THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY FOR PALLIATIVE TREATMENT IN METASTATIC LIVER CANCER : A CASE REPORT

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ABSTRACT

A case of metastatic liver cancer from CA colon who failed to systemic therapy was treated with 3D-CRT and periodical irradiation with deep inspiration breath- hold technique. This technique permits the precise delivery of high radiation dose to the target while sparing the most of normal liver tissue. The radiation dose was 66Gy in 20 fraction encompassed the target at the 90 percent isodose line. The tumor was decreased in size and pain was relief. The CEA level was decreased from 1466 to 371 in one month after radiation therapy .The second course of radiation with 30 Gy in 2 weeks was given to the residual tumor. The tumor in the liver was controlled for more than 18 months. The patient could tolerate to the treatment procedure well without any complications inherent to the technique. This technique is an effective and safe treatment for liver metastatic tumor especially in single lesion .

INTRODUCTION

The present of metastases in the liver is usually fatal. Chemotherpy has been accepted to be the treatment of choice. There are documented palliative role of chemotherapy in term of symptomatic relief and slightly increased survival in some study.[1,2] However some type of tumor dose not response to chemotherapeutic agent.So the treatment of patient with liver metastases is principally based on the origin of the primary tumor. Surgery is a well established method on the treatment of liver metastases from colo-rectal cancer. But only a small proportion of these patients will be in a satisfactory condition for surgery.[3,4]

Radiation therapy play a very important role for palliative treatment of metastatic tumours to brain and bones but not for metastatic diseases to liver. The restricted tolerance of the normal liver limits the use of this modality to treat the metastatic diseases to the liver which are usually multiple and occupy the major part of the liver. The radiation doses exceeding 25-30 Gy delivered in 2-3 weeks to the entire liver leading to a fatal complication of hepatitis especially in patient who has poor liver function and minimum liver reserve.[5,6]

The improvement of radiation technique such as stereotactic radiotherapy or three dimensional conformal radiotherapy facilitates treatment by providing a mechanism for conforming the high - dose radiation to the target volume, thus minimizing the dose to adjacent uninvolved normal structures. This process involves graphic reconstruction of 3- dimensional images from multiple cross-sectional CT

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images, beam's-eye-views display, rapid dose calculations and dose display, and the interactive modification of beam parameters to provide adequate target tumor dose coverage and avoid uninvolved normal tissue. However, the movement of intrathoracic and intraabdominal target during treatment still be the major problem for conforming radiation technique. The periodical irradiation with the corresponding of patient's respiratory phase technique for lung metastasis and hepatoma was reported with encouraging response and improving survival.[7,8] Thus, the deep inspiration breath-hold technique is used to treat a case of metastatic liver tumor from colon cancer who failed to chemotherapy and not suitable to surgery.

CASE REPORT

A 69 years old man with a history of CA ascending colon was referred for consultation about role of radiation therapy in metastatic liver cancer. He had a tumor at ascending colon diagnosed in April 1998, and right half colectomy was done there after. The pathological report was well differentiated adenocarcinoma with 2/37 positive lymph node metatstasis.

He received 6 courses of 5FU + Leucovorin as an adjuvant chemotherapy from July 1998 to January 1999. After the treatment, the CEA level was still persisted around 15.

Feb 1999, the CEA level raised to be 23. The abdominal CT was done. Liver and lung metastases were found. The chemotherapy was changed to campto or CPT-11. The treatment was stopped in June due to the progression of disease to be 5x5.5x4.2 cm. and the CEA level was raised to be 206.3.

Oct 1999, the CT scan showed progression of the liver had mass to be 6X6X5.4 cm. and the CEA level had raised to be 591. New combination chemotherapy composed of Oxaliplatin+ 5FU + leucovorin was given. After 3 courses of chemotherapy, the CEA level was 575 while the tumor still progress to be 8x6x5.4 cm.(Figure 1a-1c).The patient was sent to consult for radiation due to pain at the right flank in Feb 2000.The CEA level at that time was 1466. The patient was treated with 3DCRT with the deep inspiration breath-hold technique .

Figure 1a

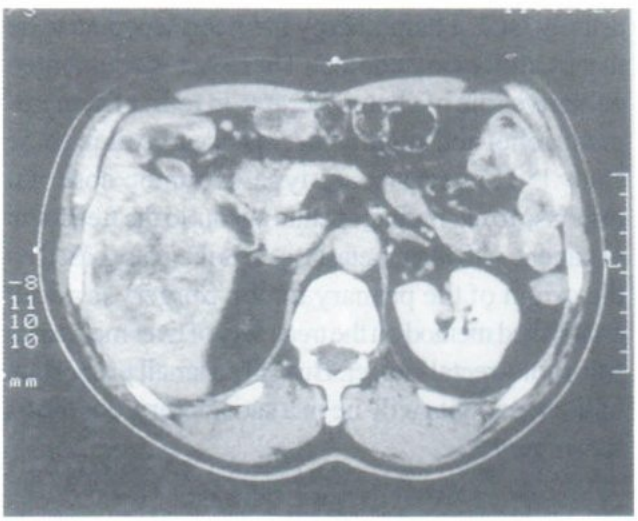

Figure 1b

Figure 1 A-C A large liver mass measuring 8 cm occupied the whole lower portion of right lobe.

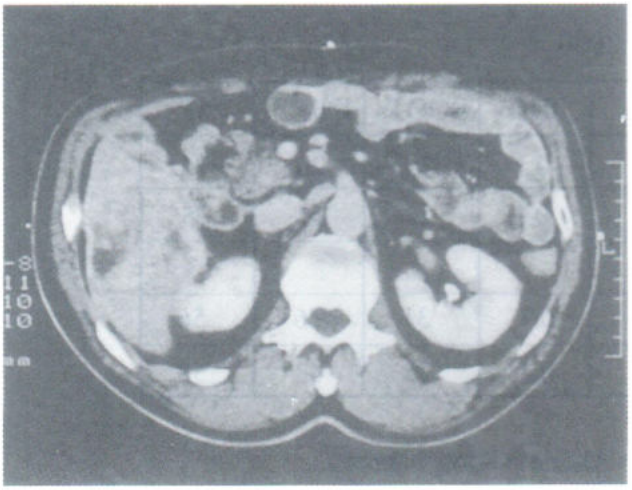

Figure 1c

RADIATION TECHNIQUE

The patient were positioned and immobilized on the CT-scanner couch with the marker wires placed at midline and lateral side of the body along the laser beams. This position was set with these markers through out the treatment couses. Axial CT images, with 0.5 cm slice thickness through the liver were obtained during full inspiration. The CT images were transfered directly to the treatment planning system (Focus 3D-planning system). The processes were done systematically by labeling the external contour to the normal critical organs. Then the treatment volume was defined. In this case we used the gross tumor volume or GTV as the planning treatment volume because it was a palliative treatment. The treatment planning were done according to the shape of the tumor and the critical organs nearby. Multiple static beams of different angles were used. The ninety per cent isodose line was encompassed the target while sparing the most of the liver tissue. After the treatment plan was approved, the alignment was transfer to the central level of the treatment field and CT scan at isocenter slice was done to confirm the same slice as in the treatment plan, while the patient was set in the same position.

To correct the effect of organ movement from breathing, irradiation was given during the period of full inspiration. Thus the treatment had to be divided into small multiple sessions relating to the inspiratory phase. The patient was trained to keep his full inspiration as long as he could and 80 per cent of the duration he could hold his breath would be used for the period of irradiation in each session.

In the treatment room, the patient was set and immobilized by the same position as for the CT scanning. At least two radiation technologists were needed for this treatment procedure. The first one worked on the treatment machine while the other controlled the patient respiration during treatment through the intercom, and observed the patient from the closed-circuit television. According to the biological effect, the 276 cGyX20 fractions which is equivalent to 66 Gy of 200 cGy per fraction, 5 fractions a week by TDF calculation was given.

RESULT

The patient tolerated the treatment procedure very well, no immmediate complication was found. The pain was relief. One month after treatment, the CT scan of upper abdomen was done. The lesion was decreased in size (figure 2a-c) with no reaction outside the tumor. The CEA level was decreased to 371and the liver function test was within normal limit. The CEA level and liver function test were followed up as shown in table 1

Table 1 The CEA and liver profile from Feb to Dec 2000

Date	CEA	Alb	Glob	DB	IDB	SGOT	SGPT	AP
1/2/00	1466	3.9	3.1	0.5	0.1	28	26	76
4/4/00	371	3.9	3.2	0.5	0.1	25	17	75
16/5/00	225							
16/6/00	182	3.9	4.0	0.5	0.1	31	26	56
23/12/00	234	3.9	2.7	0.7	0.3	25	43	58

DB, IDB, AP
DB = Direct Bilirubin , IDB = Indirect , AP = Alkaline Phosphatase

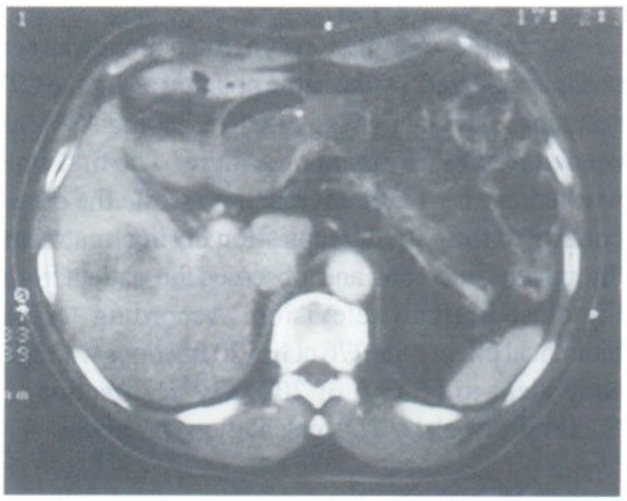

Figure 2a

Figure 2b

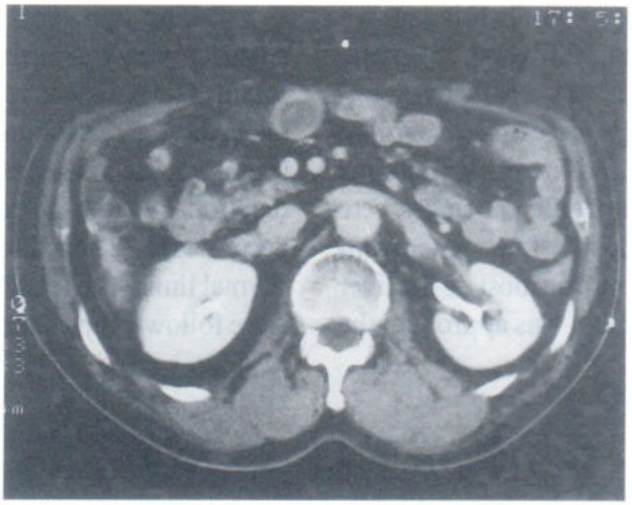

Figure 2c

Figure 2a-c The CT scan showed decreasing in size of the liver in comparison with the lesion before radiation.

In May 2000 , Xeloda that had been claimed to be a very effective drug in colo-rectal cancer, was given to the patient due to the persistence of high CEA level for the purpose of palliative treatment for residual tumor and micrometastasis. But unfortunately the patient suffered from hand foot syndrome after one course of treatment. Because of the CEA level still persisted in July 2000, 3D-CRT was plan to retreat the residual tumor in the liver. Ten fractions of 256 cGy was given to the lesion. At this time we found metastatic lesions in the right lung as in figure 3a. We also treat the metastatic lesions in the right lung lesion by 3DCRT with a radiation dose of 622 cGyx 5 fractions that is equivalent to 70 Gy of conventional dose.

Dec 2000, the lesions in the lung almost disappear (Figure 3b) and also further decreasing in size of the lesion in the liver (Figure 4a-c)

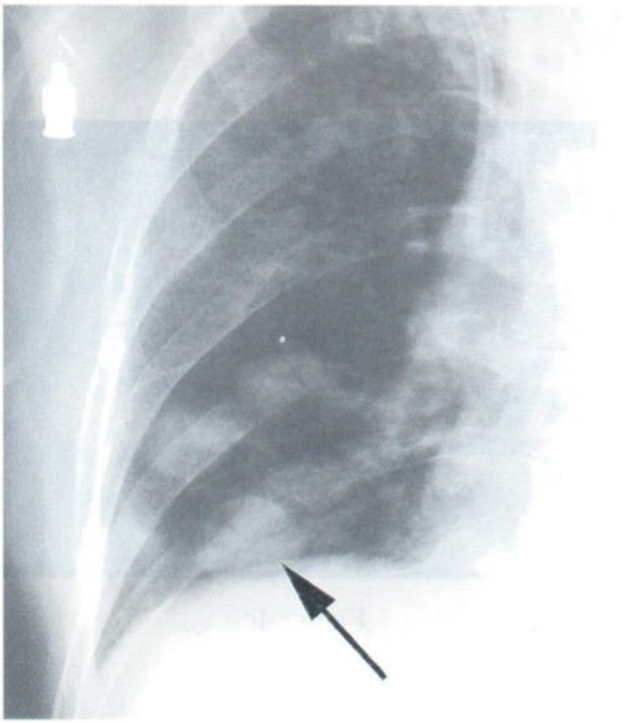

Figure 3a

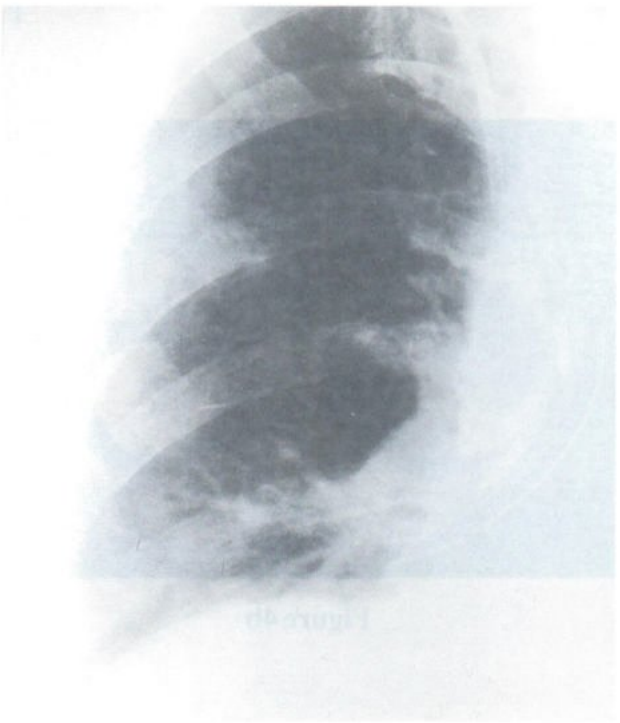

Figure 3a

Figure 3a (left) Chest x-rays showed a large tumor in right lower lobe (arrow) which almost disappeared in **figure 3b (right)** 4 months after 3D-CRT

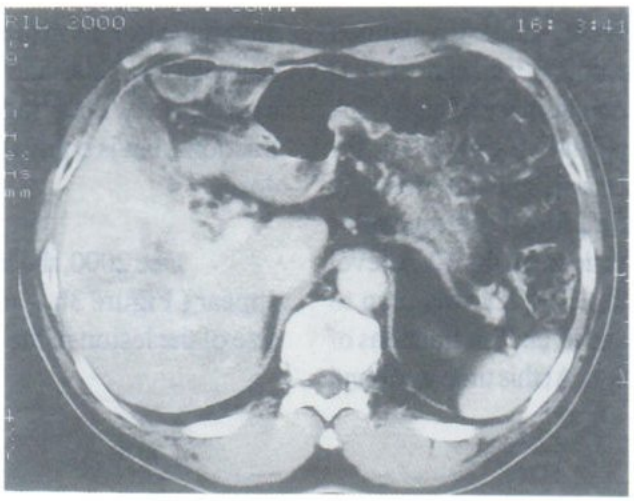

Figure 4a

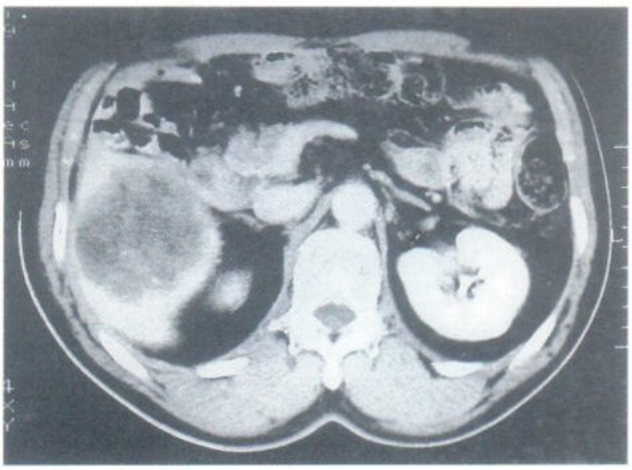

Figure 4b

Figure 4c

Figure 4a-c The CT scan showed mark decreased in size of the tumor in the liver 4 months after 3D-CRT

Jan 2001, there were multiple lung metastasis outside the radiation field. Supportive treatment was given because the patient had no symptom. The CEA level continue to rise up to 1370 in Aug 2001. The patient developed brain metatstasis in Oct 2001. He was treated by conventional 40 Gy to the whole brain and 66 Gy for the metastatic lesion using stereotactic radiation therapy. The patient's clinical condition was well, but the CT scan showed new multiple metastatic lesions in the liver beyond the radiation field as shown in figure 5a-b

DISCUSSION

This patient got the standard adjuvant chemotherapy, 5FU and leucovorin, after surgery for colorectal cancer , but failed to control the disease . The second line chemotherapy regimen

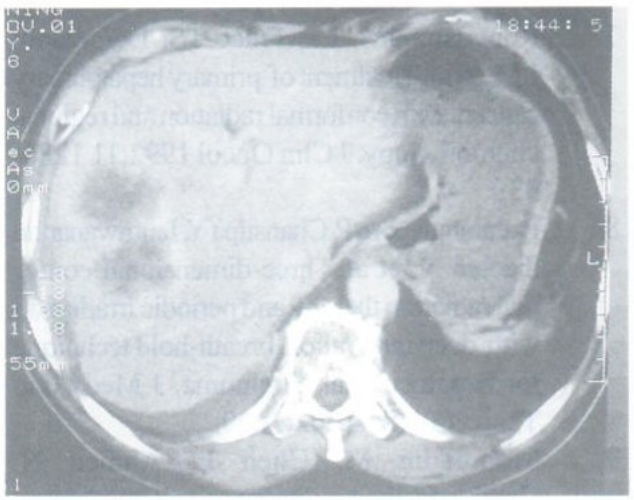

Figure 5a

Figure 5a

Figure 5a-b The abdominal CT scan showed new multple metastatic lesions in the liver beyond the previous radiation fields

with Campto and Oxaliplatin were given. The CEA level and the disease still progressed with pain at the right flank. So the patient was sent to consult for radiation.

Liver irradiation with or without chemotherapy has been used for the palliation of symptom caused by non-resectable hepatic metastatic tumor which had been failed to chemotherapy.[9]

The major concern is that the tumor receives a dose high enough to achieve a reasonable probability of local control while the radiation dose to normal tissue should be kept low enough to an acceptable complication level. Three dimentional computerized planning system provides a mechanism for increasing the tumor dose to the CT-defined target as a mean of enhancing local tumor control and increasing in overall survival.[10-14] One of the most difficult problems in the treatment procedures for these precisely method is the movement of the target organ in the thorax and abdomen. Even if the body can be positioned and immobilized, the visceral organs, such as liver, still move up and down with breathing. The deep breath-hold technique was then developed to solved the problem and showed a good result without any acute complications.[8] This study warrant the high dose, more than 60 Gy , local radiation therapy for metastatic hepatic tumor which was high enough to relieve the pain symptom .The CEA level was dramatic response after stereotactic radiation therapy. The liver profile still in normal limit even after the second course of radiation to the liver in July 2000 showing the successful sparing of normal liver tissue. With the use of active breathing control during treatments, we were able to decrease the amount of normal liver tissue danrage leading to lessen the risk of radiation induced liver abnormality.

However , because of the natural history of the disease , the patient developed brain ,lung and the liver metastases outside the radiation field. The patient survived more than 20 months from the starting of palliative treament for liver metatstases. The patient tolerated the treatment well and also had a good quality of life except during the course of chemotherapy that he felt suffered from the toxicity.

CONCLUSION

Three dimensional conformal radiation and periodical irradiation with the corresponding deep

insipiration breath-hold technique is a simple and feasible irradiation technique for a metastatic liver tumor which is a movable target. The method decrease the toxicity of treatment and therefore, facilitate further dose escalation. This technique should be considered in metastatic liver tumor as:

1. An alternative to open surgery for metastatic liver tumor both in curative and palliative aims.

2. To be used as the booster technique for delivering the high dose to the well defined volume after whole liver irradiation up to maximal liver tolerance dose.

REFERENCES

1. Scheithauer W, Rosen H, Kornek GV, et al. Randomized comparison of combination chemotherapy plus supportive care with supportive care alone in patients with metastatic colorectal cancer. BMJ. 1993;306:752-5.
2. Glimelius B, Hoffman K, Graf W., et al. Quality of life during chemotherapy in symp tomatic patients with advancd colorectal cancer. Cancer.1994;73:556-562
3. Stehlin JS, de Ipolyi PD, Greeff PJ, et al. Treatment of cancer of the liver. Annuals of Surgery.1998;208:23-35.
4. Elias D, Lasser PH, Montrucolli D, Bonvallot S, Spielmann M. Hepatectomy for liver metastasis from breast cancer. Eur J of Surg Oncol.1995;21:510-513.
5. Ingold JA ., Reed GS.,Kaplan HS., Bagshaw MA. Radiation hepatitis. AJR. 1965;93:200 -203.
6. Russel AH., Clyde C., Wasserman TH. Ac celerated hyperfractionated hepatic irradiation in the management of patients with liver metastases results of the RTOG dose escalating protocol. Int J Radiat Oncol Biol Phys. 1993;27-117-123.
7. Robertson JM. Lawrence TS, Dworzanin LM., et al. Treatment of primary hepatobiliary cancers with conformal radiation and regional chemotherapy. J Clin Oncol 1992;11 1286-93.
8. Pattaranutaporn P, Chansilpa Y, Ieumwananon thachai N, et al. Three-dimensional confor mal radiation therapy and periodic irradiation with deep inspiration breath-hold technique for hepatocellular carcinoma. J Med Asso Thai. 2001;84:1692-1699.
9. Mohiuddin M, Chen E, Ahmed N. Combined liver radiation and chemotherapy for palliation of hepatic metastases from colorectal cancer. J of Clin Oncol. 1996 ;14: 722-8
10. Ha CS, Kijewski PK, Langer MP. Gain in target dose from using computer controlled radiation therapy (CCRT) in the treatment of non small cell lung cancer. Int J Radiat Oncol Biol Phys 1993; 26:335-359.
11. Leibel SA. The biologic basis for conformal three-dimensional radiation therapy. Int J Radiat Oncol Biol Phys 1991;21:805-811.
12. Lichter AS. Three-dimensional conformal radiation therapy : A testable hypothesis. Int J Radiat Oncol Biol Phys 1991;21:853-855.
13. Fuks Z, Leibel SA, Wallner KE, et al. The effect of local control on metastatic dissemination in carcinoma of the prostate:Long term results in patients treated with I125 implantation. Int J Radiat Oncol Biol Phys 1991; 21:537-547.
14. Leibel SA, Scott CB, Mohiuddin M,et al. The effect of local-regional control on distant metastatic dissemination in carcinoma of head and neck : Results of an analysis from the RTOG head and neck database. Int J Radiat Oncol Biol Phys 1991;21: 805-811.