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RADIOTHERAPY AND SURGERY IN 50 CASES OF OSTEOSARCOMA TREATED WITHOUT ADJUVANT CHEMOTHERAPY

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A consecutive series of osteosarcoma patients from one hospital is described. In 1962 radiotherapy with delayed surgery according to Cade was replacing surgery alone as the adopted treatment programme. Statistically the results were the same before and after this time with 5 out of 29 and 6 out of 21 patients, respectively, surviving 5 years. With radiation alone none out of eight survived. Surgery alone produced 3 out of 14 and radiation with delayed surgery 6 survivors out of 15. As surgery with or without radiotherapy is equally ineffective in controlling osteosarcoma a prospective randomized trial of the relative merits of chemotherapy and interferon as adjuvant therapy seems highly desirable.

Key words: osteosarcoma; radiotherapy; amputation

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Over the last 5 years the traditional methods of treatment for osteosarcoma including surgery with or without radiotherapy have gradually been replaced by new programmes combining surgery with chemotherapy. Before the introduction of modern programmes of this type the results of earlier regimes have been reviewed.

Evaluation of the results of therapy for osteosarcoma is often made difficult by the fact that consecutive series from single hospitals are generally small. Larger series are always collected from several different clinics and are reliable only when tumour registers are used (Larsson & Lorentzon 1974) but in such series there is always greater variation in therapy. The material may give valuable information when added to similar series from other clinics and, in the future, assessment of the results in series of this type will also be influenced by the effects of chemotherapy.

In 1962, it was decided at the University Clinic in Lund, to change the principle of therapy for osteosarcoma from surgery alone to radiotherapy with delayed surgery according to Cade (1955). This paper presents the results obtained with the former and the latter programmes both without adjuvant chemotherapy, and discusses the latest trends in the new programmes with chemotherapy.

Table 1. Basic data of all cases of osteosarcoma tabulated in the order of survival time.

Case no.	Sex	Age	Location	Therapy	Duration of symptoms (months)	Biopsy year	Time in months from biopsy to: metastases	Time in months from biopsy to: death
32	M	12	PH	R	1	1968	at diagnosis	2.5
23	F	29	PF	S	3	1951	not shown	3
1	F	52	DT	S	7	1962	not shown	3
26	M	70	PFe	R	8	1969	not shown	3
10	M	5	PH	R	1	1954	2.5	3.5
3	F	12	DF	R	0.5	1958	1	5
16	M	21	DF	RS	6	1959	3.5	5
29	F	33	DF	S	2	1957	not shown	5
33	M	14	DF	SR	1	1948	3	5
40	M	47	DF	R+6+S	8	1967	at diagnosis	6
44	F	9	DF	SR	3	1962	4.5	6
9	M	22	PFi	R+6+S	3	1969	2.5	6.5
2	F	13	PT	RS	2	1956	not shown	7
6	F	8	DF	R	3	1967	2	7
24	M	9	PF	R	2	1953	4.5	8.5
20	F	41	Mand	SR	7	1946	4.5	9
27	F	64	PT	S	2	1957	8	9
18	F	70	Calc	S	6	1952	2	10
39	M	17	DF	RS	1	1946	7	11
8	F	19	PHu	RS	7	1959	4	11
41	F	7	DF	R+6+S	1	1972	4	11
36	F	3	PF	R+6+S	1	1970	8	11.5
45	M	19	DF	S	4	1968	5	11.5
15	M	18	DF	R+6+S	3	1953	5.5	12
25	F	69	PH	RS	8	1968	not shown	12
28	M	30	DF	RS	7	1964	2	14
49	F	10	DF	R+6+S	?	1962	6	15
34	F	38	DF	S	1	1958	13.5	17
42	M	7	PH	R	1	1952	14	17.5
17	M	21	DF	R+6+S	12	1965	12	19
43	M	11	PH	R+6+S	4	1968	4	19.5
35	M	26	DF	S	10	1948	13.5	22.5
7	F	33	DR	S	5	1957	8	32
31	M	44	PH	R+6+S	6	1969	7	37.5
4	M	17	DF	S	2	1960	26	41
21	F	32	PT	SR	?	1945	not shown	59
48	M	19	PT	R	5	1966	35	72
13	F	35	PT	S	16	1947	98	102
50	F	22	PH	SR	?	1952	132	156
12	M	10	PT	R+6+S	9	1972	None	Alive (5 years)
11	F	33	Sca	S	3	1970	None	Alive (7 years)
46	M	22	DF	RS	2	1969	None	Alive (8 years)
30	F	41	PT	R+6+S	4	1967	4	Alive (10 years)
5	M	11	DF	R+6+S	11	1965	None	Alive (12 years)
47	M	20	PT	R+6+S	4	1963	16	Alive (14 years)
37	F	11	DF	R+6+S	6	1959	None	Alive (18 years)
22	M	18	PT	S	2	1958	47	Alive (19 years)
14	M	16	DF	R+6+S	3	1953	None	Alive (24 years)
19	M	13	DF	S	3	1953	None	Alive (24 years)
38	M	8	DF	RS	?	1949	None	Alive (28 years)

D = distal. F = femur. H = humerus. P = proximal. R = radiotherapy only. RS = radiotherapy followed immediately by surgery. R+6+S = radiotherapy followed by surgery delayed 3–6 months. S = surgery only. T = tibia.

MATERIAL

During the period 1945 through 1972, 74 patients with a diagnosis of osteosarcoma were registered at the University Hospital in Lund, Department of Orthopaedic Surgery or Radiotherapy. After reviewing our records and histological preparations, 50 were accepted as osteosarcoma according to the WHO classification. Twenty-four cases were rejected by the histopathologist as chondrosarcoma (8), fibrosarcoma (4), undifferentiated sarcoma (3), giant cell tumour (2), chondromyxosarcoma (2), osteoblastoma (1), fracture (1), Ewing sarcoma (1). In two patients the histological preparations were unacceptable for a diagnosis and the cases were rejected. In three, cytological needle-biopsy preparations alone were accepted at the review.

The distribution of age was typical and there were 27 males and 23 females (ratio 1.3:1). If only patients below 25 are considered the ratio is 2.4:1. Table 1 presents the basic data of all 50 patients with osteosarcoma.

METHODS

Up until 1962 the principle of therapy was amputation when surgically possible. For sarcoma in the distal femur transmedullary amputation was used. For sarcomas in the diaphyseal region or more proximally disarticulation was performed. Radiotherapy was used only for cases where surgery was impossible or where it had been tried but proven insufficient at pathology.

From 1962, biopsy was followed by radiotherapy according to Cade (1955) but using high voltage equipment. Doses of 6,500–7,500 rad were given and amputation was carried out 4–6 months later. In cases where fracture or continuation of tumour growth occurred in spite of radiotherapy, amputation was performed earlier.

RESULTS

Table 1 describes the cases in order of survival time. Sex, age and location of tumour are shown as well as therapy,

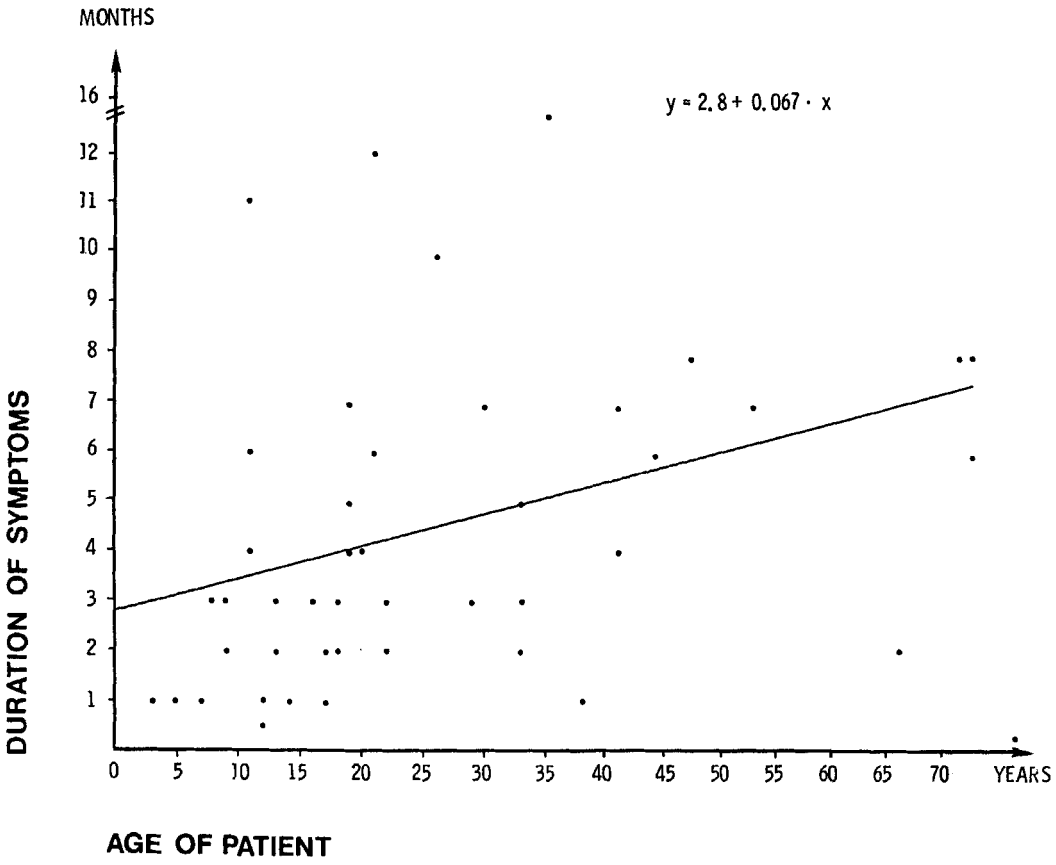

Figure 1. Age versus duration of symptoms.

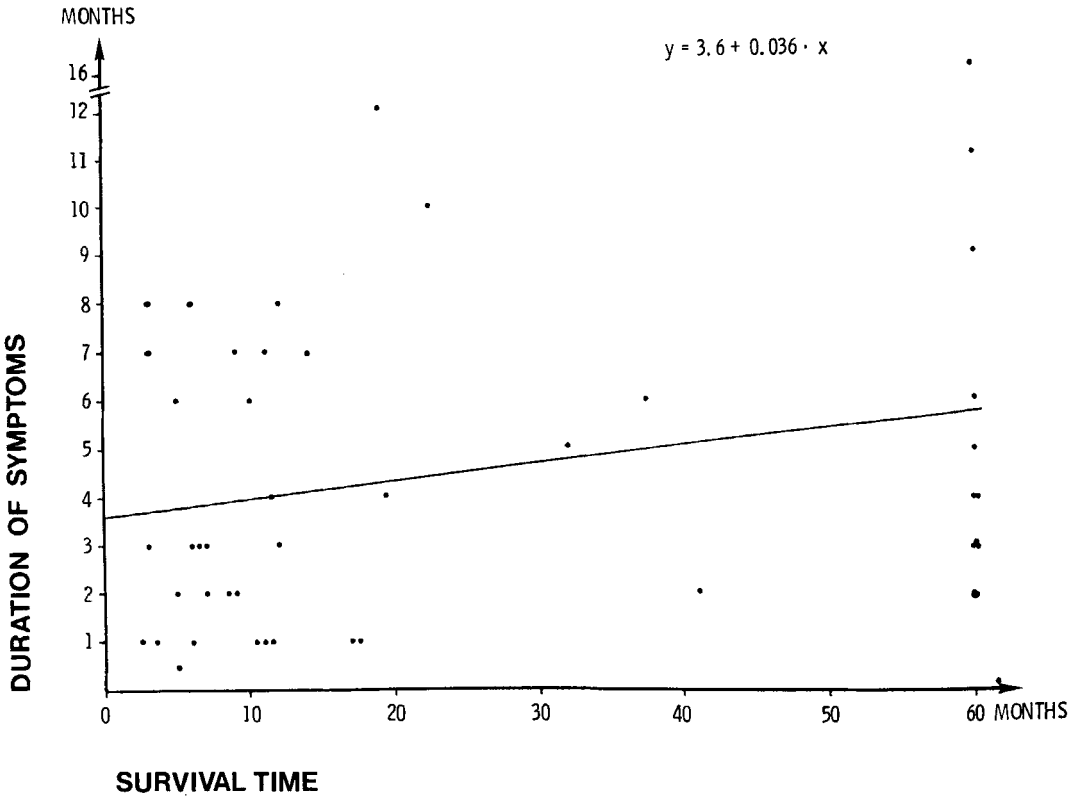

Figure 2. Survival time versus duration of symptoms.

duration of symptoms in months before biopsy, and the time interval in months before evidence of metastases and before death ensued. There is some correlation between age and duration of symptoms (Figure 1). Survival time versus duration of symptoms is shown in Figure 2. No case with symptoms for 2 months or less were among the survivors, but in general the correlation in this material is weak. Before 1962, 5 cases out of 29 survived 5 years, from 1962, 6 out of 21 survived 5 years. Before 1962, 12 out of 29 patients were treated with surgery alone. From 1962, 2 out of 21 were treated with surgery alone. The general 5-year survival was 17 per cent before 1962 and 29 per cent since 1962 but the difference is not statistically significant according to Fischer's test ($P = 0.054$ for the combined material). In the total material of 50, 8 patients treated with radiation alone produced no survivors. Surgery alone produced 3 out of 14 and delayed surgery after radiation six 5-year survivors out of 15 (Tables 1, 2, 3).

Table 2. Survey of planned therapy and disease-free survival.

Therapy	No.	5-year survival
Amputation only	14	3
Amputation + secondary radiotherapy	5	0
Radiotherapy for delayed amputation	15	6
Radiotherapy + immediate amputation	8	2
Radiotherapy only due to metastases	8	0
Total	50	11

Table 3. High voltage radiation before delayed surgery; primary plan and final outcome.

Therapy	No.	5-year survival
Amputation after 6 months	8	6
Amputation before time due to complications	2	0
Amputation not carried out due to metastases	5	0
Total	15	6

DISCUSSION

This consecutive and unselected series shows a 5-year cure rate and a 5-year survival rate of 18 and 26 per cent, respectively. Four patients had pulmonary metastases resected, two were disease-free 5 years later. When the material is divided according to therapy, the group with radiation and delayed surgery has a survival rate and a cure rate which is greater than those with surgery alone but the differences are not statistically significant.

In 1962 the Cade principle was adopted When the results after this time are compared with those from the earlier period the survival rate is a bit better but again the difference is statistically not significant. Many materials support this conclusion (Cederlöf et al. 1960, Dahlin & Coventry 1967, Lindblom et al. 1961, Poppe et al. 1968). Sweetman et al. (1971) recorded 14 out of 61 surviving amputation alone and 22 out of 80 surviving radiotherapy with delayed amputation. In France, Trifaud & Meary (1972) made a broadbased review of the literature studying this question and recorded a 21 per cent 5-year cure rate with amputation alone in 903 cases and a 23.8 per cent rate with delayed surgery after radiotherapy in a series of 501 cases studied. The material presented in this paper agrees with this. It should therefore be remembered that in cases where immediate surgery for one reason or another is not feasible, radiotherapy with the surgery postponed for 4 to 6 months does not adversely influence the results. This type of programme should not be used in cases where the tumour has already made the function of the limb inferior to that of a prosthesis. When the function is good and the pain is controlled by the radiotherapy the possibility of delaying surgery must be kept in mind for special cases. Campannacci & Cervellati (1975) from Italy reviewing 345 cases came to the same conclusion.

Since the first trials with chemotherapy (Phenylalanin mustard in Huston, Texas, in 1963) Adriamycin alone or in combination with other drugs has produced encouraging early results. Pritchard (1976, personal communication) at the Mayo Clinic believes that during the last 5 years the general prognosis of osteosarcoma may be better than before, thereby making historical controls for evaluating the effects of chemotherapy misleading. The 2-year survival rates seem to rise from around 30 per cent without chemotherapy to between 50 and 75 per cent with chemotherapy (Cortes et al. 1972, Jaffe & Watts 1976, Rosen et al. 1974, Sutoff et al. 1974).

Other types of adjuvant therapy for osteosarcoma which have been tried with hopeful early results are adoptive immunotherapy (Neff & Enneking 1975) and interferon (Nilsonne et al. 1975). Interferon as an effective adjuvant to surgery may support the theory of a viral aetiology.

Although it is not proven that these adjuvant programmes are producing better results in the long run, the early figures have given a new interest in reducing the magnitude of mutilating surgery for these patients. Marcove (1975, 1977, personal communication) as well as Sneath (1976, personal communication) are concentrating on extirpation of the bone involved with preservation of the

limb and replacing the structure with a custom-made prosthesis. Jaffe & Watts (1976) conclude that a transmedullary amputation through the involved bone rather than removal of the entire bone should now be safer than before (Foss et al. 1966).

The rarity of osteosarcoma and the delicacy of cytostatic adjuvant programmes now, more than ever, make centralized treatment with coordinated programmes a necessity. As soon as the results of adjuvant interferon are finally analyzed it should be possible to begin a Scandinavian programme comparing interferon with chemotherapy. Surgery alone or preoperative radiotherapy with delayed surgery both have proven insufficient but statistically comparable. From now on adjuvant programmes are running prospectively to make contemporary controls possible.

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