22) were treated using Das Gupta's subtotal scapulectomy (Das Gupta, 1970); one of them who had periosteal osteogenic sarcoma of proximal tibia (Case No.16) was treated with wide resection, and the resection site was covered with a gastrocnemius flap; and one of them who had chondrosarcoma of iliac wing (Case No.19) was treated with an Enneking Type I iliectomy (Enneking and Dunham, 1978).

6) Postoperative treatment

In the osteogenic sarcoma cases, all cases received chemotherapy except Case No.13 who refused the therapy. The regimen was mostly combination therapy using bleomycin, cytoxan, and dactinomycin from 3 to 7 cycles.

Case No. 7 who did not take preoperative chemotherapy was treated with 9 cycles of cisplatin and adriamycin with radiotherapy. Three cycles of cisplatin and adriamycin were tried in Case No.16.

Two cases of malignant fibrous histiocytoma and 3 cases of chondrosarcoma (Case No.19, 20, 22) were treated with radiotherapy. Six cycles of chemotherapy with adriamycin, vincristine, and methotrexate were

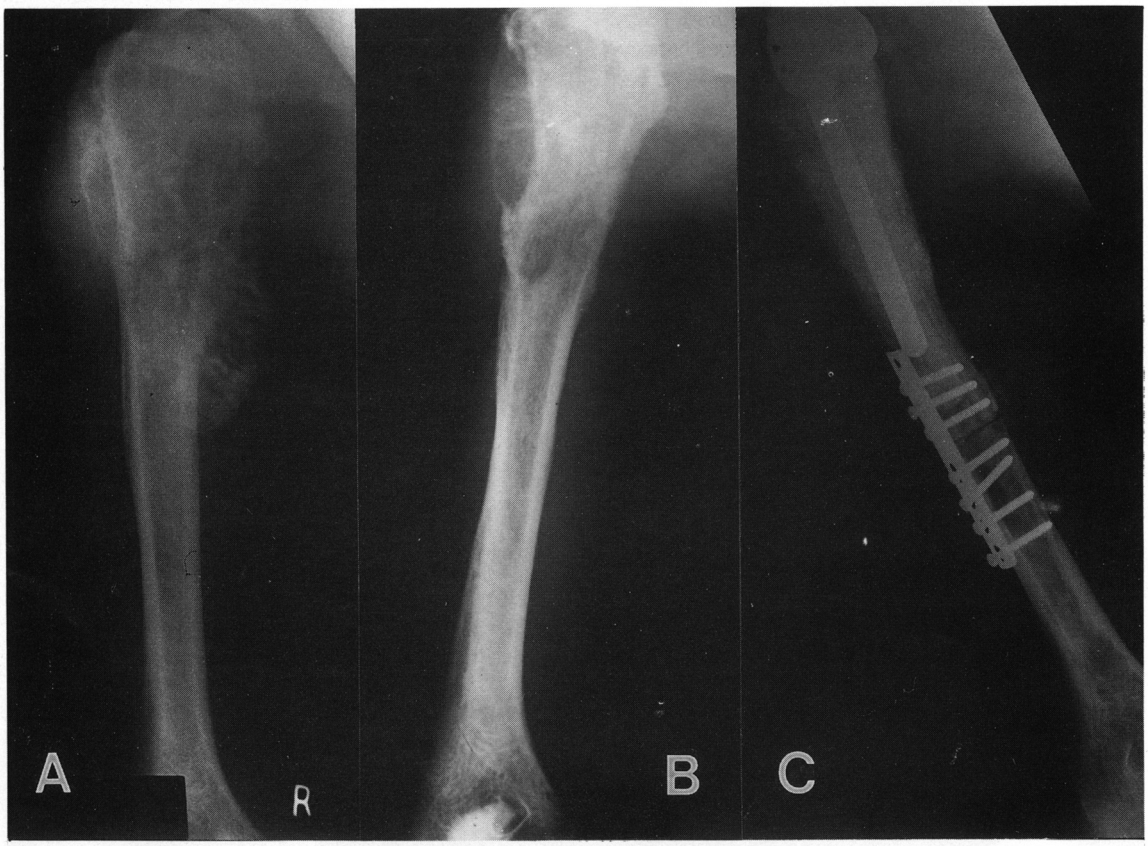

Fig. 2. IIB osteosarcoma of the proximal humerus in a 26-year-old patient (A). Definite reduction of tumor mass is observed after preoperative chemotherapy (B). A wide resection and reconstruction with autoclaved autograft, Neer prosthesis, and compression plate was done (C). (Case No. 1)

done in 2 cases.

7) Functional analysis of limbs

We analyzed 17 cases who could be followed up for more than one year postoperatively. We used Enneking's functional evaluation system of the surgical treatment of musculoskeletal tumors (Enneking, 1987) for functional grading.

8) Survival rate

We used a calculation method of nonparametric estimation from incomplete observation by Kaplan and Meier (Kaplan-Meier survival rate) (Kaplan and Meier, 1958) for the estimated survival rate of the patients.

RESULTS

1) Survival

At final follow-up, 10 cases (40%) were continuously disease-free, 3 cases (12%) lived with metastasis, and 12 cases (48%) died.

The estimated Kaplan-Meier 3.5-year survival rate was 39.5% in the overall cases (Fig. 5).

In 15 cases of osteogenic sarcoma, the estimated Kaplan-Meier 34-month survival rate was 46.2% (Fig. 6).

The average duration from diagnosis to death in 12 expired cases was 22.6 months (ranging from 10 to 52 months).

2) Functional evaluation

Fourteen cases were excellent; 3 cases good; 3 cases fair; and 1 case poor. One poor case was Case No.25 who had diabetes mellitus originally. After the postoperative radiation therapy, there was moderate-to-severe painful swelling with erythema on the operated field, which might have been due to radiation reaction.

Overall, 14 (82%) of the 17 cases were more than good.

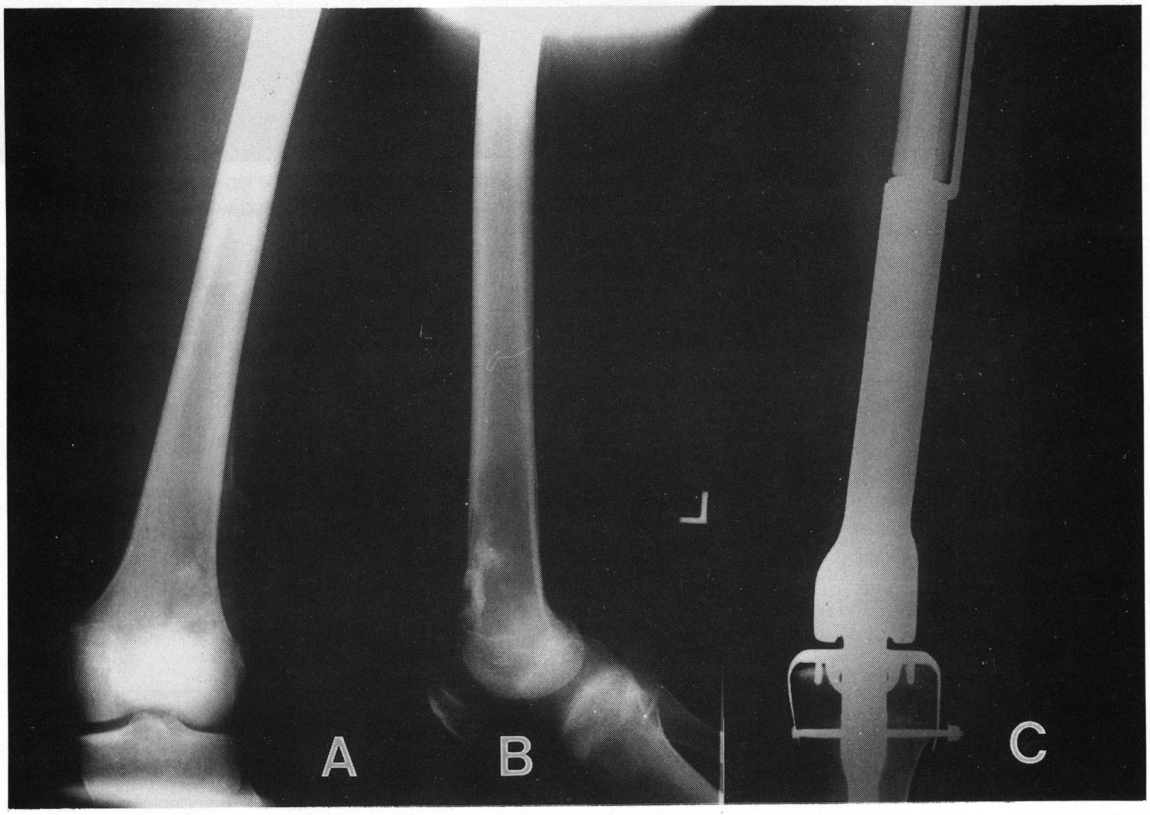

Fig. 3. A IIB osteosarcoma of the distal femur in a 17-year-old boy (A, B). His knee function was more than good before he developed spine metastasis and subsequent paraparesis (C). (Case No. 5)

3) Complications

There were 4 cases with complications. Two of them were superficial wound infection which could be controlled with conservative treatment for about 4 weeks; local recurrence was noted in Case No. 3, who showed pulmonary metastasis during radiotherapy of recurred local lesion; and Case No.21 had broken screws due to the loosening of the femoral stem fixation, which was re-fixed at the 7th postoperative month.

4) Metastasis

Metastasis was noted in 15 cases (osteogenic sarcoma; 10, chondrosarcoma; 3, and malignant fibrous histiocytoma; 2). Twelve of them expired. The most common location was the lung (13 cases). In the osteogenic sarcoma, 4 cases (Case No. 5, 6, 10 and 15) among 10 cases of the metastasis showed bone-to-bone metastasis: 2 cases (Case No. 6 and 15) were only bone-to-bone metastasis without pulmonary metastasis; and 2 cases (Case No. 5 and 10) were

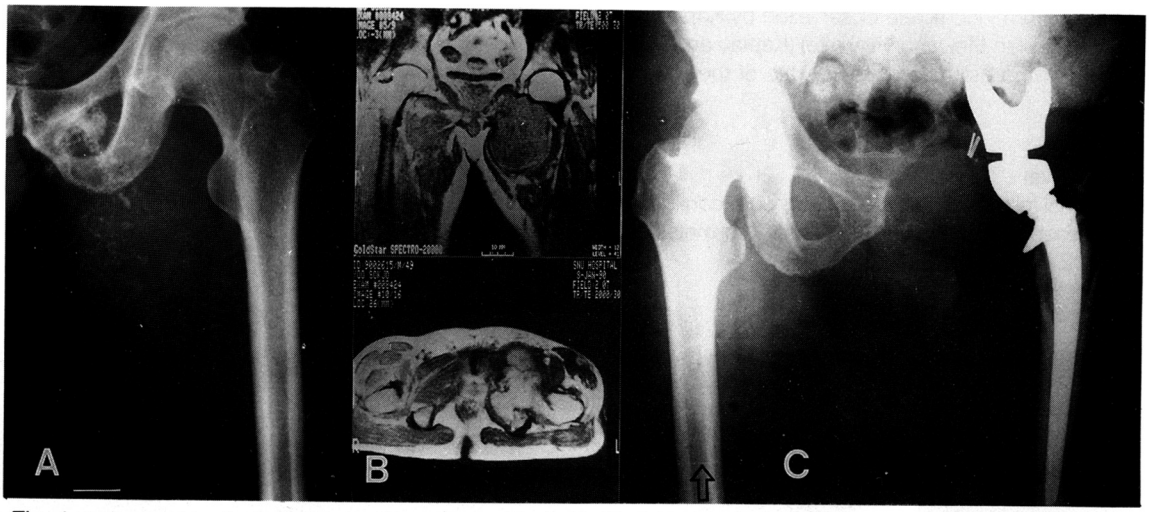

Fig. 4. A 49-year-old patient with IIB chondrosarcoma of the pubis (A). Adductors and flexors of the hip were invaded significantly in magnetic resonance image (B). Though the function of this patient was fair, his limb was saved with a wide resection and reconstruction using a custom-made prosthesis (C). (Case No.18)

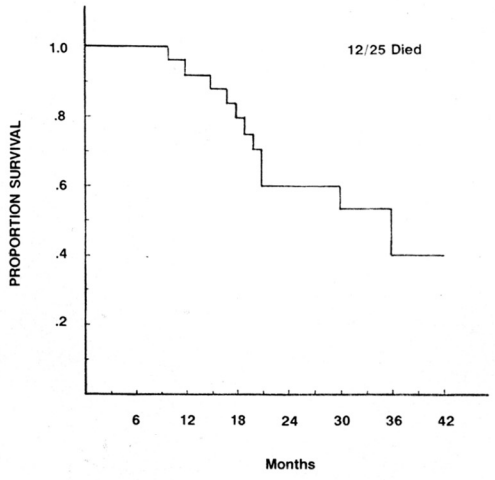

Fig. 5. Survival of all patients: 12 out of 25 patients died, giving an estimated Kaplan-Meier 3.5-year survival rate of 39.5%.

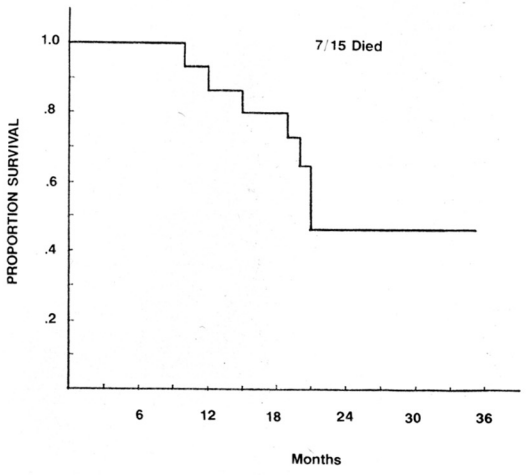

Fig. 6. Survival of patients with osteogenic sarcoma: 7 out 15 patients died, giving an estimated Kaplan-Meier 34-month survival rate of 46.2%.

bony metastasis concomitant with pulmonary metastasis.

The average duration from diagnosis to detection of the metastasis was 16.7 months (ranging from 6 to 46 months).

DISCUSSION

Since the 1980's, there has been remarkable improvement in the surgical management and survival of patients with primary malignant bone tumors. This is mainly due to the development of chemotherapy and modern radiographic tools.

In osteogenic sarcoma, Edmonson et al. (1980) and Sim et al. (1978) improved survival rates to over 30% with chemotherapy, and recently Rosen and Nirenberg (1985) reported that 77% had 5-year survival with high dose methotrexate, adriamycin, bleomycin, and cisplatin.

While the chondrosarcoma is still resistant to chemotherapy and radiotherapy, radical resection combined with preoperative and postoperative chemotherapy is the treatment of choice in malignant fibrous histiocytoma (Boland and Huvos, 1986).

So far chemotherapy was effective especially in osteogenic sarcoma. In addition to controlling the subclinical metastasis, preoperative chemotherapy helped to consolidate the local tumor mass, which in turn allowed for ease in wide resectioning for limb-salvage procedures. Magnetic resonance imaging (Sundaram et al., 1986), computed tomography, and bone scan play a major role in assessing the extent of local and metastatic leions.

Furthermore, Simon et al. (1986) and Springfield et al. (1988) reported that there is no difference in the survival and tumor recurrence rate either with amputation or limb salvage operation in osteosarcoma.

In chondrosarcoma and malignant fibrous histiocytoma, post-operative radiotherapy was used mainly to control the possible remnants of tumor cells.

In prosthetic replacements, the Kotz modular system (Kotz, 1988; Ritschl et al., 1987) was mainly used in our series. A technical problem we faced was the reconstruction of the ligamentum patellae in the cases of proximal tibia lesion in which tibial tuberosity should be sacrificed. The ventral transposition of a gastrocnemius head (Malawer, 1983) was used in such cases.

We performed temporary resection arthrodesis modifying the technique of Campanacci et al. (1987) in patients who refused prosthetic replacement because of its high cost and/or uncertainty of long-term survival. These temporary fixations can be changed into allograft or autograft after chemotherapy, which can affect bony union if immediate postoperative chemotherapy is to be done.

According to Enneking's functional evaluation system (1987), scales with motion, pain, stability, emotional acceptance, and complication were good enough to satisfy almost all of the patients, but only the strength scale was different. Most of the patients showed only 2+ to 4− muscle power. This might have been due to the wide resection of the surrounding musculature of the bony lesion.

In our series of 25 patients with limb salvage operations, the local recurrence rate was 4.0% (1/25) at 25.2 months of average follow-up. Low local recurrence rate in limb salvage operation may be attributed to preoperative chemotherapy. The importance of preoperative chemotherapy in any limb salvage protocol was emphasized by the Mayo Clinic's experience of local recurrence rate of 23.7% in limb salvage patients who did not receive preoperative chemotherapy (Sim et al., 1983). Compared with this high recurrence rate, Lane et al. (1983), Eckardt et al. (1985) and Marcove and Abou-Zahr (1984) reported a local recurrence rate of zero to 7.8% with preoperative chemotherapy.

The single incidence of the loosening of the femoral stem was revised at the 7th postoperative month, and the patient is presently in excellent condition.

The estimated 3.5-year (42 months)survival rate was 39.5% based on the Kaplan Meier Survival plots.

The survival rate of the osteogenic sarcoma group (15 cases) was analyzed separately. This resulted in a 46.2% survival rate at 34 months. This survival rate in osteogenic sarcoma was similar with those of UCLA (Eckardt et al., 1985), in that the estimated Kaplan-Meier 2-year survival rate was 65%, and the 5-year survival rate was 36%.

From these results, we carefully suggest that the multidisciplinary limb salvage program for malignant bone tumors is promising in terms of survival rate, function, surgical morbidity, and psychological benefits. We also agree that proper diagnostic tools for accurate preoperative assessment of the patients, facilities to administer chemotherapy and radiotherapy, and skillful surgical oncologists are the prerequisites for better results (Rosen and Nirenberg, 1985). Finally, we admit that our long-term results remain to be evaluated again.

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