
RADIATION RESPONSE OF PULMONARY METASTATIC OSTEOSARCOMA

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ABSTRACT

Pulmonary metastatic osteosarcoma still has fatal outcome in the Eastern country due to the low socioeconomic problem. Many of the patients cannot afford chemotherapy. Radiation treatment combined with chemotherapy has shown to be a very good response with some survivors. This study showed the benefit of the irradiation combined with chemotherapy over chemotherapy alone in 5 cases of pulmonary metastatic disease, the other 4 acted as a good adjuvant. Only one case, the lung nodule increased in size after radiation and chemotherapy but the pleural effusion has been controlled.

INTRODUCTION

The overall survival rate among patients with osteosarcoma has improved dramatically in the past decade partly due to the improved outcome of treatment of patients with pulmonary relapse. Gross metastatic disease in the lung was detected at diagnosis in 10-20 percent of all patients with osteosarcoma in the first presentation.¹ Eight percent of relapses occur in the lung alone and 90 percent of relapses occur within the first two years of initial diagnosis. During the past decade the universally poor 5 year survival rates, which range from 0 to 30%, have stimulated the active role to combat pulmonary spreading.² Treatment of pulmonary metastasis includes chemotherapy and aggressive resection of the tumor but very limited use of pulmonary irradiation. Whole lung irradiation has been used extensively in the treatment of pulmonary metastases from various malignant tumor, with an extremely radiosensitive nature such as Ewing's and Wilms's tumor.³ In the cases of osteosarcoma, elective whole lung irradiation of 15 Gy in 12 days showed no significant differences in either survival or postponing the appearing of metastasis.⁴ Therefore, pulmonary irradiation was not found to be of value as an adjuvant

measure in the treatment of pulmonary metastatic osteosarcoma.

The purpose of this study was to emphasize the adjuvant role of radiation in controlling pulmonary metastasis and leading to increase chance for cure.

MATERIALS AND METHODS

Multidisciplinary preoperative therapy was a new approach of osteosarcoma in Faculty of Medicine, Ramathibodi Hospital. The treatment consisted of preoperative intraarterial infusion of cisplatin combined with intravenous chemotherapy, with or without local irradiation, surgery and prophylactic whole lung irradiation.⁵⁻¹⁰

From the total 125 cases of osteosarcoma, 10 cases of osteosarcoma with pulmonary metastases, admitted to Ramathibodi Hospital between March 1986 to March 1995, were treated with irradiation and chemo-therapy. All patients received 23.40-35.00 Gy (100-180 cGy daily, 5 fractions per week) to the affected whole lung with or without booster dose of 18-30 Gy at the pulmonary nodules. In the cases of bilateral lung disease, the worse lung was irradiated and the effectiveness of the adjuvant chemotherapy

was determined by the response of the other non irradiated lung. The criteria for selecting the lung for irradiation included number of nodules and size of the metastasis. The treatment were given by using two parallel opposing fields with Cobalt-60 teletherapy or from 6 MeV linear accelerator with mid line depth without lung inhomogeneity correction. All patients received additional cisplatin 100-120 mg/m² IV infusion during the irradiation treatment every 3 weeks combined with either doxorubicin, epirubicin, etoposide or bleomycin, cyclophosphamide and dactinomycin, according to the whole group randomization.

There were 2 female and 2 male patients with unilateral lung disease. The other female and 5 males had bilateral metastases. (Table 1). The mean age of the patients was 17.03 ± 7.7 with the range of 4 to 29 years old. The main criteria for evaluating the effectiveness of adjuvant lung irradiation was the disappearance or reduction in size of the pulmonary nodule or pleural effusion.

RESULTS

Among 10 patients, one 26 years old female survives for more than 43 months after initial diagnosis of the disease and gave birth to a healthy baby girl weight 3015 gms. Her lung lesion disappeared with asymptomatic mild irradiation effect at her right middle lung field (Fig. 1-2). All other 8 patients showed very good radiation responses. All pulmonary nodules in the

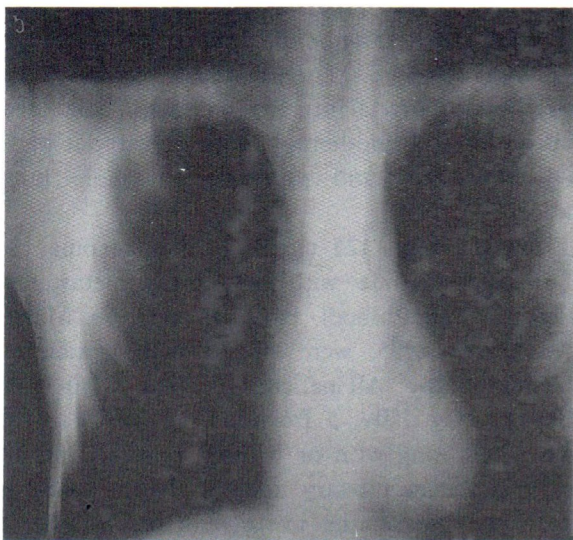


Fig 1 Tomogram of the chest showed nodular lesion in the right lower lobe, differentiated from the nipple shadow.

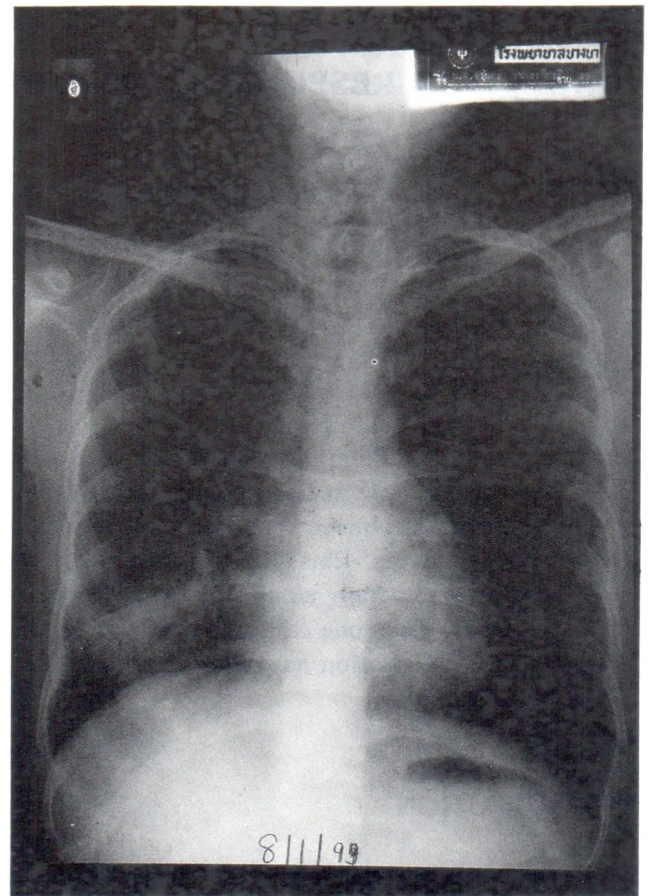


Fig 2 Plain film of the chest in the same patient after 4350 cGy local irradiation combined with chemotherapy. The nodule was disappeared with asymptomatic radiation infiltration.

irradiated lung dissolved or disappeared in contrast with the controlled unirradiated lung. All but one of the patients with bilateral diseases, the lung nodules in the unirradiated lung increased in size even they were on chemotherapy (Fig. 3-5). One girl who still survived for more than 17 months now, had one calcified lung nodule which was proved to be negative on lung resection, but another nodule was positive and she was continued on chemotherapy.

Only one 16 years old boy had increased in size of the pulmonary nodule in the previous irradiated thoracotomized lung, but the pleural effusion was under controlled. He returned to school with a very good health, even his lung still had pulmonary nodule and he was continued on chemotherapy but the regimen was changed from cisplatin combined with epirubicin to ifosfamide added to cisplatin. The status of the

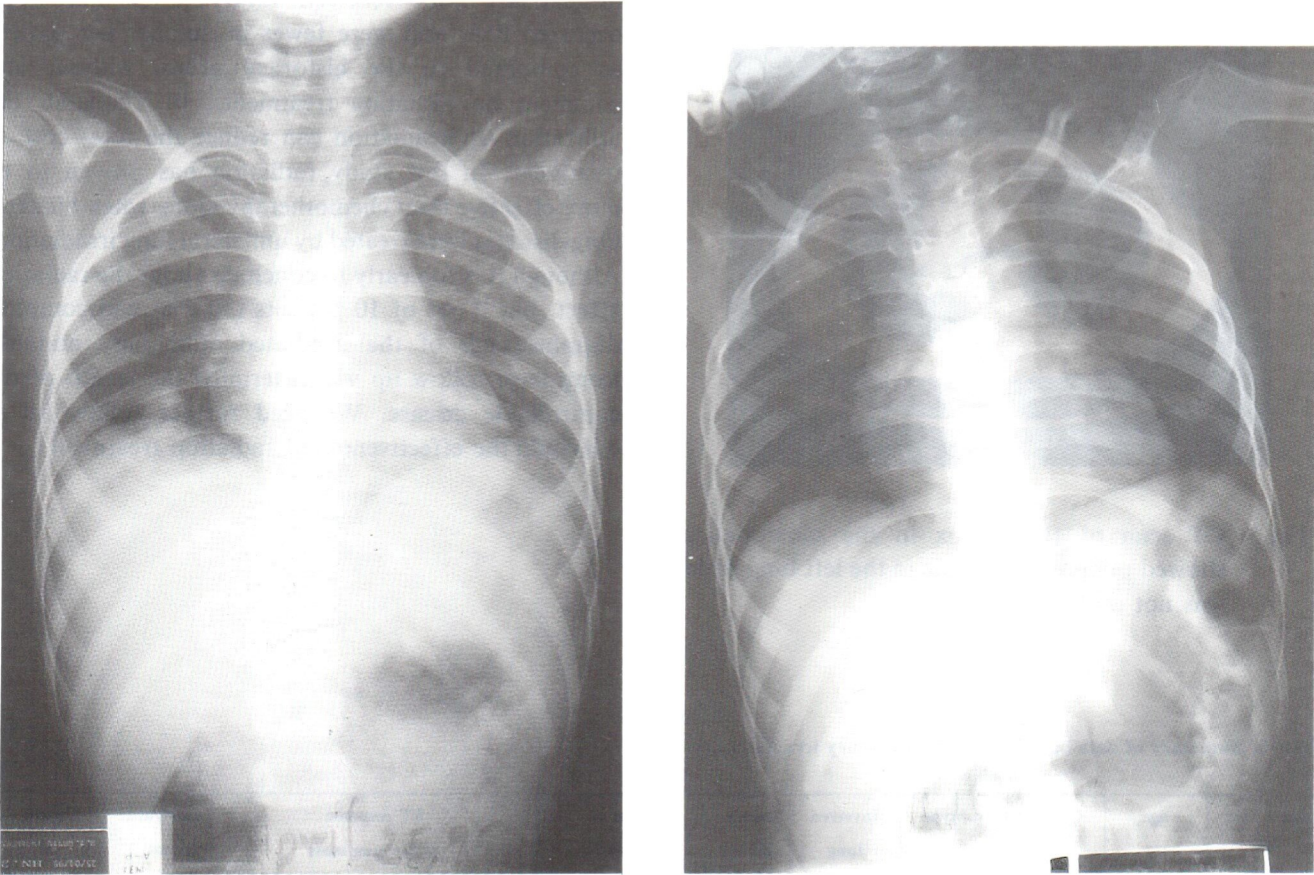


Fig 3-4 Plain film of the chest before and after irradiation of 2520 cGy at the right lung field combined with chemotherapy.

patients was shown in Table 2, among these 10 cases, 2 patients developed bony disease, one with bone and spinal cord lesion, another had stump recurrence.

DISCUSSION

Metastases which were detectable on the chest x-ray, have a diameter of at least 6-10 mm. and contain 10^8 or more tumor cells.¹¹ Experience has shown that these metastases can seldom, if ever, be completely destroyed by radiation even in a much higher dose. Apart from the specific radiosensitivity of the certain tumor, a chance of cure by radiation is also depended on the number of viable tumor cells. Observation and calculations by Breur and Abbattucci had shown that the radiosensitivity of osteosarcoma is sufficient to eradicate tumor nodule of 10^5 cells with a dose of 20 Gy over 10 days, that is, the maximum dose which was tolerable for both lungs. So prophylactic lung

irradiation may play important role to prevent lung metastasis.¹¹⁻¹⁵ In the cases of fullblown pulmonary metastasis, patients receiving chemotherapy combined with aggressive resection of the tumor survived for more than 41% in Western country,¹ but in Eastern country even in Thailand, there were no survivor left. Aggressive lung irradiation adjuncted with chemotherapy, may control pulmonary metastasis. From March 1986 to March 1995 a total of 125 cases of osteosarcoma were treated in Ramathibodi Hospital. There were 49 lung metastases in this study 39 cases had already terminated with other 5 still survived with disease. The rest of the patients were lost to follow up and suspected to be dead due to far advanced diseases. Only 2 patients were still survived without disease detectable 79⁺ and 43⁺ months after treatment. One was treated by chemotherapy alone, the other by combined chemotherapy and radiation. The other 9 cases were excluded in this study.

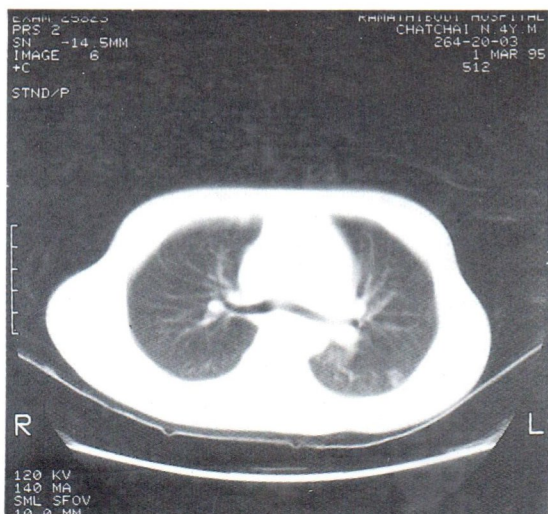


Fig 5 CT scan of the thorax in the same patient showed pulmonary nodule in the left lung which was not radiated.

Jaffe et al. suggested that pulmonary metastases in patients who received adjuvant chemotherapy occurred later and were fewer in number per patient as compared to the historical group without any comment on radiation treatment.¹ In Thailand, the utilization of irradiation can reduce the total cost of treatment. In this study, radiation has proven to be more effective than chemotherapy alone when bilateral lung diseases were treated by unilateral lung irradiation. Although it is too early to conclude about the radiation effect, but 9 out of 10 patients (90.0%) had complete disappearance of the irradiated pulmonary nodules. Long term follow up will determine the length of the controllable disease. We need further follow up to conclude the effectiveness of radiation treatment.

Table 1 Summary of data on 10 cases of pulmonary irradiation.

case	sex	age	site	subtype	Involved lung		chemo-therapy	dose of irradiation cGy		RT response of the lung mass			survival 1 mos	Course of disease
					Rt	Lt		1°	booster dose	disappeared	decreased	increased		
1	F	26	fibula	osteoblastic	/		epi	2550	1800	X			43 ⁺	survive
2	F	14	fibula	chondroblastic	/		VP-16	2550			X		17 ⁺	second bone
3	F	16	tibia	chondroblastic	/	/	epi + BCD	3500		X			16	loss
4	M	17	femur	osteoblastic		/	epi + BCD	2550	3000	X			15	bone, cord
5	M	14	tibia	fibroblastic	/	/	doxo	2550	-	X			12	loss
6	M	12	tibia	osteoblastic	/	/	epi	2520	-	X			7 ⁺	jaw other lung progressed
7	M	29	femur	MFH variant	/	/	epi	2550		X			8 ⁺	stump recur other lung progressed
8	M	23	femur	osteoblastic	/	/	epi	2340	-	X			5 ⁺	stable
9	M	4	femur	chondroblastic	/	/	epi	2520	-	X			4 ⁺	other lung progressed
10	M	16	tibia	telangiectasis	/		epi	2520				X	3 ⁺	stable

Epi = epirubicin, doxo = doxorubicin, BCD = bleomycin - cyclophosphamide + dactinomycin.

Table 2 Status of the diseases

Metastasis	
bone	2
bone + cord	1
stump recur	1

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