

Radiotherapy in the treatment of hepatocellular carcinoma and its metastases*

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Summary. A study was conducted to evaluate the effect of external radiation therapy on hepatocellular carcinoma (HCC) and its metastatic lesions. A total of 33 patients with cytopathologically proven HCC were subjected to radiation therapy over a 4-year period, and treatment was discontinued in 8 cases due to jaundice, severe discomfort, or early mortality. Thus, 25 patients with 28 lesions underwent irradiation with a total dose ranging between 3000 and 5600. Of these, seven were irradiated for liver tumors, and the results showed that two lesions decreased in size, the symptoms improved in 1 case, and another patient maintained stable disease for 4 months. Among the 21 metastatic lesions treated, only 2 patients failed to respond to the treatment. Nine subjects were irradiated for bone metastases, and the bone pain subsided in all but one case. The survival for bone metastasis was as long as 23 months when the primary tumor was treated effectively. Three of the four cases of irradiated skin nodules disappeared and had not recurred after 5 months, 1 year, and 4 years, respectively. Tumor shrinkage or symptoms of relief were noted for three abdominal lymph nodes, one neck lymph node, one pleural tumor, and one lung tumor. Clinical improvement associated with a stable lesion was observed in two patients with brain metastasis. Follow-up revealed regrowth of the tumor or recurrence of symptoms in most of the patients. However, none of the patients died as a direct result of a metastatic lesion. Although external radiation therapy is palliative in intent, it appears to be useful in the treatment of HCC and its metastatic lesions.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies. Surgery is considered to be the best method of treatment. In patients for whom surgery is contraindicated, transcatheter arterial embolization (TAE) has been used to improve survival. However, since both surgery and TAE are unsuitable or ineffective in some patients, some other kind of treatment must be used in such cases. In addition, the prolongation of life might result in increased development of extrahepatic metastasis; therefore, treatment of metastatic lesions is also important. As radiotherapy has long been used in cancer therapy, we felt that it might be of benefit in the treatment of both primary and metastatic HCC lesions. We therefore conducted a clinical study on irradiation of HCC and its metastatic lesions.

Patients and methods

A total of 33 patients with cytopathologically confirmed HCC were selected for treatment with radiotherapy, and treatment was discontinued in 8 cases due to the development of jaundice, severe discomfort, or early mortality. Therefore, only 25 patients with 28 lesions completed the treatment course, including 23 men and 2 women whose ages ranged from 33 to 72 years. The lesions consisted of 7 liver tumors, 9 bone metastases, 4 skin nodules, 3 abdominal lymph nodes, 1 neck lymph node, 2 brain tumors, 1 pleural tumor, and 1 lung tumor. Among the 7 liver tumors, 5 were irradiated after failure or a poor response to TAE. The irradiation was performed with a linear accelerator at doses ranging from 3000 to 5600. The tumor size and location and the irradiation field were determined by ultrasound, CT, and conventional X-rays according to the characteristics of the tumors.

Results

The patients' background data and the results obtained are presented in Table 1. In all, 43% of the liver tumors failed to respond to the irradiation. Only 2 of 7 liver tumors displayed a decrease in size after the irradiation (Fig. 1);

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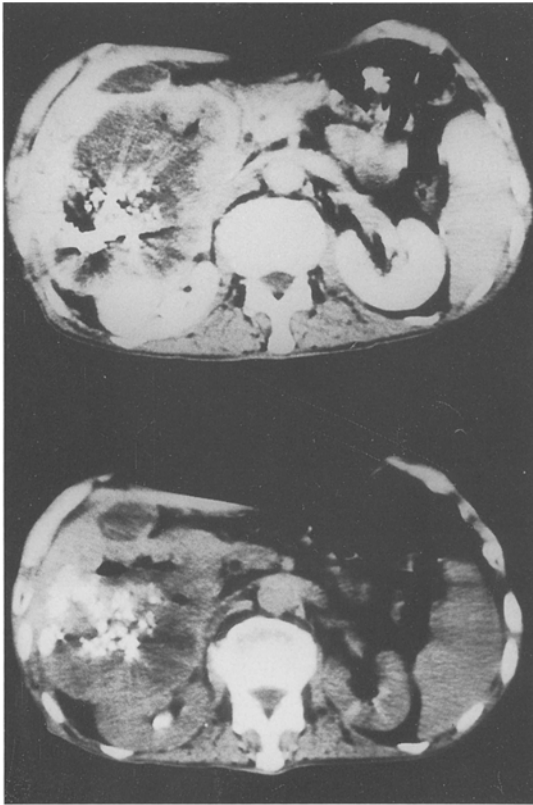


Fig. 1. Abdominal computed tomography demonstrates necrosis and shrinkage of a right abdominal tumor after irradiation. The *upper image* was obtained prior irradiation, and the *lower image* was obtained after irradiation

1 showed a stable condition, and the other showed an improvement in symptoms. Of the 21 metastatic lesions treated, 17 showed some improvement after irradiation (Fig. 2). Two patients with bone metastasis survived for longer than 1.5 years and finally died due to tumor recurrence. In all, 13 of the 17 responding lesions recurred

Table 1. Results of external irradiation in the treatment of HCC and its metastases

Tumor		Response	Follow-up result	
Number	Site			
Liver:				
1	8 cm	Size decrease		2 m l
2	7 cm	No response		8 m d
3	8 cm	No response		6 m d
4	6 cm	Subjective improvement	Recurred	10 m f
5	8 cm	No response		8 m f
6	5 cm	Stationary for 4 m		6 m f
7	3 cm	Size decrease		4 m f
Bone:				
8	Spine	Pain relief	Recurred	11 m l
9	Spine	Pain decrease	Recurred	2 m l
10	Pelvis	No response		1 m l
11	Spine	Pain decrease	Recurred	23 m d
12	Shoulder	Pain relief	Recurred	19 m d
13	Pelvis	Pain decrease	Recurred	4 m d
14	Spine	Pain decrease	Recurred	2 m f
15	Spine	Paralysis subsided	Recurred	3 m d
16	Spine	Pain decrease	Recurred	5 m f
17	Skin nodule	Disappeared	No recurrence	4 y f
18		Disappeared	No recurrence	5 m l
19		Disappeared	No recurrence	1 y f
20		No response		2 m d
21	Abd. LN	Pain and ileus subsided	Recurred	3.5 m d
22		Pain decrease	Recurred	6 m f
23		Size and pain decrease	Recurred	6 m l
24	Neck LN	Size decrease		2 m l
25	Pleural	Pain decrease	Recurred	5 m d
26	Lung	Size decrease	Recurred	3 m d
27	Brain	Stable		8 m d
28	Brain	Stable		4 m l

l, Lost to follow-up; d, dead; f, follow-up continues; m, months; y, year(s); Abd., abdomen; LN, lymph node

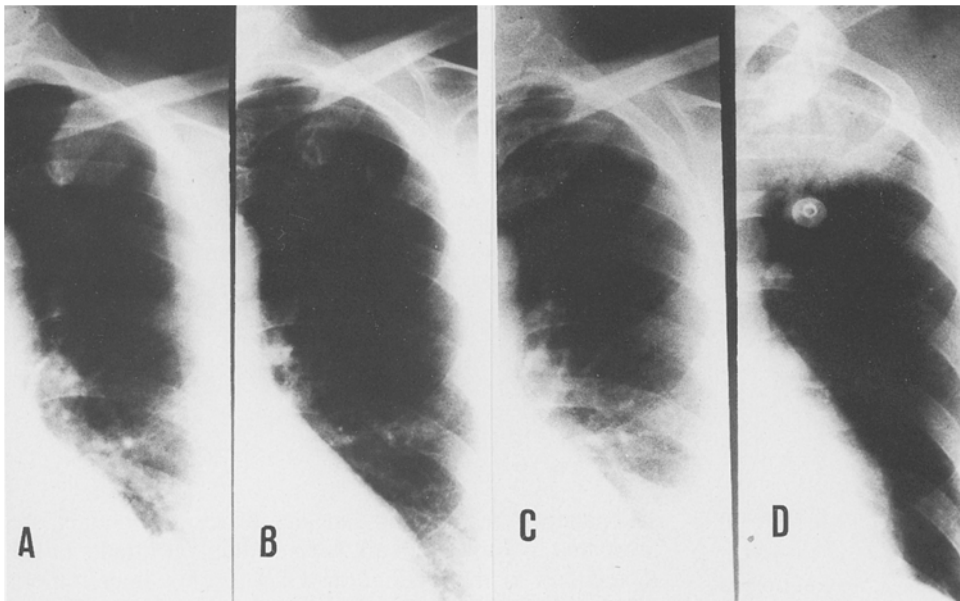


Fig. 2 A-D. Chest films of a patient with HCC reveal shrinkage of a left upper lung tumor after irradiation (A-C) and recurrence 2 months later D

during the follow-up period. None of the patients died as a direct result of a metastatic lesion.

Discussion

Most HCC cases are complicated by liver cirrhosis, which contraindicates surgical treatment. In Taiwan, the currently favored therapeutic modality is TAE in most cases [1]. However, since TAE is sometimes impossible due to distorted vessels or to repeated TAE, radiation therapy is a viable alternative. However, a large dose of irradiation might cause radiation hepatitis [4], and poor results have been reported several decades ago [2]. Nevertheless, improvements in imaging techniques and better localization of the irradiation have decreased the likelihood of radiation hepatitis and might achieve favorable results [3, 6]. Although we irradiated only 7 patients with HCC for liver tumors, 4 of them maintained a decrease in size or stable disease for some duration (Fig. 1). Of these subjects, 5 either had undergone repeated TAE and could not be embolized or did not respond to TAE. We thus consider irradiation to be a valuable palliative treatment.

Metastatic lesions have been found at high incidence in an autopsy study of primary liver cancer deaths [5]. Although metastasis may not be detected at diagnosis, the prolongation of life by effective treatment [7] provides more time for the appearance of metastasis. The management of metastatic lesions from HCC is becoming increasingly important.

The most frequently encountered extrahepatic metastases were detected in the lung, bone, and lymph nodes. Lung metastases are usually multiple and not suitable for irradiation, but solitary cases can be irradiated (Fig. 2). Bone metastasis frequently causes troublesome pain, but most patients fortunately respond well to irradiation. The pain usually disappears or decreases in intensity. Although the symptoms usually recur, they can be managed by repeated irradiation. This is important because some patients might survive for a long time after proper treatment of a liver tumor. Metastases to the abdominal lymph nodes are not

symptomatic when they are small. When they are enlarged and show symptoms, irradiation is usually helpful. The best effect was obtained in irradiation of skin nodules. Three of four nodules disappeared after irradiation, and no recurrence has been observed for as long as 4 years. The one nonresponsive lesion was a rapid-growing tumor in a noncooperative patient, and it measured 5 cm and showed central necrosis at the time at which irradiation was started. The reason for the excellent response in the other three cases might have been the good localization with a full irradiation dose.

We believe that external radiation could be used either in combination with or as an alternative to surgery and TAE in only some patients with HCC, particularly for local control of distant metastases. Radiotherapy is also effective in the management of metastatic lesions and should help improve the patient's quality of life.

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