

The Role of Porta Hepatis Irradiation in Relieving Malignant Obstructive Jaundice

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We have analysed 13 patients with malignant obstructive jaundice due to metastasis who were treated with local radiation therapy to the area of porta hepatis at the Radiation Therapy Department of Paik Hospital attached to the Inje University between 1984 and 1988. A good response was observed in 6 out of 7 evaluable patients receiving a total radiation dose ranging from 2600 to 5480 cGy in 2.6 to 6 weeks. A complete response was noted in 5 patients, a partial response in 1 patient, and no response in 1 patient. The overall median survival for 13 patients was 3 months. But two patients lived more than a year without recurrence of jaundice.

Moderate dose, localized field radiation therapy appears to be beneficial in relieving obstructive jaundice and gives a good symptomatic relief.

Key Words: Porta hepatis irradiation, Malignant obstructive jaundice

INTRODUCTION

The jaundice developed in cancer patients is usually an ominous sign. It frequently indicates the presence of diffuse parenchymal metastatic liver disease and /or extrinsic pressure in the major biliary system by metastatic lymph nodes in the porta hepatis (Table 1)¹⁾.

Obstructive jaundice is distressing because of: (1) frequent ascending cholangitis, fever and toxic effect of infection (2) toxic effect of retained bile and liver degradation products leading to hepatic coma (3) epigastric and right upper quadrant pain (4) pruritus and (5) skin discoloration²⁻⁵⁾.

Thus surgery (primary resection or palliative

bypass), radiologic intervention (percutaneous transhepatic biliary drainage, endoscopic biliary drainage or endoprosthesis), radiation therapy or chemotherapy are needed to relieve the distressing conditions. Among others, radiation therapy is frequently used as an alternative measure to surgical bypass in relieving malignant obstructive jaundice.

In order to illustrate the value of radiation therapy using the standard porta hepatis field by Dr. Hopfan⁶⁾, we would like to report on 13 patients with malignant obstructive jaundice due to metastasis in porta hepatis who were treated at the Radiation Therapy Department of Paik Hospital attached to the Inje University between 1984 and 1988.

METHOD AND MATERIALS

We have analysed 13 patients who developed malignant obstructive jaundice with metastatic diseases in porta hepatis proved by computed tomography scan or ultra sonography and were treated with local radiation therapy to the area of porta hepatis. The characteristics of the patients and their diseases are summarized in Table 2.

1. Definition of Response

We quoted from Kopelson's definition of response in radiation therapy for the patient with obstructive malignant jaundice secondary to biliary tract metastasis of primary breast cancer.

A complete response was defined as a fall of bilirubin to normal level. A partial response was defined as a fall of bilirubin (but not to normal

Table 1. Cause of Biliary Obstruction

| | No. of Patients |
|---------------------------------------|-----------------|
| Pancreatic Carcinoma | 15 (36) |
| Benign Stricture | 7 (16) |
| Obstructing Common Bile Duct Stones | 6 (14) |
| Metastatic Carcinoma to Porta Hepatis | 6 (14) |
| Cholangiocarcinoma | 4 (9) |
| Recent Operative Trauma | 3 (7) |
| Carcinoma of Gall Bladder | 1 (2) |
| Duodenal Diverticulum | 1 (2) |
| Total | 43 (100%) |

Modified from Pollack, T.W.¹⁾

Table 2. Patients Characteristics

| Patient No. | Sex/Age | Primary Site | RT. Dose (cGy) | F.S. (cm) | T.B. (mg%) Initial/Last | Response | Duration of Survival (mon) |
|-------------|---------|--------------|----------------|-----------|-------------------------|----------|----------------------------|
| 1 | F/57 | S | 5480 | 9 X 10 | 11.8/ 0.8 | CR | 10.5 |
| 2 | M/53 | S | 700 | 12 X 12 | 14.4/ ? | | 0.2 |
| 3 | M/64 | S | 4180 | 10 X 10 | 13.5/ 1.0 | CR | 4.0 |
| 4 | M/52 | S | 3800 | 10 X 10 | 13.7/ 0.4 | CR | 12.0 |
| 5 | F/53 | S | 3050 | 10 X 10 | 7.5/24.8 | NR | 4.0 |
| 6 | M/62 | S | 1000 | 10 X 10 | 13.0/ ? | | 3.0 |
| 7 | M/50 | S | 2600 | 13 X 18 | 7.8/ 5.9 | PR | 2.0 |
| 8 | M/44 | S | 3800 | 15 X 22 | 2.4/ 0.4 | CR | 5.0 |
| 9 | F/63 | S | 300 | 10 X 10 | 21.6/ ? | | 0.1 |
| 10 | F/35 | S | 5040 | 10 X 10 | 8.9/ 0.4 | CR | 12.0 |
| 11 | M/68 | G B | 1500 | 13 X 13 | 3.4/ ? | | 1.0 |
| 12 | M/68 | G B | 4400 | 14 X 10 | 2.4/ ? | | 1.0 |
| 13 | F/69 | P | 250 | 10 X 10 | 27.5/ ? | | 2.0 |

S : Stomach, GB : Gall Bladder, P : Pancreas, RT : Radiation Therapy, F.S. : Field Size, T.B. : Total Bilirubin, CR : Complete Response, PR : Partial Response, NR : No Response

level), or a decrease in pain, pruritus, or mass shrinkage. No response was defined as no change in icterus, pruritus, mass size, pain or deterioration. Length of response was analysed from the date of beginning of therapy. Survival data were calculated from the date of diagnosis of biliary tract metastasis via the actuarial method.

2. Radiotherapeutic Technique

All patients were treated with a 4 MeV linear accelerator. Radiation ports were designed to cover the area of the porta hepatis. We used the standard porta hepatis field illustrated by Dr. Hopfan. Sometimes radiation field, however, were modified by the result of computed tomography scan or ultrasonography. Field sizes ranged from 9×10 cm to 15×22 cm (standard field size is 10×10 cm). In Fig. 1, the construction of porta hepatic field of irradiation by Dr. Hopfan is shown. In Fig. 2, the simulation film of standard porta hepatis field used in our hospital is shown. All patients received a total radiation doses ranging from 250 to 5480 cGy. Seven evaluable patients, however, received a total radiation doses ranging from 2600 to 5480 cGy.

RESULTS

Informations of diagnosis, therapy and results in each of our 13 patients were presented in Table 2. The evaluable patients consisted of 7 patients who checked a total bilirubin level after completion of

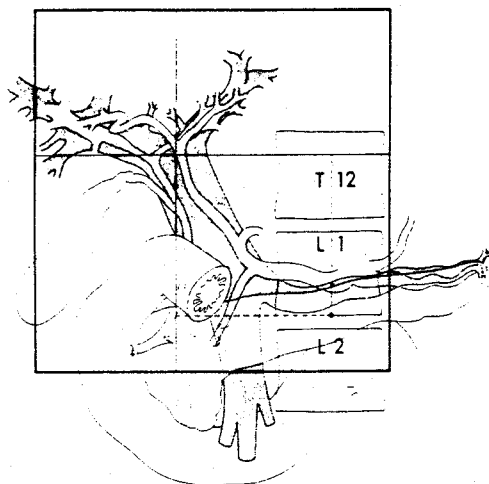


Fig. 1. Relationships in the porta hepatis region. The construction of the porta hepatis field of irradiation is shown. (Modified from Hopfan. S.)⁶⁾

radiation therapy. A good response was observed in 6 out of 7 evaluable patients receiving a total radiation doses ranging from 2600 to 5480 cGy in 2.6 to 6 weeks. A complete response was noted in 5 patients, a partial response in 1 patient and no response in 1 patient. The change of bilirubin levels in entire group before and after radiation therapy was shown in Fig. 3. The average total bilirubin value decreased from 9.47 mg% before to 4.81

mg% after radiation therapy. The time-course change in bilirubin level in 7 evaluable patients after the beginning of radiation therapy was shown in Fig. 4. Each patient did not have a level drawn at each time interval. In most of the patients, total bilirubin level was transiently increased till delivery of about 2000 cGy, and then was decreased. The patients survival following radiation therapy for the entire

group of 13 patients was shown in Fig. 5, with the median survival being 3 months post treatment (range 0.1~12 months). The 3 stomach cancer patients with good general conditions received sufficient irradiation with doses ranging from 3800 ~5480 cGy. Two out of the 3 patients lived more than a year without recurrence of jaundice. But 2 gallbladder cancer and 1 pancreatic cancer patient did not receive the planned dose of irradiation and they all died within 2 months. The patients who had objective response to radiation therapy survived longer than no responders (median survival 10.5 months for responders). Actuarial survival for 13 patients was shown in Fig. 6. Three months actuarial survival was 46%.

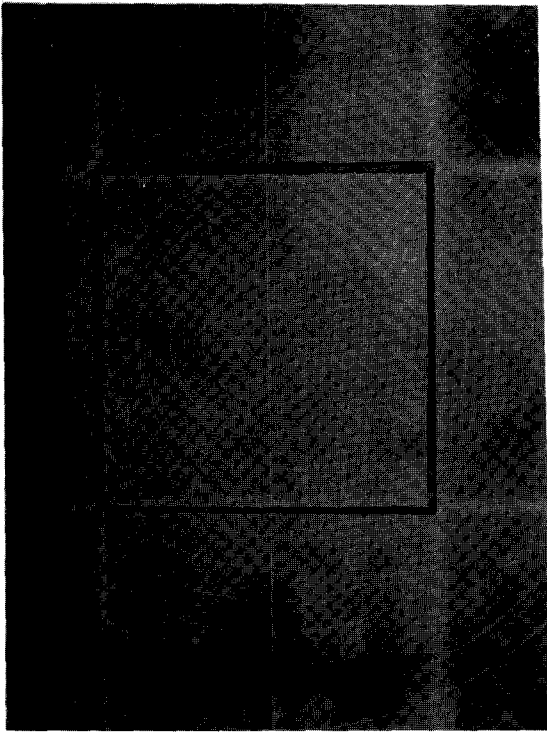


Fig. 2. The simulation film of standard porta hepatis port.

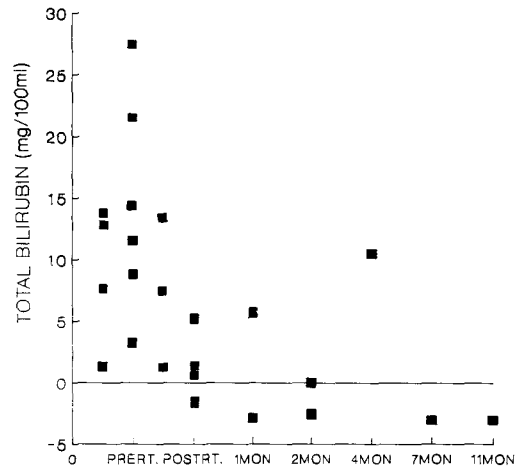


Fig. 3. Time-course change in bilirubin levels in entire gorup after radiation therapy.

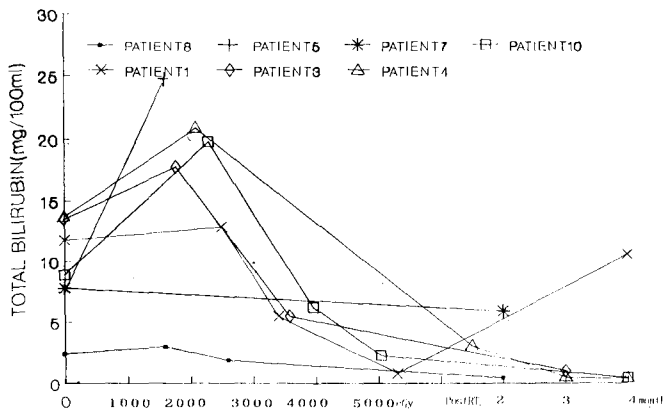


Fig. 4. Time course change in bilirubin levels in the 7 evaluable patients.

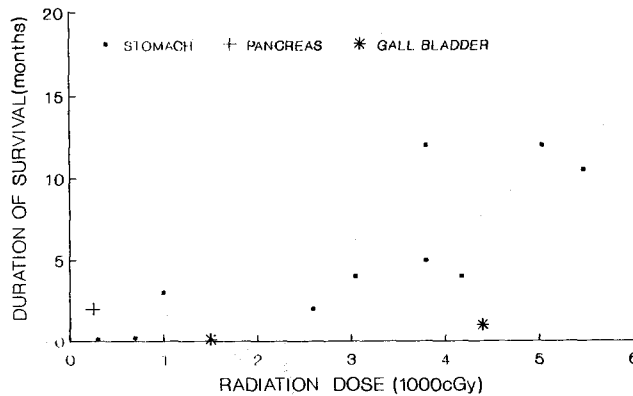


Fig. 5. Duration of survival for each different radiation doses.

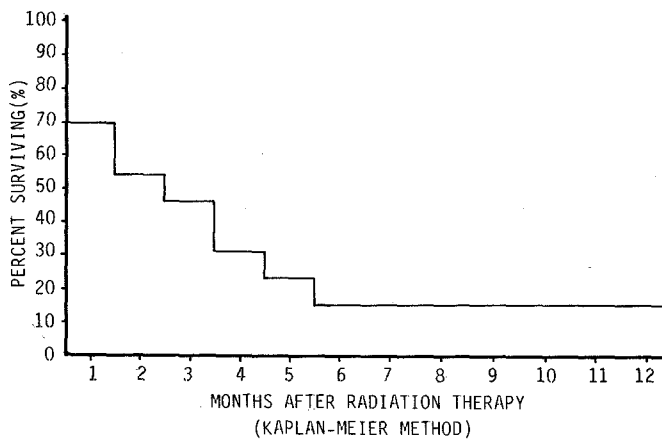


Fig. 6. Observed survival for 13 patients after radiation therapy.

DISCUSSION

In the patient of malignant obstructive jaundice, treatment aim is not only to prolong life but also to improve the quality of life.

Recent studies show overall 5 year survival rate of 6~7% in the patients with malignant obstructive jaundice secondary to gallbladder cancer, less than 5% in the patients with malignant obstructive jaundice secondary to extra hepatic bile duct cancers and especially worse in the patients with malignant obstructive jaundice secondary to metastatic disease in *prota hepatis*. If the patients with obstructive jaundice are not treated, duration of survival is about less than 2 months^{7,8)}.

The surgical (bypass surgery) and non-surgical (percutaneous biliary drainage, endoscopic drainage, endoprosthesis or radiation therapy)

methods may apply in treatment of malignant obstructive jaundice. The bypass surgery may result in higher postoperative mortality (15~30%) and is scarcely applied to metastatic lesion after primary cancer surgery. Successful palliation in 80~90% of the patients with malignant obstructive jaundice is observed in use of percutaneous transhepatic biliary drainage, endoscopic biliary drainage and endoprosthesis.

The patients with pancreatic cancer or diffuse intra abdominal metastasis, however, rarely survived regardless of the types of drainage¹⁰⁾. In a certain cases using these methods, serum concentration of bilirubin decreased during the 3 weeks drainage period but not to normal value and more slowly than would be expected from normal hepatic bilirubin elimination in spite of adequately drained bile volume. The decrease was most pronounced during the first week of drainage.

Thus, the methods are more useful in a reduction of postoperative mortality¹¹⁻¹³.

5~10% of severe acute (hemorrhage, sepsis, biliary peritonitis etc.) and 40~50% of delayed complication (usually relate to catheter dysfunction) may occur in using these methods. Percutaneous transhepatic biliary drainage is not used in massive metastatic disease of liver with marked distortion of intrahepatic bile duct. Disadvantages of endoscopic approach are poor suitability for high obstruction and scarcity of skilled endoscopists. Endoprosthesis insertion is technically more complex and long term patency rate is yet to be established. Thus, there has been particular reawakening of interest in local irradiation of the portal hepatis.

There has been little attention devoted to potential value of irradiation for malignant obstructive jaundice due to metastasis in porta hepatis.

Hudgins and Meoz treated 8 patients with obstructive jaundice secondary to metastatic cancer with palliative radiation therapy². The doses delivered ranged from 1500 to 5000 cGy given through small (average 8×10 cm) opposed field. In three of the patients, the jaundice had disappeared by completion of radiation therapy. In the remaining five, improvement occurred within 4 weeks following completion of therapy. All of these patients experienced improvement from jaundice, the symptom free interval varying from 3 weeks to 11 months. All patients tolerated the radiation therapy well and no adverse side effects were recorded during therapy.

Kopelson treated 49 patients with obstructive malignant jaundice secondary to biliary tract metastasis of primary breast cancer with palliative radiation therapy⁷. Overall radiation therapy produced a response in 6 of 9 patients. Field size ranged from 10×10 cm to 21×23 cm. In the patients who were treated with larger fields, field size often was reduced after 2200~2500 cGy. Dose ranged from 999 to 4960 cGy. The complete response after irradiation occurred in 3 of 3 patients who were treated with relatively high dose (TDF>40), small field size (<225 m) compared to 1 of 2 patients who were treated with low dose (TDF≤40), small field size. For patients who were treated with large field size (>225 m), complete response occurred in 1/1 patient treated with high TDF (>40) versus 1/6 treated with low TDF (≤40). The bilirubin fell to normal by the end of therapy in only 1 of 6 complete responders to irradiation but the bilirubin fell to normal by 2 months after completion of therapy in

the remaining 5 patients.

Median survival of the irradiated group (6 months) was better than the non irradiated group (3.3 months). Chu suggested that 3500 cGy in 3~4 weeks could effectively treat metastatic porta hepatis nodal obstruction from breast cancer¹⁴. Meyer et al, described 3 patients with metastasis from carcinoma of the stomach, breast, and rectosigmoid who irradiated on a 4 MeV linear accelerator¹⁵. Two of 3 patients received 3000 cGy via opposed 8×8 cm portals coupled with 5-fluorouracil. There was marked improvement of obstructive jaundice which was documented clinically by bilirubin level. Warshaw and Welch described 2 patients with colon cancers with definitive radiation therapy alone (3750 and 4000 cGy) and who survived 5 and 14 months after irradiation¹⁶. Papachristou and Fortner described 7 patients with metastasis from carcinoma of stomach who received radiation therapy. There was no radiation response in 2 of the 7 patients in whom palliative surgery was precluded. However, bilirubin levels declined in the 5 patients who were treated by radiation therapy plus surgical decompression. In our study, jaundice caused by malignant metastatic diseases in porta hepatis were treated by localized standard porta hepatic field (10×10 cm) with moderate dose (ranged from 2600 to 5480 cGy) in 7 evaluable patients.

A complete response was observed in 5 patients. Median survival of all patients and 7 evaluable patients were 3 months and 10.5 months. Two patients lived more than a year without recurrence of jaundice. Three months actuarial survival was 46 percents. Although average total bilirubin value decreased from 9.37 mg% to 4.81 mg% after radiation therapy, a normal total bilirubin level was observed in the 5 complete responders.

Bilirubin level after radiation therapy was changed with time. Each patient did not have a level drawn at each time interval. Beginning radiation therapy, total bilirubin level was transiently increased till delivery of about 2000 cGy, and then was decreased. This result appears to be related to the transient edema at the biliary tract in early period of radiation therapy. It is not considered as radioresistance. Most of responders received sufficient dose with standard field (2600~5480 cGy, 10×10 cm). Thus, these patients may yield improved duration of survival.

In summary, it appears to us that moderate dose, localized field (standard porta hepatis field) radiation therapy plays a definite role in palliative

treatment of malignant obstructive jaundice due to metastasis in porta hepatis. In order to improve the response rate and prolong the duration of jaundice free in the patients with malignant obstructive jaundice, combination of radiation therapy and systemic chemotherapy may need to be considered.

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== 국문초록 ==

악성 폐쇄성 황달 환자에 있어서 간문에 대한 방사선치료의 역할

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1984년부터 1988년까지 인제대학교 의과대학 치료방사선과에서 전이성 암에 의해 발생한 악성 폐쇄성 황달환자 13명을 대상으로 간문을 포함하는 국소방사선치료를 시행하였다.

총 3명의 환자중 추적가능한 7명은 표준 방사선 조사야에 2.6주에서 6주 동안에 걸쳐 2600~5480 cGy의 방사선 조사를 받았으며 이중 5명은 완전관해, 1명은 부분 관해를 보여주었다. 전체 13명의 환자에서의 평균 생존기간은 3개월 이었으며 7명의 추적가능한 환자에서는 10.5개월이었다. 완전 관해를 보인 환자 5명중 2명은 황달의 재발없이 1년 이상의 생존기간을 보여주었다. 따라서 간문의 전이성 암으로 인해 발생한 악성 폐쇄성 황달 환자에 있어서 간문을 포함하는 조사야의 국소적 방사선 치료는 황달 해소와 증상완화에 많은 도움을 줄 수 있는 것으로 생각된다.