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CHOLANGIOCARCINOMA

A place for brachytherapy

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Primary malignant tumors of the extrahepatic duct are relatively rare (WALTERS & OLSON 1935, LAM 1940, ARIEL & PACK 1960, VAN HEERDEN et coll. 1967, WHELTON et coll. 1969, ACKERMAN & DEL REGATO 1970). Because of the proximity of the extrahepatic duct to the major organs and the fact that this area is so richly supplied by blood vessels and lymphatics, malignancies of the extrahepatic duct tend to spread quickly to neighboring organs and metastasize early to the regional lymph nodes (LAM, VAN HEERDEN et coll., WHELTON et coll., ACKERMAN & DEL RAGATO). Survival rates are distressingly poor for this tumor. Recent investigations show an overall 5-year survival rate of less than 5 per cent in extrahepatic duct carcinoma (ACKERMAN & DEL REGATO, TERBLANCHE 1976, PILEPICH & LAMBERT 1978).

Surgery has been recognized as the only form of treatment either for curative or palliative intent possibly due to the nature and clinical behavior of the tumor (TERBLANCHE). Various types of bypass procedures have been documented in the literature primarily designed for palliative purpose with little hope for cure (TERBLANCHE). Radiation on the other hand, has been regarded as having no role in the management of these tumors and to our knowledge, this has never been substantiated (GREEN et coll. 1973, HUDGINS & MEOZ 1976, KOPELSON et coll. 1977).

The cell type of the tumor and its location made the oncologist reluctant to manage this disease by irradiation either for palliation or cure.

Recently, there has been a renewed interest in radiation treatment of carcinoma of the extrahepatic biliary system because of some successes that have been made by using external beam therapy or intraoperative therapy (GREEN et coll., HUDGINS & MEOZ, KOPELSON et coll., PILEPICH & LAMBERT, TODOROKI et coll. 1980). These successes have stimulated many radiation oncologists and surgeons to take a serious look at the possibility and feasibility of applying external irradiation to this carcinoma preoperatively or postoperatively or alone.

The following is a case report of cholangiocarcinoma of the common hepatic duct treated successfully by drain catheter choledochostomy, brachytherapy and subsequently hepaticojejunostomy.

Case report

A 46-year-old well developed, somewhat obese man, was admitted with complaints of jaundice and diarrhea of 4 days duration. Previous medical history indicated that he has been treated for peptic ulcer for several years mainly by medications. His total bilirubin at the time of admission was 8.7 mg/100 ml and alkaline phosphatase 121.0 units. A $^{99}Tc^{m}$ sulphur colloid liver and spleen scan was normal. Upper gastrointestinal examination done one day after admission was reported to be consistent with chronic duodenal ulcer disease.

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Upper abdominal ultrasound showed the liver to be normal in size but there was suggestion of slight dilatation of the intrahepatic biliary ducts. Diagnosis of extrahepatic biliary duct obstruction was suggested and he was referred to University of Maryland Hospital for further management. A repeat total bilirubin, two weeks later, was 12.3 mg/100 ml.

Two and a half weeks after initial symptoms, an abdominal exploration was performed. There was a tumor at the common hepatic duct just below the bifurcation of the right and left hepatic ducts. The tumor appeared to encircle the common hepatic duct and it measured 1.5 cm in diameter with no spreading beyond the common hepatic duct. Biopsy of the tumor showed adenocarcinoma. The regional lymph nodes were negative for tumor. Because of the obstruction of the common bile duct a catheter was inserted with the tip at the left hepatic duct to drain the excessive bile. Retrograde cholangiography was performed to demonstrate the tumor through the catheter (Fig. 1).

One month after the exploratory laparotomy, the patient was admitted for radiation therapy.

It was decided to use ^{192}Ir inserted retrogradely through the drainage catheter and positioned at the tumor site with the aid of a localizer (Fig. 2). A total dose of 30 Gy calculated at 1.0 cm around the source was delivered in 72 hours.

Two and a half weeks after the first iridium therapy, a second ^{192}Ir treatment was given in the same manner as before, delivering a dose of 30 Gy in 72 hours with the aid of the localizer (Fig. 2).

One month after the completion of iridium therapy, evaluation of the patient showed some improvement of his jaundice but never completely cleared.

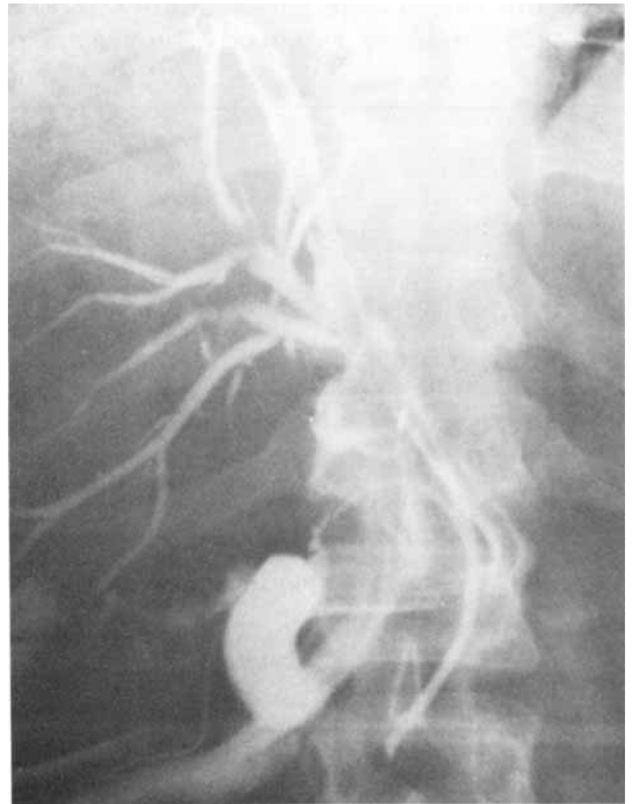

Fig. 1. Retrograde cholangiography. Tumor of the common hepatic duct (→).

Dosimetric analysis

Fig. 3 shows the composite dose (Gy) distribution from two implant applications of ^{192}Ir seeds. A single nylon ribbon containing 12 seeds, each of 47 MBq activity and a separation of 4 mm between seeds was implanted twice through an indwelling catheter. The duration of each implant was 72 hours and the time interval between the 2 applications was 18 days.

The elliptic distribution profile shown is typical of a single ribbon (or line) source. A total of 30×2 Gy was specified as the tumorcidal dose; the profile of the prescription dose was elliptic in shape with a minor axis of 2.0 cm and a major axis of 4.8 cm. The expected rapidity of dose fall-off is observed by noting that the tumorcidal dose is 50 and 25 per cent, respectively, at 0.6 cm and 1.5 cm away from the treatment volume measured along the minor axis.

The placement of the indwelling catheter in the

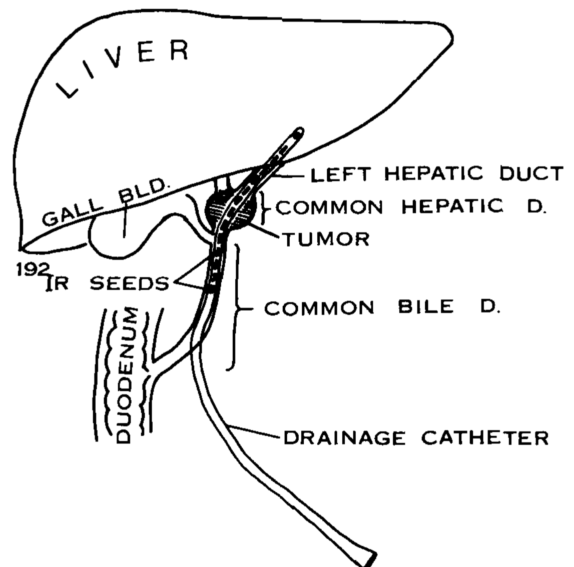

Fig. 2. Anatomic location of the tumor in the present case and the relationship with liver, gall bladder and common bile duct. A ribbon of ^{192}Ir seeds was inserted retrogradely through a drainage catheter and its position was controlled by a simulator.

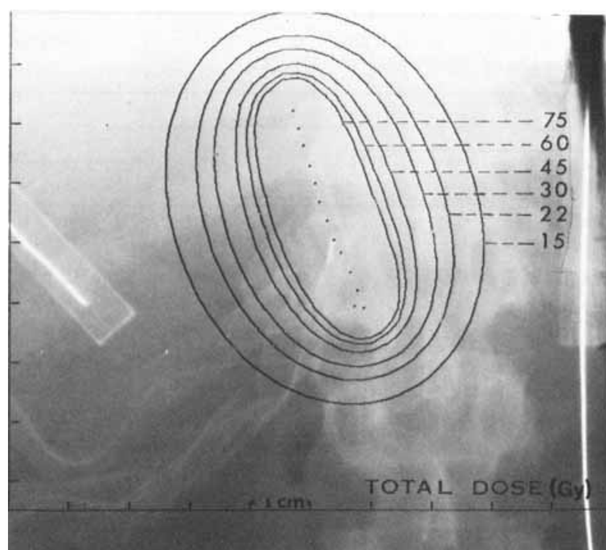

Fig. 3. A.p. view. Composite dose distribution from 2 implant applications of ^{192}Ir seeds. A total of 12 seeds, each with 47 MBq (0.71 mg radium equivalent) and seed separation of 4 mm was maintained for 72 h for each implant. The 60 Gy isodose line was chosen for the treatment.

common bile duct at surgery greatly facilitated the ease and speed with which the implant was done; the high localized dose and rapid fall-off make this application especially suited to cases such as this.

Two months after the completion of the treatment, he was re-explored to: (1) examine the response of the tumor to irradiation and possibly resection of the residual tumor, and (2) do a by-pass procedure if necessary to decompress the liver.

Exploratory laparotomy failed to show any evidence of tumor either by palpation or by visual inspection. Marked fibrosis around the area of the common hepatic duct was encountered. Biopsy of the tissue surrounding the common bile and regional lymph nodes showed marked fibrosis and some tumor cells with pyknotic nuclei.

Six months after the completion of the treatment, the patient's general condition returned to normal with no jaundice observed. His bilirubin was back to normal.

Three years after the treatment, his bilirubin was normal as well as his general condition.

Discussion

The present case serves as an ideal case to illustrate that a localized common bile duct carcinoma can be successfully treated by brachytherapy using drainage catheter as a path to guide and position the ^{192}Ir ribbon following its insertion retrogradely. The total dosage delivered by this innovative technique was 60 Gy for 2 applications and obviously sufficient to destroy all tumor cells with minimal untoward effect. It was our impression and that of others that this type of carcinoma is relatively sensitive to radiation as shown by lack of gross tumor seen in the area of the common bile duct and its vicinity following the re-exploration of the patient 2 months after the completion of brachytherapy. His clinical course also supported the impression and at the present time the patient is doing quite well, more than 3 years after the treatment with no evidence of recurrence of his tumor.

The placement of drainage catheter to decompress the obstruction at the common hepatic duct through exploratory laparotomy is a necessity not only to determine the extent of the tumor but also to mark the area to be irradiated. Re-exploration 2 months after irradiation confirmed our belief in that a tumor in the common hepatic duct in a highly selected case such as this one can be treated by appropriate intracatheter irradiation by ^{192}Ir provided that the tumor volume is small enough and there is no spread beyond the common hepatic duct. The case presentation should serve as a stimulant to pursue this type of management further. In the event that the tumor has spread beyond the common bile duct (CDB) or the common hepatic duct (CHD), intracatheter irradiation could be used in combination with external beam therapy to achieve a good palliation as demonstrated in several reports (HERSKOVIC et coll. 1981, CHITWOOD et coll. 1982, CONROY et coll. 1982).

Review of the literature

External irradiation for carcinoma of the common bile duct. Most of the literature (Table) regarding external beam irradiation dealt primarily with palliative radiation therapy. Because of low radiation tolerance of the surrounding structure around the CBD and porta hepatis, most radiotherapists in the past used a moderate dose of external beam therapy to obtain relatively short-term results. GREEN et coll. and HUDGINS & MEOZ gave the tumor dose anywhere from 20 Gy/2 weeks to 50 Gy/5 weeks to achieve a good palliation such as decreasing bilirubin level, jaundice free status or minimizing pain with almost complete success. KOPELSON et coll.

Table

Carcinoma of the extrahepatic duct. Review of the literature

Authors	No. of cases	Site*	Method of treatment		Outcome
			Surgery	Irradiation	
External therapy					
GREEN et coll. (1973)	4	CBD	Biopsy	30 Gy/3 weeks	1) Bilirubin drop from 15 to 1.2 in 5 months
			Biopsy and T-tube drainage	20 Gy/2 weeks	2) Bilirubin drop from 29 to 2.9, survived 12 months
			Biopsy and drainage	50 Gy/5 weeks	3) Bilirubin drop from 22 to 1.9, died after 7 months
			Biopsy	53 Gy/5 ½ weeks	4) Bilirubin drop from 30 to 1.0, died after 10 months
HUDGINS & MEOZ (1976)	3	CBD	Not specified	Palliation 50 Gy/32 days	1) Improved, jaundice free interval 6 months
				32.5 Gy/59 days	2) Improved, jaundice free interval 6 months
				49.5 Gy/43 days	3) Improved, jaundice free interval 1 month
KOPELSON et coll. (1977)	8**	CBD	T-tube drainage and biopsy	^{60}Co, 4 MeV, rtg rays, 22.5 MV. Dose range 38–70 Gy/32–52 days (50–60 Gy most)	1) Palliation obtained in 7/8 (decreased pain, pruritis, mass) 2) Total bilirubin, reduction in 5/5 (3 not recorded)
PILEPICH & LAMBERT (1978)	5	CBD	T-tube drainage in 4, incomplete resection in 1	2 cases, radical treatment 60 Gy/30 fractions	NED 6 and 26 months, duct open
				2 cases, palliation treatment, 40 and 43 Gy/20 and 21 fractions	Palliation achieved, jaundice relieved, died after 3 and 5 months
				1 case after surgery, 44 Gy/22 fractions	Died of the disease after 10 months
Brachytherapy					
WALTERS & OLSON (1935)	1	CBD, bifurcation	Incomplete resection, T-tube drainage	Ra needles, 10 mg, placed in duct, 14 h, total dose 11.55 Gy/14 h	Decreased jaundice, survived 2½ months, died of the disease
HERSKOVIC et coll. (1981)	10	Bile duct	Percutaneous transhepatic cholangiography and placement of indwelling catheter	6 cases, 50 Gy was given for palliation by ^{192}Ir seeds/ 1–2 days	
				4 cases treated with curative intent, 50 Gy given by ^{192}Ir seeds/ 1–2 days plus 50 Gy external beam therapy with 15 MV rtg rays, small field	Local control achieved in 1, too short follow-up
CONROY et coll. (1982)	5	CBD obstruction due to carcinoma of lung 2, pancreas 2, stomach 1	Percutaneous transhepatic cholangiography and placement of biliary drainage catheter	Ra needles inserted at site of obstruction and left in place for 72 h, total dose around duct 200 Gy	Palliative response achieved in all 5 patients with level of bilirubin down to normal value

Authors	No. of cases	Site*	Method of treatment		Outcome
			Surgery	Irradiation	
Present report	1	CHD	Explorative laparotomy, drainage catheter, choledochostomy plus hepaticojejunostomy	Insertion of ^{192}Ir through drainage catheter delivering total dose of 60 Gy (72 h treatment, twice)	Alive NED 3 years after completion of treatment
Intraoperative therapy					
TODOROKI et coll. (1980)	1	CHD	Cholecystectomy, ext. bile drainage	Intraoperative irradiation, 15 MeV 30 Gy/10–20 min	Survived 8 months, died of the disease, palliation achieved, bilirubin drop from 28 to 2.6
	1	CHD	Cholecystectomy, ext. bile drainage	Intraoperative irradiation, 11 MeV 30 Gy/10–20 min	Survived 5 months, died of the disease, palliation, bilirubin drop from 27.2 to 10.4
	1	L and R hepatic duct	Cholecystectomy, gastrectomy, ext. bile drainage	Intraoperative irradiation, 18 MeV 30 Gy/10–20 min	Survived 33 days, decreased gastrointestinal bleeding and bilirubin
	1	L and R hepatic duct	Cholecystectomy, gastrectomy, ext. bile drainage	Intraoperative irradiation, 18 MeV 30 Gy/10–20 min	Survived 18 months, recurrence with metastasis

* CBD = common bile duct, CHD = common hepatic bile duct.
** Three cases also received 5-fluorouracil.

reported the same result in conjunction with T-tube bile drainage. PILEPICH & LAMBERT were the first group to give a higher dose with an attempt to achieve a long-term palliation and a possible cure in cases whose disease were incompletely resected. The total doses of radiation was 60 Gy/6 weeks. They achieved excellent palliation in the majority of cases treated and 2 cases were reported to be free of disease in 6 and 26 months after completion of the treatment.

Important information can be identified from the experiences of PILEPICH & LAMBERT and others: (1) CBD tumors are relatively sensitive to irradiation. (2) The patients can tolerate the radiation treatment to the porta hepatis region very well with minimal untoward effect. (3) Decreased jaundice and bilirubin level are evidenced in almost all cases treated. (4) It is possible to achieve cure from a highly selected group of patients whose diseases have been debulked by surgery. Palliation by external beam therapy can be achieved with a moderate dose of radiation.

Brachytherapy for carcinoma of the common bile duct. From extensive literature search (Table) it was clear that there were limited experiences regarding brachytherapy for extrahepatic duct carcinoma probably due to dismal prognosis of the disease, technical difficulty and lack of interest. Before 1981, there was only one report by WALTERS & OLSON who placed a 10 mg radium needle at the tumor of bifurcation of CBD for a duration of 14 hours following an incomplete resection of the tumor and T-tube drainage. Decreased jaundice was observed and the patient survived for 2½ months. It was obvious that the dose delivered by radium therapy in this fashion was too low (11.55 Gy) to achieve any long-term palliation.

HERSKOVIC et coll. and CHITWOOD et coll. reported their experiences using ^{192}Ir seeds treating CBD tumors through percutaneous transhepatic cholangiography and placements of indwelling catheter. Six cases were treated with a dose of 50 Gy and achieved mainly palliation. Four cases were treated by brachytherapy with 50 Gy in 1 to 2 days and followed by 50 Gy of external irradiation (16 MV roentgen rays, small field). They obtained local control in one case but the follow-up was too short to substantiate further comments. It was obvious that

selection of the cases with early disease for this type of treatment is essential for the success. For the advanced cases with CBD obstruction, this technique appeared to be superior than surgical by-pass because of the less invasive procedures with lower morbidity and mortality.

This technique of treating carcinoma involving the CBD by placing radioactive source in the indwelling catheter inserted through percutaneous transhepatic cholangiography was extended further to treat some extrabiliary obstruction by other tumors (CONROY et coll.). Intracatheter radium needles were used and usually kept in place to deliver a dose of 200 Gy around the CBD in 72 hours. CONROY et coll. treated metastasis causing obstruction to the CBD in 5 patients (2 cases with carcinoma of the lung, 2 with carcinoma of the pancreas and one with carcinoma of the stomach). Palliation response with normal level of bilirubin was obtained in all 5 patients.

Early carcinoma with no spreading beyond the CHD and CBD can be treated very effectively by intracatheter brachytherapy alone as shown in the present case. Careful selection of cases for brachytherapy with curative intent is probably one of the most important factors. In the event that the tumor has spread beyond the CHD or CBD, a combination of external beam therapy and intracatheter brachytherapy as shown by HERSKOVIC and his associates appears to be the best approach to achieve palliation and sometimes cure (HERSKOVIC et coll., CHITWOOD et coll.).

Intraoperative therapy. This technique of radiation treatment is relatively new to most oncologists but it has already shown its efficacy with some promising results (Table). TODOROKI et coll. treated 4 relatively advanced cases with carcinoma of the common hepatic, right and left hepatic ducts following exploration and bile drainage in the operating room with electron beam therapy of various energy from 11 to 18 MeV. Palliative results with drastic decrease in bilirubin level were achieved with a dose of 30 Gy in 10 to 20 min. Obviously, the radiation dosage, the extent of the area to be treated and type and extent of surgery to be made have to be evaluated further if a better result is to be obtained. Although the preliminary results of TODOROKI et coll. appear promising, it is felt that there still is a need to evaluate the possibility of combined therapy including intraoperative irradiation, brachytherapy and surgery in order to obtain improved results.

SUMMARY

Carcinoma arising from the common hepatic duct is unique in its clinical course and is difficult to manage due to its dismal prognosis. The case reported and the treatment reflected not only the highly selective process but also the innovation of the intracatheter brachytherapy technique available to date. Exploratory laparotomy appears essential to identify the extent of the tumor and localize the area for brachytherapy. Percutaneous transhepatic cholangiography and placements of the indwelling catheter should be reserved for non-surgical candidates whose long-term survival is limited. Review of pertinent literature also shows various roles of irradiation in the management of this disease. The potentials of intraoperative therapy, brachytherapy, external beam therapy and their combinations were examined to implement the future recommendation of the treatment.

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