# CONCURRENT CHEMO-RADIOTHERAPY FOR LIVER METASTASIS FROM BREAST CANCER: TWO CASES REPORT

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## ABSTRACT

Two cases of multiple liver metastases from breast cancer, failed to the previous chemotherapy, were treated with concurrent chemo-radiotherapy. Thirty Grays of external irradiation was given to the whole liver in 3 weeks and 300 mg/m²BSA of carboplatin on day 1 and 750 mg/m²BSA of 5FU from day 1 to day 4 were also combinely given. After then, chemotherapy of the same regimen were repeated every four weeks. The tumor showed good response within 1-2 months after treatment. The metastatic areas in the liver were replaced with regenerating nodules in one case at one and a half year later. The patients could tolaterate the treatment very well without any complications, both clinicals and liver function test. Concurrent chemo-radiotherapy might be an alternative treatment for metatstatic breast cancer to the liver.

**Key Words :** Breast Cancer, Liver metastasis, Concurrent chemo-radiotherapy.

## INTRODUCTION

Forty-one per cent of the cancer patient will develope liver metastases during the course of their illness because of the high blood flow through its capillary bed. Especially in breast cancer patient, the evidence of liver metastases is as high as 64 per cent.(1-2) Multiple liver metastatic sites were found in 70-75 per cent. The average survival for the patients with clinically evidences are about 5 months.(3-5) Radiation therapy for liver metastases has been limited by the low radiation tolerance of the hepatocyte with a threshold dose of 25-30 Gys, dose related venous occlusion and parenchymal fibrosis.(6,7)

The application of chemotherapy for metastatic breast cancer has improved overall survival modestly. Nonetheless, in the good response group, it has effectively ameliorated many tumor related symptom, but also has increased treatment-related toxicity , often at the expense of life.(8)

Several investigators have attempted to use chemotherapy as a radiosensitizer in various organs and showed a promising result, not only in the squamous cell carcinoma but also adenocarcinoma and transitional cell carcinoma. Thus the concurrent chemo-radiation was used to provide benifit without a corresponding increased toxicity. Chemotherapy such as carboplatin and 5 FU have shown the good radiosensitizing activity and have also been investigated as a single agent for treatment of breast cancer with 25-30 per cent response.(9-10)

From the rational of concurrent chemo-radiation therapy , and from effectiveness of

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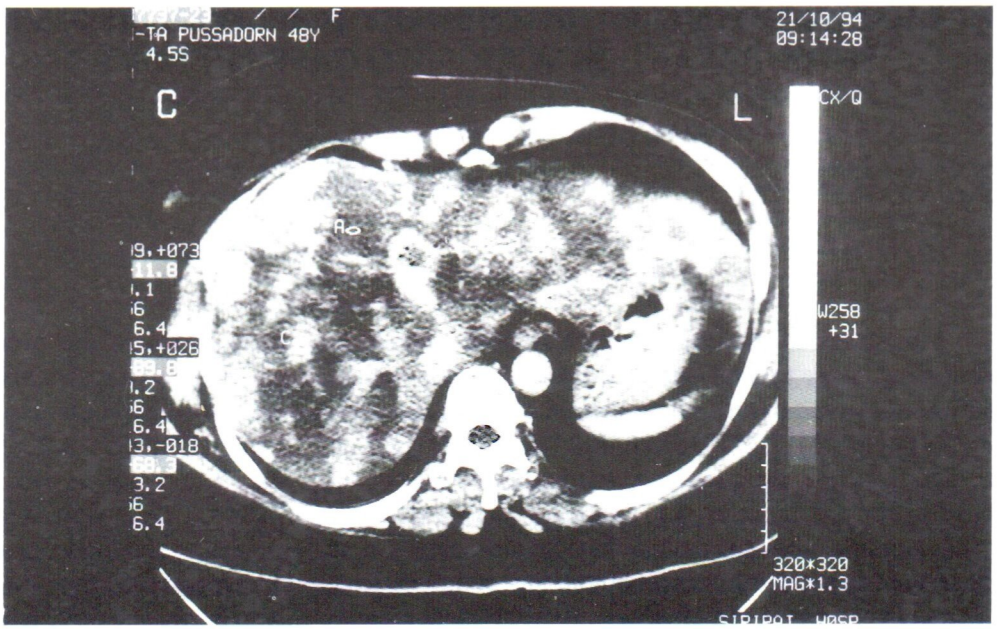


Fig.1 The CT scan showed multiple liver metastatsis in both lobes.

platinum compound and 5FU, we used carboplatin and 5FU as the chemotherapeutic agents in conjunction with 30 Gys of radiation to the whole liver. Two breast cancer patients with multiple liver metastases were treated.

**Case No. 1**

A known case of stage 4 breast cancer patient having a large 10x6 cm2 primary tumor mass with skin invasion was treated with 6 courses of chemotherapy (CMF) followed by modified radical mastectomy 4 years ago. The pathological report was invasive ductal carcinoma, moderate differentiation with negative estrogen and progesterone receptors. Postoperative radiation with the dose of 46 Gy was given to the chest wall. Three years later, she suffered from moderate to severe pain at right costal margin. Physical examination showed no abnormality detectable except enlarged liver about 4 cm. below right costal margin with moderate tenderness. CT scan showed massive metastasis in both lobes of liver as shown in figure 1.

The whole liver were irradiated daily with 2 Gy per fraction to a total dose of 30 Gy. The 300 mg/m$^2$ of carboplatin was given on day 1 and 700 mg/m$^2$ of 5FU per day were infused from day 1-4. After completion of radiation treatment, the chemotherapy was given intravenously every 28 days for 12 courses.Liver function test at the beginning and during chemotherapy were shown in the table 1 and CT scan were repeated at 1, 6 and 12 months after radiation respectively for evaluation of the response
and toxicity.

Table 1. Liver function test at the beginning and during treatment.

| | before treatment | 3rd month | 1 year |
|---|---|---|---|
| SGOT | 133 | 52 | 43 |
| SGPT | 67 | 51 | 44 |
| AP | 267 | 213 | 312 |

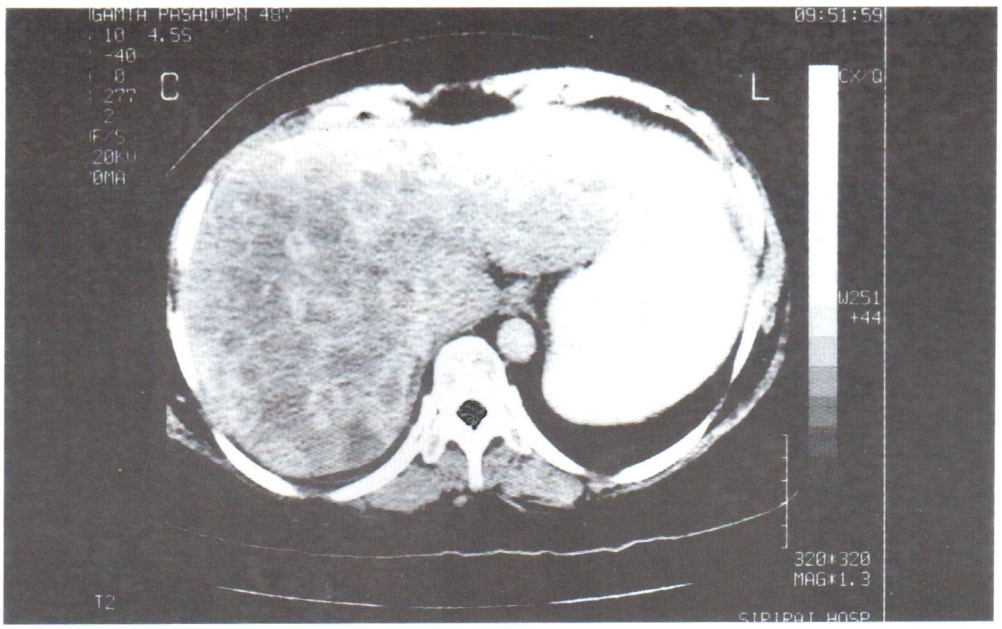


Fig.2 One months after completion of radiation, CT scan showed significant changes of the tumor.

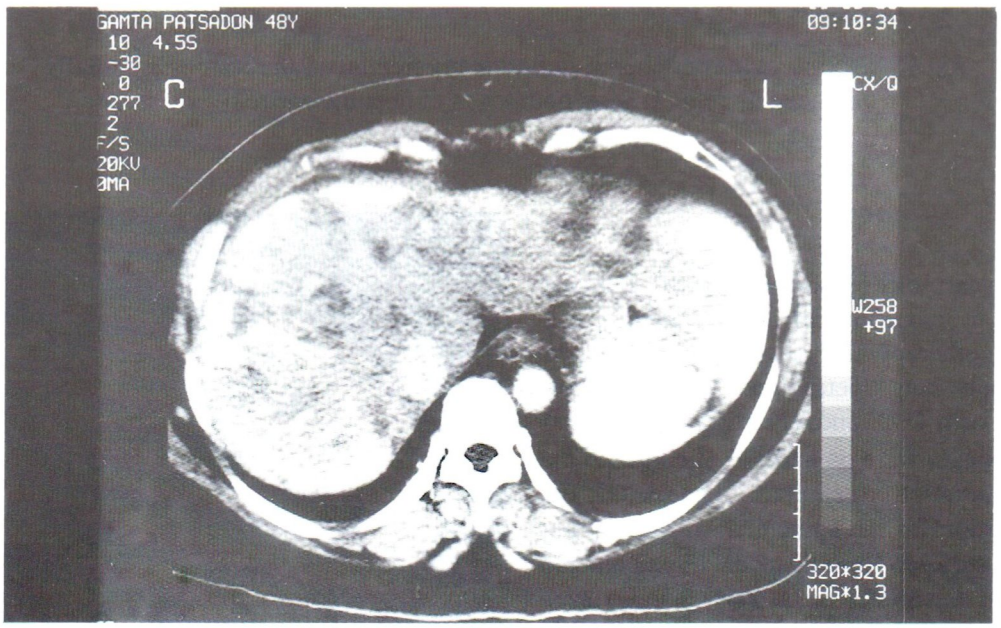


Fig.3 At 6 months after radiation treatment.

One months after completion of radiation, the liver showed more homogeneous than before irradiation and chemotherapy. The patient looked healthy. There was no sign of hepatic dysfunction. Chemotherapy was kept on.

At the 6th month of chemotherapy, CT scan showed significant changes of the liver. The size was decreased and the inhomogenicity was much improved.

At one year after treatment, the patients was very healthy. The liver function still showed a high level of alkaline phosphatase, but SGOT and SGPT were normal. CT scan revealed homogeneous liver with regenerating nodule, no definite space occupying lesion was seen. The last course of chemotherapy ,the twelfth course, were given.

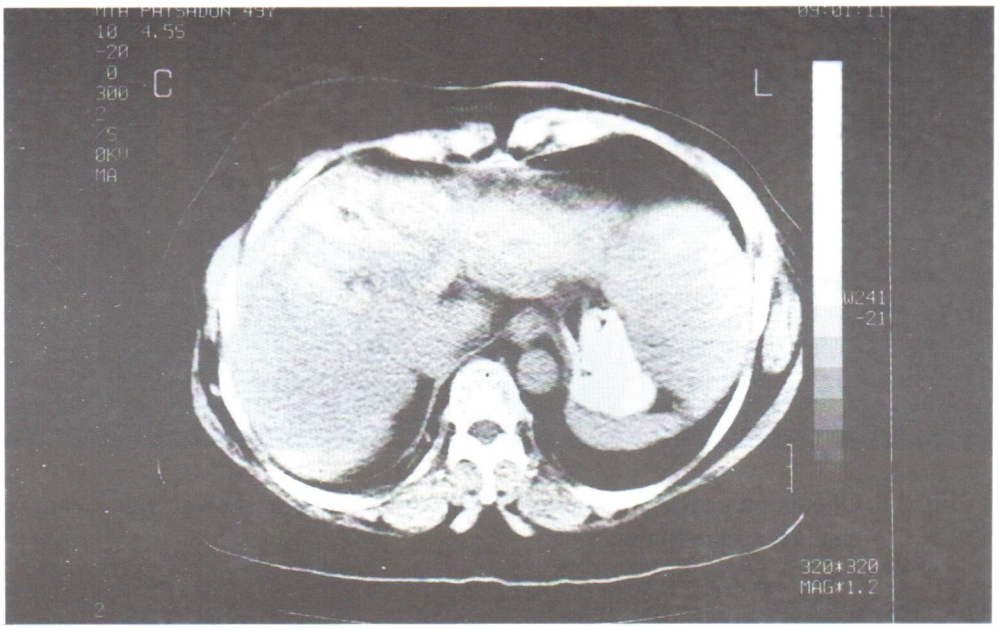


Fig.4 At one year after chemo-radiotherapy treatment, the lesions are totally replaced by regenerating nodules in almost the entire liver.

**Case No. 2**

A 48 years old female with stage 2 breast cancer treated by modified radical mastectomy and adjuvant chemotherapy 2 years ago, developed bone, brain and lung metastases. Multi-agents chemotherapy with CAF and Taxol were given and the tumor responses were on and off. She has got the brain bath radiation for brain metastases, and palliative radiation for the spine metastatsis. On her later visit, she suffered from dyspnea, bone pain and abdominal pain due to livermetastasis. The CT scan of the upper abdomen were shown to have multiple hypodensed areas in the liver as in Fig.5 and liver function test were shown in table 2.

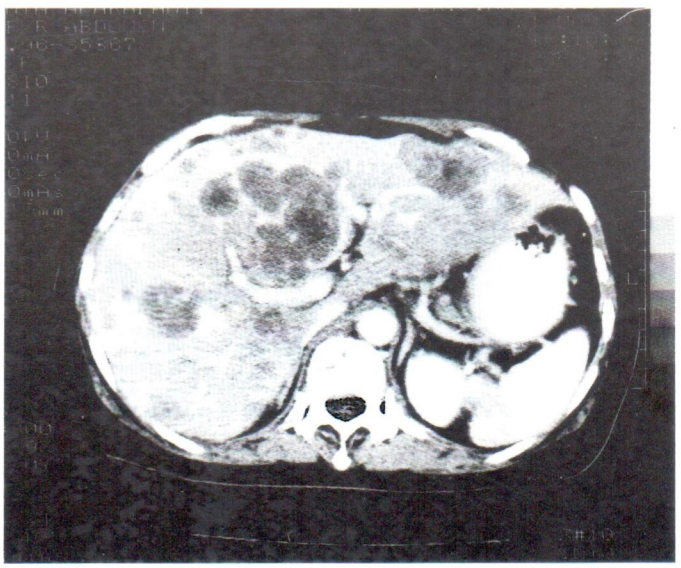

Fig. 5 CT scan showed multiple liver metastases occupied in both lobe of liver.

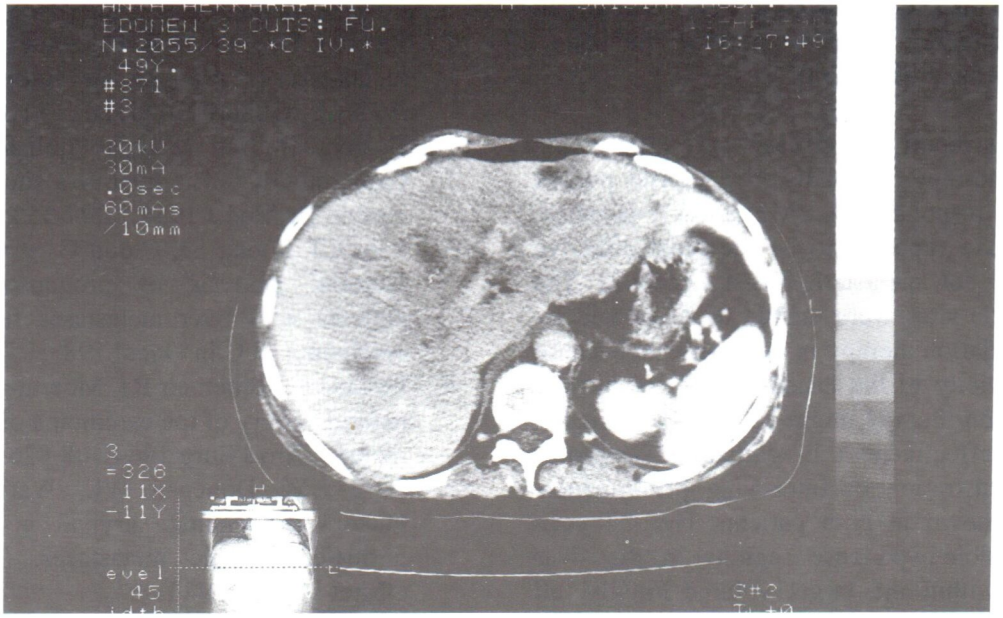


Fig 6. At the end of radiation treatment, the liver showed significant improvement of the lesion and the reduction in size of the liver.

She refused chemotherapy due to scarring of the previous toxicities, but she requested for the palliative treatment to relieve the discomfort from liver and lung symptoms. Concurrent chemo-radiation therapy was then offerred, base on the rationale of improving or enhancing each other with minimized toxicities. The treatment procedures were the same as in the patient No.1, with additional radiation lung bath to the right lung. After completion of radiation treatment, the discomfort at the right costal margin was relieved. CT scan of the upper abdomen revealed reduction in size of the liver with the improvement of metastatic lesions.

Table 2. Liver function test at the beginning and during treatment.

| | before treatment | 3 month after |
|---|---|---|
| SGOT | 365 | 97 |
| SGPT | 247 | 38 |
| AP | 595 | 408 |

## DISCUSSION

Extensive experience in the treatment of liver metastases has shown that the external radiation is effective in palliating symptom with 50-90 per cent relieving of the symptoms and 25 percent demonstrating of improving performance status. However, most of the disease will progress within a few months, resulting in a median survival of 3-6 months.11-13

Various schemes of radiation dose, techniques and combinationsof chemotherapy or radiosensitizer were studied . All are under the clinical investigations with comparable results. 14-18.

Recently, high-dose radiation therapy to the liver performed by using overlapping portals defined by a three-dimensional treatmentplanning system (conformal radiation therapy) is a new method for treatment of hepatic tumors. Meanwhile, the combination of the intraarterial hepatic chemo-therapy were also initiated.19-20

Anyhow, the cases of multiple sites of liver metastasis and failure to chemotherapy are still the

major problems. Concurrent chemo-radiation therapy were reported in several diseases that can reduce the radiation doses or provide the better result with the same radiation doses.

In this report, the disease were progressing after chemothe-rapy.Especially the second patient who failed to respond after CMF and 3 courses of Taxol that were reported to be the most effective chemotherapy for metastatic breast cancer.21 The liver metastatic sites were unable to be treated by conformal radiation therapy in both patients because of the multiplicity of the lesions. The concurrent chemo-radiation therapy might be the most suitable method. The effectiveness in palliating symptoms and the demonstration of improving performance status were shown in both patients. The CT scan showed reversible hypodense regions in the liver parenchyma within the target volume. Finally, all metastatic sites were replaced by the regenerating nodules. The liver fuction test did not show the hepatitis features. On the contrary, it showed an improvement of the liver functions in comparison with the ones prior to the treatment.

This report suggested that concurrent chemo-radiation therapy might be the alternative treatment procedure that can palliate the metastatic symptoms and prolong the survival in patients who response well to this scheme of treatment. The synergistic effect could provide a good response with minimizing the toxicity from each therapeutic modalities.

## CONCLUSION

1. Concurrent chemo-radiation therapy is an alternative treatment for liver metastasis from breast cancer.

2. Radiation dose of 30 Gy may be the optimal dose for whole liver irradiation with no acute and late complications.

3. Carboplatin and 5FU might be a good radiosensitizer and also a candidate for palliative chemotherapeutic agent for metastatic breast cancer.

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