Hiroshima J. Med. Sci.
Vol.42, No.2, 89~96, June, 1993
HIJM 42-11

Ewing's Sarcoma: Evaluation of Chemotherapy in 17 Cases

Toshifumi OZAKI[1)], Hajime INOUE[1)], Shinsuke SUGIHARA[1)], Masanori HAMADA[1)], Yukou NAKAGAWA[1)] and Kohji TAGUCHI[2)]

1) Department of Orthopaedic Surgery, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama 700, Japan
2) Department of Pathology, Okayama University Hospital, 2-5-1 Shikata-cho, Okayama 700, Japan

ABSTRACT

Seventeen patients with Ewing's sarcoma were divided into 3 groups according to treatment. Ten patients were treated with complete chemotherapy; 9 with VACA protocol, composed of vincristine, actinomycin-D, cyclophosphamide and doxorubicin, and the remaining 1 with T-11 protocol. Four were given incomplete VACA protocol, and another 3 received no chemotherapy. Clinical results were evaluated in the three treatment subgroups described above. All patients without systematic chemotherapy died from lung metastasis within 1 year of the initial treatment. Three of 4 patients who were given incomplete chemotherapy died after a mean survival period of 17.7 months, and one developed cancerous pleuritis after 38 months. In the group receiving complete systematic chemotherapy, 5 of 10 patients are alive, and 2 have been disease-free for more than 3 years.

Distant metastasis is likely when viable cells persist at the site of the primary tumor, even if the tumor size has been considerably reduced by preoperative chemotherapy. Therefore, immediate initiation of intensive chemotherapy and maintenance for the full course of therapy can improve the prognosis of Ewing's sarcoma.

Key words: *Ewing's sarcoma, Chemotherapy, Prognosis*

Ewing's sarcoma has a predilection for teenagers, but is rare in blacks and Chinese[9)]. In Japan, only 20 cases are reported annually[23)]. However, its clinical features and laboratory profiles resemble those of osteomyelitis and other malignant bone tumors making the differentiation difficult[1)]. In addition, histopathological differentiation from small round cell tumors often poses a problem[3)].

Since Ewing's sarcoma is sensitive to anticancer drugs and radiation therapy, these adjuvant therapies have been introduced in many institutions since the 1970's. With the increased availability of intensive chemotherapy such as T-protocol by Rosen et al[19)], the treatment of Ewing's sarcoma has rapidly improved when combined with the more definite surgical resection of tumors investigated by MRI and other imaging techniques. Therefore, early diagnosis and prompt initiation of appropriate treatments is important for the prognosis of Ewing's sarcoma.

We experienced 17 cases of Ewing's sarcoma since 1965. Systematic chemotherapies (VACA protocol, composed of vincristine, actinomycin-D, cyclophosphamide and doxorubicin) shown in Fig. 1 were introduced in 1979[15,16)]. In the present study, clinical and laboratory data are shown and analyzed, and the treatments and prognoses of the cases are discussed with respect to three treatment subgroups.

PATIENTS and METHODS

Seventeen patients with Ewing's sarcoma were examined in this study (Table 1). Patient age at initial examination ranged from 9 to 38 years (mean 18.3 years). There were 11 males and 6 females. Of 15 tumors with bone origin, 4 were in the ilium, 3 in the scapula, 2 in the femur, and 6 in other locations. In two cases originating from soft tissues, one occurred in the thigh, and the other in the upper arm. All cases were in Enneking's stage IIB[4)]. The mean period of follow-up was 25 months (3-106 months).

As shown in Table 2, radiographic findings of Ewing's sarcoma of the bone revealed typical osteolytic changes in 11 patients, and moth-eaten images in 5 patients. Sclerotic changes were found in 6, typical onion-peel appearance in 4,

Address for correspondence: Toshifumi Ozaki, M.D.
Department of Orthopaedic Surgery, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama 700, Japan.

Table 1. Clinical summary of cases

Case No.	Age	Sex	Site	Stage*	Period of follow-up (months)	Outcome
1	38	F	spine	IIB	11	DOD[a]
2	9	M	scapula	IIB	3	DOD
3	13	F	femur	IIB	12	DOD
4	27	F	humerus	IIB	29	DOD
5	21	F	clavicle	IIB	17	DOD
6	27	M	scapula	IIB	41	NED[b]
7	15	M	ilium	IIB	7	DOD
8	16	M	scapula	IIB	21	DOD
9	13	M	rib	IIB	106	CDF[c]
10	11	M	ilium	IIB	7	DOD
11**	21	M	thigh	IIB	44	AWD[d]
12	10	F	talus	IIB	38	CDF
13	20	M	ilium	IIB	23	DOD
14	16	M	femur	IIB	26	DOD
15	21	M	ilium	IIB	25	NED
16**	19	M	upper arm	IIB	23	DOD
17	13	F	5th metacarpal bone	IIB	4	CDF

Case 16 is a large cell type (14, 17).
*: Enneking's surgical stage (4)
**: Extraskeletal Ewing's sarcoma
a: dead of disease. b: no evidence of disease.
c: continuous disease free. d: alive with disease.

Table 2. Radiological findings of cases

Case No.	Lytic change	Sclerotic change	Soft tissue mass	Onion-peel apperence	Sun-ray spicula
2	+	–	+	–	–
3	+	–	–	–	–
4	+	+	+	+	+
5	+ (ME)	+	+	+	–
6	+ (ME)	–	–	–	–
7	+	+	++	+	–
8	+	–	+	–	–
9	–	–	–	–	–
10	–	+	+	–	+
11*	–	–	++	–	–
12	+	+	+	–	–
13	+ (ME)	–	++	+	–
14	–	+	++	–	–
15	+ (ME)	–	++	–	–
16*	–	–	++	–	–
17	+ (ME)	–	++	–	–

Case 16 is a large cell type.
We cannot check the X-ray film of Case 1.
*: Extraskeletal Ewing's sarcoma.
ME: moth-eaten

and spicula formation in 2. Histologically, small round cells with highly uniform round nuclei were found in all except Case 16, a large cell variant of Ewing's sarcoma[14,17]. Symptoms and laboratory findings of each patient are shown in Table 3. High fever (>37.5 °C) was noted in 10 patients, and local spontaneous pain in 13, superficial warmth in 6, swelling in 14, and redness in 3. Anemia (hemoglobin concentration <12.5 g/dl) was observed in 7, leukocytosis (>9,000/mm^3) in 4, high erythrocyte sedimentation rate (>30 mm/hr) in 5, increases in the lactate dehydrogenase (LDH) level (>450 IU/liter) in 5, and positive C-reactive protein (CRP, >0.4 mg/dl) in 8.

In principle, Ewing's sarcoma was treated surgically with 1 cycle of preoperative chemotherapy and 3 cycles of postoperative chemotherapy (Fig. 1). The treatment and results were assessed by dividing the patients into three subgroups: no chemotherapy group (Cases 1–3), incomplete chemotherapy group (Cases 4–7) and complete che-

motherapy group (Cases 8–17) (Table 4). The survival rate was calculated by the Kaplan-Meier method[10], and compared by a generalized Wilcoxon test[5]. According to the Huvos' method, we classified the histological effect of preoperative chemotherapy in 4 grades: grade I, 0–50% of the tumor was necrotic, grade II, 50–90% of the tumor was necrotic, grade III, more than 90% of the tumor was necrotic, and grade IV, 100% of the tumor was necrotic[8].

RESULTS

Three patients were not treated systemic chemotherapy (Cases 1–3). Intralesional resection of the tumor was performed in Case 1, marginal resection was performed in Case 2, and surgery was not performed in Case 3. All 3 patients died due to lung metastasis within 1 year after initial treatment (Table 4).

In the incomplete VACA protocol group, chemotherapy was discontinued in the middle of the course in 4 patients (Cases 4–7), surgery was performed in Case 5 (marginal resection of the tumor) and Case 6 (wide resection). In Cases 4 and 7, radiation therapy was performed instead of surgery, and Case 5 received only radiation therapy after surgery without chemotherapy. Three patients (Cases 4, 5, and 7) died after a mean survival period of 17.7 months. Although one patient (Case 6) survived after only 1 course of postoperative chemotherapy (VACA), he developed cancerous pleuritis 38 months after cessation of chemotherapy (Table 4).

After preoperative chemotherapy, most of the cases showed reduction of the tumor volume (Fig. 2a and b). Of 10 patients with complete systemic

Table 3. Symptoms, physical findings, and laboratory findings of cases

Case No.	Abnormal fever	Pain	Local heat	Swelling	Redness	Hb (g/dl)	WBC (/mm^3)	ESR (mm/hr)	ALP (IU/l)	LDH (IU/l)	CRP (mg/dl)
1	+	+	−	−	−	13.4	4,850	21	65		0
2	−	+	+	+	+	12.0	5,750		180		
3	+	+	−	+	−	13.2	7,300	54	187	695	0.4
4	+	+	+	+	−	11.3	8,200	71	120	390	0.4
5	−	+	−	+	+	13.2	6,400	7	60	364	0.2
6	−	+	−	+	−	14.6	10,500	19	116	348	3.3
7	+	+	−	+	−	10.7	11,300	120	275	601	21.0
8	−	−	−	+	−	15.5	6,000	3	132	349	0
9	−	−	−	−	−	12.4	3,500	22	166	411	0
10	+	+	−	+	−	15.5	10,400	29	181	2285	6.5
11*	+	+	+	+	−	11.1	9,700	2	57	315	5.6
12	+	+	+	+	+	11.4	5,000	32	224	427	0.2
13	+	+	−	−	−	15.5	4,500	30	140	794	0.6
14	−	+	−	+	−	14.2	8,700	11	217	460	0.5
15	+	+	−	+	−	13.5	8,900	52	106	139	7.2
16*	+	−	+	+	−	13.8	4,700		81	402	5.6
17	−	−	+	+	−	12.4	3,300	5	262	356	0

*: Extraskeletal Ewing's sarcoma.

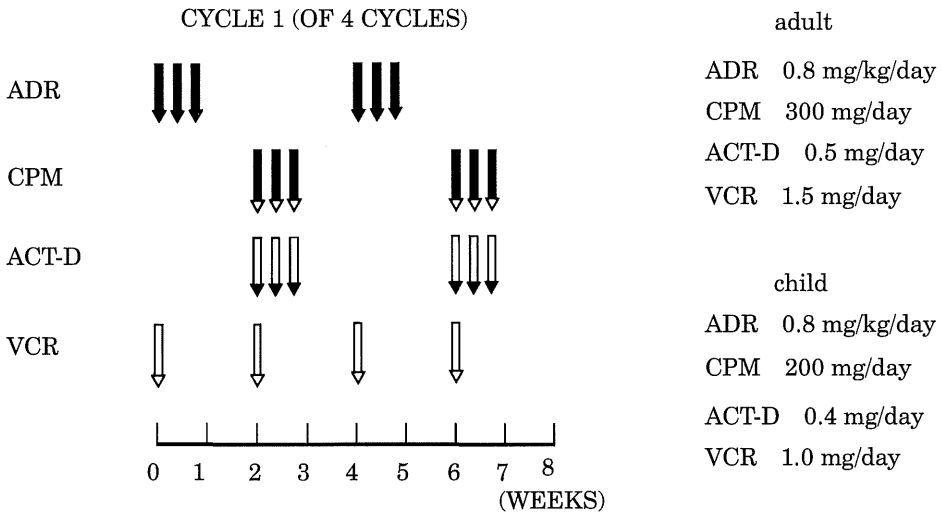

Fig. 1. VACA protocol for Ewing's sarcoma. ADR: doxorubicin (adriamycin), CPM: cyclophosphamide, ACT-D: actinomycin-D, and VCR: vincristine. We administered these drugs intravenously every other day (3 days) in a week, and every other week.

Table 4. Summary of treatment in cases

Case No.	Preoperative therapy	Surgical procedure[a]	Postoperative therapy	Treatment after relapsing	Histological evaluation[b]	Metastasis (months)	Prognosis (months)
1.	—	intralesional	—	—		lung	DOD (11)
2.	radiation (12Gy)	marginal	radiation (40Gy)	—		lung	DOD (3)
3.	radiation (30Gy)	—	—	—		lung (12) bone (12)	DOD (12)
4.	ADR, VCR radiation (60Gy)	—	—			lung (19) bone (20)	DOD[e] (29)
5.	VACA[c]	marginal	radiation (40Gy)	radiation (40Gy)		lung (13) bone (13)	DOD (17)
6.	—	wide	VACA	T-11[d]		cancerous pleuritis (38)	NED[f] (41)
7.	VACA, radiation (50Gy)	—	—			lung (2)	DOD (7)
8.		marginal	ADR, radiation (40Gy)	VACA→ radiation (70Gy)		lung (5)	DOD (21)
9.	—	marginal	VACA, radiation (50Gy)				CDF[g] (106)
10.	VACA, radiation (60Gy)	—		VACA→ radiation (40Gy)		lung (1) bone (1)	DOD (7)
11.	—	curative wide	VACA	VACA→CDDP→ IFOS + Etop[i] (thoracotomy)		lung (13)	AWD[h] (44)
12.	VACA	curative wide	VACA		IV		CDF (38)
13.	VACA, radiation (60Gy)	wide	VACA	VACA+CDDP→ radiation (50Gy)		bone (17)	DOD (23)
14.	VACA	curative wide	VACA	IFOS + Etop (thoacotomy)	II	lung (12)	DOD (26)
15.	VACA	wide	VACA	IFOS + Etop	II	lung (10)	NED (25)
16.	VACA	wide	VACA	IFOS + Etop	III	axilla lymph node(8), lung (18)	DOD (23)
17.	T-11, radiation (30Gy)	wide	T-11		IV		CDF (4)

a: Resection margin (22). b: Histological evaluation of preoperative chemotherapy, I: 0–50% necrosis, II: 50–90% necrosis, III: >90% necrosis, IV: 100% necrosis (8). c: VACA, composed of vincristine, actinomycin-D, cyclophosphamide, and doxorubicin (Fig. 1). d: T-11 regimen (19). e: dead of disease. f: no evidence of disease. g: continuous disease free. h: alive with disease. i: IFOS + Etoposide + THP + CPM (See Fig. 3).

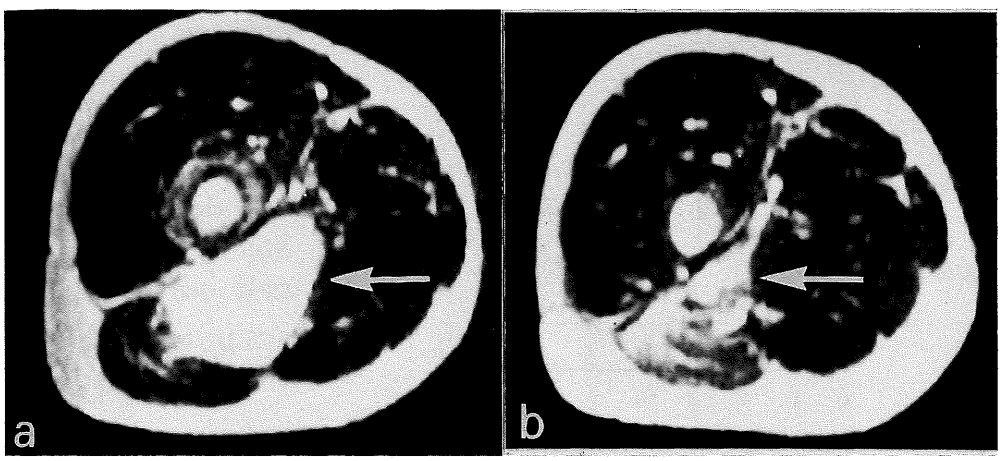

Fig. 2. Case 14. MR images (T2) before VACA protocol (a). MR images (T2) after VACA protocol (b). White arrows indicate the tumor.

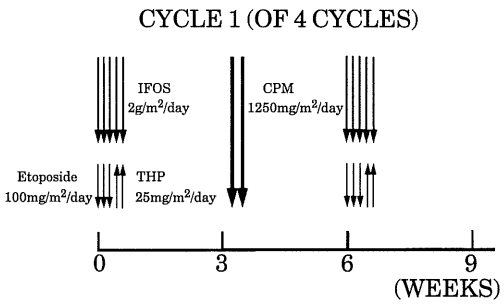

Fig. 3. The protocol for relapsed cases of Ewing's sarcoma. IFOS: ifosfamide, THP: pirarubicin, and CPM: cyclophosphamide. IFOS was administered intravenously every day (5 days), etoposide was administrated day 1 to 3, and THP was day 4 and 5. CPM was also administrated every day (2 days). This is a modified Rosen' T-16 protocol (using THP instead of ADR).[21]

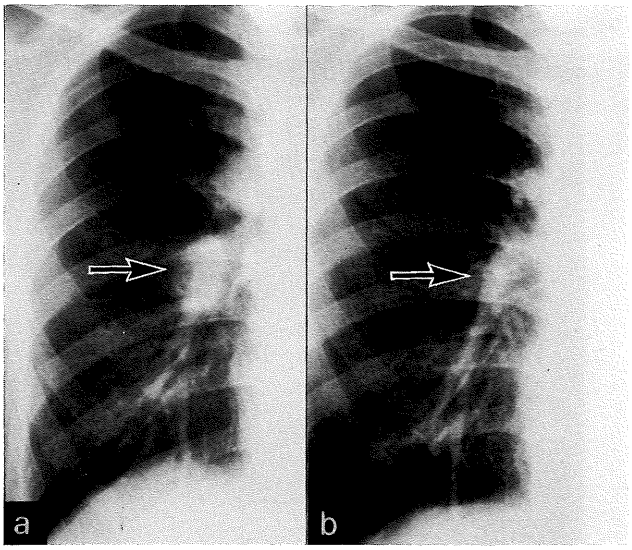

Fig. 4. Case 14. Lung metastasis appeared 12 months after starting the initial treatment (VACA) (a). Lung metastasis had almost disappeared after administration of 1 course of IFOS, etoposide and a high dose of CPM (b). Black arrows indicate the tumor.

chemotherapy (Cases 8–17), 9 received surgery; curative wide resection in 3, wide resection in 4, and marginal resection in 2. Five of these 9 patients are alive, and 2 (Cases 9 and 12) have been continuously disease-free for more than 3 years. The remaining case (Case 17) has had a short follow-up period since the beginning of treatment. In two other survivors, chemotherapy was changed to a regimen consisting primarily of ifosfamide (IFOS) after the development of lung metastasis (Case 11 and 15) (Fig. 3). A patient with Ewing's sarcoma of the rib (Case 9) has survived for the longest period (106 months) (Table 4). The cumulative 3-year survival rate was 0% for those who received no chemotherapy, and 40% for those with complete chemotherapy ($p<0.02$).

In the 17 patients with Ewing's sarcoma treated in our department, relapse was observed after remission in 11 of 14 patients given chemotherapy (8 complete and 3 incomplete). After relapse, 1 patient (Case 5) was treated by radiation therapy alone, 2 (Cases 8 and 10) by VACA and radiation therapy, 2 (Cases 11 and 13) by VACA and cisplatinum (CDDP), and 1 (Case 4) by other treatments. However, 4 recent patients (Cases 11, 14, 15, and 16) were treated by a regimen consisting primarily of IFOS (Fig. 3). In these 4 patients, responses were observed after the first administration (Fig. 4a, 4b, 5a, and 5b). Three

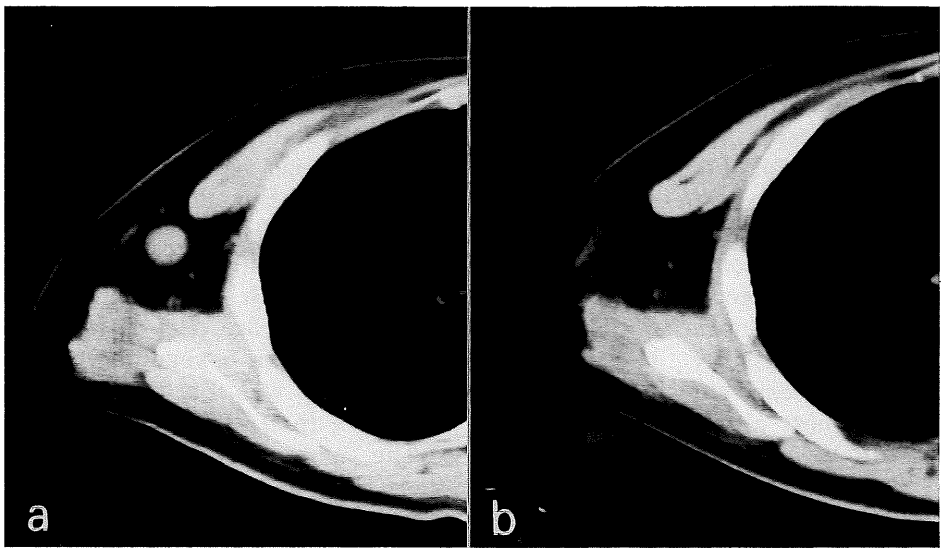

Fig. 5. Case 16. Metastasis to the axillary lymph node was detected by CT scan (a). Metastatic lesion had almost disappeared after administration of 1 course of IFOS, etoposide, and high dose of CPM (b).

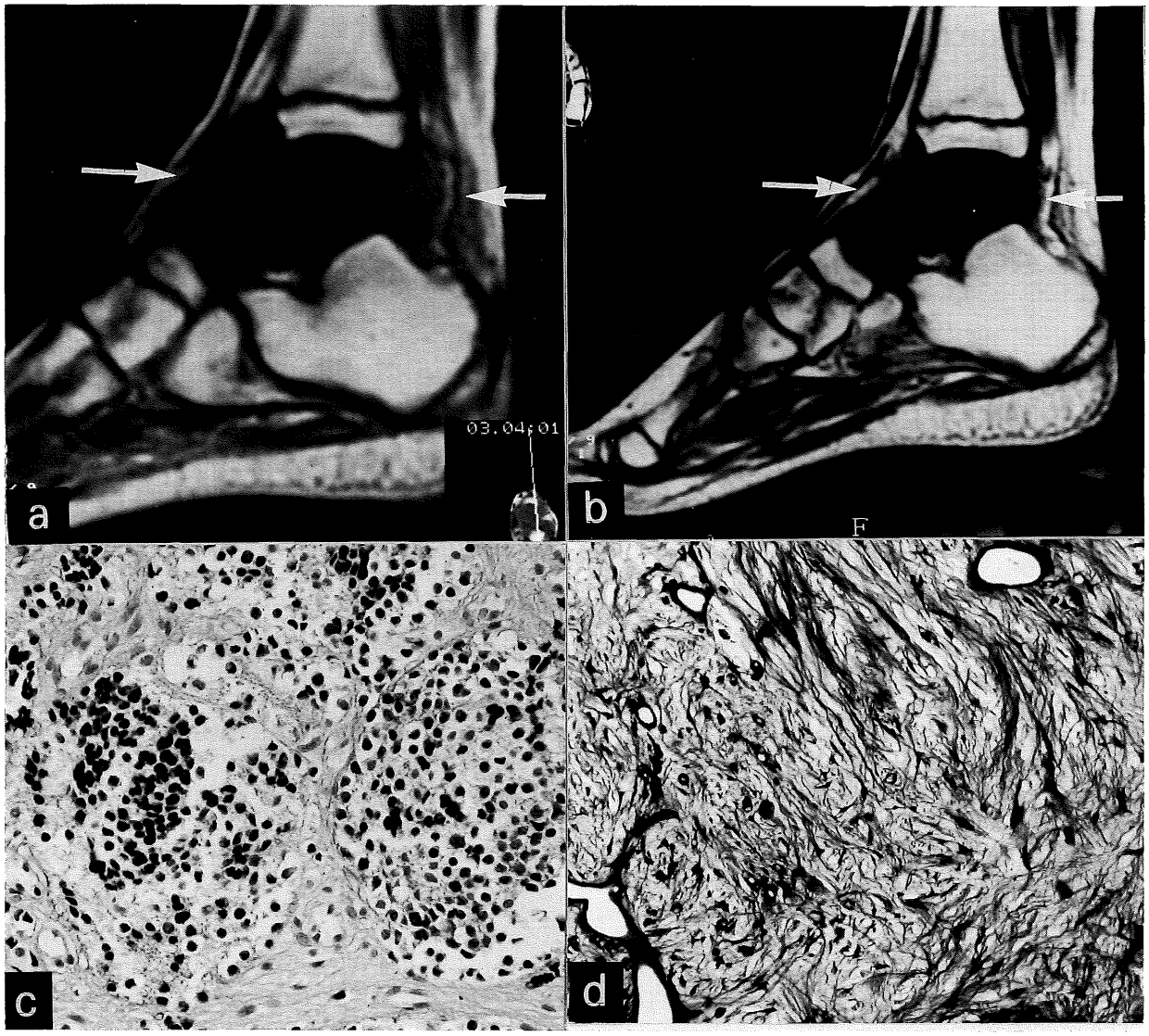

Fig. 6. Case 11. T1 weighted imaging before preoperative chemotherapy showed tumor tissue in the talus and extension into the soft tissue (a). T1 weighted imaging after preoperative chemotherapy showed no tumor mass out of the talus (b). Biopsy specimen before chemotherapy (H.E. stain, ×200)(c). No viable tumor cells were detected in the resected primary lesion after VACA protocol (H.E. stain, ×200)(d). White arrows indicate the tumor.

(Cases 14, 15, and 16) showed no evidence of disease (NED) for a mean period of 8 months. In the remaining patient (Case 10), a small metastatic focus in the lung persisted. One patient (Case 15) without evidence of disease continues to be followed. In Case 6, T-11 protocol was initiated after cancerous pleuritis developed, resulting in a general improvement. Presently, the patient shows no evidence of disease, but chemotherapy is being continued. Almost all patients who did not receive either IFOS and etoposide or T-11, did not respond to other therapies.

DISCUSSION

Ewing's sarcoma more often affects teen-agers, and more frequently males than females. It often occurs in flat bones such as the pelvis[24], which have a poor clinical prognosis, while tumors occurring in the ribs and distal portions of limbs have better prognoses. Additionally, systemic symptoms including anemia, fever and those associated with an increase in ESR, LDH and positive CRP are poor risk signs[12,25]. Although the cumulative 5-year survival rate in the high LDH group was 0%, that in the low LDH group was 53% ($p<0.02$)[5].

The survival rate of patients with Ewing's sarcoma has improved as a result of the widening application of multi-drug chemotherapy.[19] The VACA regimen administrated in our department was radiologically effective, but recurrence was observed in 7 of 10 patients, even when chemo-

therapy was completed.

Histological effects of preoperative chemotherapy were examined in 5 patients receiving surgery. A patient in whom no viable tumor cells were observed (Case 12) showed neither local recurrence signs nor distant metastasis, and survived for more than 38 months (Fig. 6). Viable tumor cells are also absent in case 17, and a good outcome is expected. In the other patients, some viable cells were observed, despite the effectiveness of chemotherapy demonstrated by radiographic and imaging techniques. Local recurrence and distant metastasis were noted even after several years as in Case 6[7], and the frequency was higher than in osteosarcoma[2]. With our VACA regimen, in which the drugs were administered every other day, the blood concentrations of the anticancer agents were not considered sufficient to eradicate tumor cells. Complete disappearance of viable tumor cells was achieved in only 1 patient among those in whom preoperative VACA therapy was effective in radiographs. Thus, only a small number of patients who were given VACA therapy survived for a long period in a disease-free condition. Huvos observed that the prognosis was poor when a considerable amount of viable cells remained after chemotherapy[9]. The disease-free survival rate was 30% when the viable cell rate was 10% or higher, but 80% when the viable cell rate was less than 10%.[9]

Once lung metastasis is detected, microscopic tumor nodules are considered to be simultaneously present all over the body, and treatment becomes difficult. Conventionally, radiation therapy or chemotherapy using drugs of the same group is continued after relapse, but this has little beneficial effect on patient survival. Recently, Goebel et al and Magrath et al reported that IFOS was effective in such cases[6,11,18,20]. IFOS is nonspecific in the cell cycle, whereas etoposide acts during a specific period in the cycle. Miser et al reported that concomitant administration of IFOS and etoposide was effective in 94% of patients with recurrent Ewing's sarcoma.[13] In our department as well, partial (Case 11, 14, and 16) or complete (Case 15) response was observed radiographically in all 4 patients treated concomitantly with IFOS and etoposide, suggesting its usefulness as a second choice chemotherapy for Ewing's sarcoma. The survival period of patients with relapsed Ewing's sarcoma was prolonged by this regimen. There have been few effective drugs for relapsed Ewing's sarcomas. IFOS and etoposide may be added to the first line regimen for Ewing's sarcoma.

Although Ewing's sarcoma responds well to drugs, the tumor completely disappeared in only a few cases after VACA therapy. The anticancer effect is considered to be higher with more intensive administration of the drugs in the early stage than with sporadic administration, as in our VACA therapy (Case 17). Improvements in therapeutic results may be achieved with early diagnosis and administration of intensive systemic chemotherapy to prevent distant micrometastasis.

(Received September 30, 1992)
(Accepted March 19, 1993)

REFERENCES

1. **Akaboshi, Y., Takeuchi, S., Nagasawa, H. and Kanematu, A.** 1982. Diagnosis and treatment of Ewing's sarcoma. Orthop. Surg. Traumatol. **25:** 29-38 (in Japanese).
2. **Campanacci, M.** 1990. Ewing's sarcoma, p.509-538. *In* M. Campanacci (ed.), Bone and soft tissue tumors. Springer-Verlag, Wien and New York.
3. **Dahlin, D.C. and Unni, K.K.** 1986. Ewing's sarcoma, p.322-336. *In* D.C. Dahlin and K.K. Unni (eds.), Bone tumors, 4th ed. Charles C Thomas publisher, Springfield.
4. **Enneking, W.F.** 1986. A system of staging musculoskeletal neoplasms. Clin. Orthop. **204:** 9-20.
5. **Gehan, E.A.** 1965. A generalized Wilcoxon test for comparing arbitrarily singly censored samples. Biometrica **52:** 203-209.
6. **Göbel, V., Jürgens, H., Etspüler, G., Exner, U., Kuhl, J., Ritter, J., Winkler, K. and Göbel, U.** 1986. Effectiveness of ifosfamide (IFO) alone and in combination with cisplatinum (DDP) in patients with recurrent Ewing's sarcoma. J. Cancer Res. and Clin. Oncol. **111(suppl.):** s30.
7. **Hayes, F.A., Thompson, E.L., Kumar, M. and Hustu, H.O.** 1987. Long-term survival in patients with Ewing's sarcoma relapsing after completing therapy. Med. and Pediat. Oncol. **15:** 254-256.
8. **Huvos, A.G.** 1987. Pathologic assessment of preoperative chemotherapy in osteogenic sarcoma, p.268-273. *In* W. F. Enneking (ed.), Limb salvage in musculoskeletal oncology, Churchill Livingstone, New York, Edinburgh, and London.
9. **Huvos, A.G.** 1991. Ewing's sarcoma, p.523-552. *In* A.G. Huvos (ed.), Bone tumors, 2nd ed. W.B. Saunders company, Philadelphia, London, Tokyo.
10. **Kaplan, E.L. and Meier, R.** 1958. Nonparametric estimation for incomplete observations. J. Am. Stat. Assoc. **53:** 457-481.
11. **Magrath, I., Sandlund, J., Raynor, A., Rosenberg, S., Arasi, V. and Miser, J.** 1986. A phase II study of ifosfamide in the treatment of recurrent sarcomas in young people. Cancer Chemother. Pharmacol. **18(Suppl. 2):** s25-28.
12. **Mandenhall, C.M., Marcus, R.B., Enneking, W.F., Sprimgfield, D.S., Thar, T.L. and Million, R.R.** 1983. The prognostic significance of soft tissue extension in Ewing's sarcoma. Cancer **51:** 913-917.
13. **Miser, J.S., Kinsella, T.J., Triche, T.J., Tsokos, M., Jarosinski, P., Forquer, R., Wesley, R. and Margath, I.** 1987. Ifosfamide with mesna uroprotection and etoposide: An effective regimen in the treatment of recurrent sarcomas and other tumors of children and young adults. J. Clin. Oncol.

5: 1191-1198.

14. **Nasscimento, A.G., Cooper, K.L., Unni, K.K., Dahlin, D.C. and Pritchard, D.J.** 1980. A clinicopathologic study of 20 cases of large-cell (atypical) Ewing's sarcoma of bone. Am. J. Surg. Pathol. **4:** 29-36.
15. **Ozaki, T., Kawai, S., Yamane, T., Ito, S. and Inoue, H.** 1990. Treatment for Ewing's sarcoma. J. Jpn. Orthop. Assoc. **64:** s827 (in Japanese).
16. **Ozaki, T., Sugihara, S., Sumii, H. and Inoue, H.** 1992. Chemotherapy for recurrent Ewing's Sarcoma. J. Jpn. Orthop. Assoc. **66:** s139 (in Japanese).
17. **Reif, R.M.** 1980. Ewing's sarcoma, cytology of large cell type. Acta Cytologica **24:** 175-176.
18. **Rosen, G.** 1987. Chemotherapy of sarcomas, p.83-98. *In* F.R. Eilber (ed.), The soft tissue sarcomas, Grune & Stratton, Inc., New York, London, and Tokyo.
19. **Rosen, G.** 1987. Role of chemotherapy in the management of bone and soft-tissue sarcomas, p.280-294. *In* R. Coombs and G. Friedlaender (eds.), Bone tumor management, Butterworths & Co., London.
20. **Rosen, G.** 1988. Bone and soft tissue sarcomas. A rational approach to their curative management. Surg. Annu. **20:** 121-144.
21. **Rosen, G.** 1992. T-16 protocol for small cell sarcoma. (private communication)
22. **The JOA Musculo-skeletal Tumor Committee** 1989. Evaluation method of surgical margin for musculo-skeletal sarcoma, p.3-23. 1st ed. Kanahara-shuppann, Tokyo (in Japanese).
23. **The JOA Musculo-skeletal Tumor Committee** 1990. General rules for clinical and pathological studies on malignant bone tumors, p.5-7., 2nd ed. Kanahara-shuppann, Tokyo (in Japanese).
24. **Thomas, P.R.M., Foulkes, M.A., Gilula, L.A., Burgert, E. O., Evans, R.G., Kissane, J., Nesbit, M.E., Pritchard, D.J., Tefft, M. and Vietti, T.J.** 1983. Primary Ewing's sarcoma of the ribs. Cancer **51:** 1021-1027.
25. **Wilkins, R.M., Pritchard, D.J., Burgert, E.O. and Unni, K.K.** 1986. Ewing's sarcoma of bone. Experience with 140 patients. Cancer **58:** 2551-2555.