

A SURGEON LOOKS AT RADIOTHERAPY IN CANCER OF THE COLON AND RECTUM

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IT MAY SEEM ODD THAT A SURGEON HAS CHOSEN to speak to you on the subject of radiotherapy in the management of cancer of the colon and rectum. I certainly profess no knowledge of the finer points of ionizing irradiation or radiobiology, but I would like to rise to the occasion nevertheless and give you my point of view on this interesting topic. It is obligatory as well as interesting because the multidisciplinary attack on cancer is here to stay, as evidenced by this joint meeting, and because the Rectum and Colon Service of the Memorial Hospital, N.Y.C., has played a role in developing such an attack.

HISTORICAL

In briefly tracing the historical development of ionizing irradiation in the treatment of cancer of the rectum, there were many reasons why this mode of therapy had been tried in the 1920's and 1930's, when the Miles procedure or abdominoperineal resection carried a formidable operative mortality. This was before the refinements of surgical technique, improved anesthesia, better pre- and postoperative care, and antibiotic therapy. The low position of rectal cancer made it accessible to the application or administration of ionizing irradiation. Radiotherapy had also been proven to be efficacious in the management of other cancers, particularly of the cervix, endometrium, etc.

Binkley, the first Chief of the Colon and Rectum Service at Memorial Hospital, described the selective use of ionizing irradiation in the treatment of cancer of the rectum both for cure in poor risk patients, and palliation in advanced inoperable cases over 40 years ago.^{2,3} The sources of irradiation included external irradiation by the radium pack, or

the 200-250 kv machine and/or the insertion of radium tampon or irradiated gold seeds. For the small tumors, he reported a series of 17 of 18 patients living 5 years or more following treatment.⁴ For the advanced inoperable tumor, he described 43% good palliative results, 29% moderate palliative results, and 19% mild palliative results.⁵ This was an astonishingly good achievement in over 200 selected patients reported at that time.

I will discuss here the current management of cancer of the colon and rectum with ionizing irradiation under three headlines: preoperative irradiation, curative irradiation, and palliative irradiation.

PREOPERATIVE IRRADIATION

From this background, it was a logical step in our institution to utilize radiotherapy as a preoperative agent in the total management of cancer of the rectum. In the late 1930's and early 1940's, Binkley administered a subcancericidal dose, i.e., 1500 to 2000 rads tumor dose, to rectal carcinomas prior to abdominoperineal resection. The method of administration was usually via two anterior and two posterior pelvic ports using the 250 kv machine. If the tumor were within 10 cm of the anal verge, an additional perineal port was included. It became immediately apparent that many of the patients improved clinically under such treatment, and bleeding and tenesmus subsided. The clinician also noticed that often bulky advanced cancers which were considered to be of borderline operability became operable following such a course of radiation therapy. A retrospective study was based on the analysis of over 1700 such patients with previously untreated cancer of the rectum, seen between 1939 to 1951, at the Memorial Hospital.^{10,11,13} The 5- and 10-year results in the patients who had received no preoperative irradiation were compared with those in the ones who did receive radiotherapy. Operative mortality and such factors as age, sex, and histologic grading were similar, but unexpect-

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edly, the 5- and 10-year results in these series were comparable in all respects except in those patients whose tumors had metastasized to the mesenteric lymph nodes, i.e., those considered under the Dukes' C classification. It appeared that these patients had benefited from preoperative roentgenotherapy, because 37% were alive 5 years after treatment, in contrast to 23% of those who had not received any preoperative irradiation. Similarly, 27% were alive 10 years after treatment, in contrast to 10% of those who had not received preoperative radiotherapy.

This significant finding was tempered by the fact that it represented a retrospective study only, and that there was selectivity of patients involved. Actually the patients with poorer clinical setups were more likely to be the ones to have preoperative radiation therapy prescribed. Nevertheless, a randomized study was then carried out between the years 1957 and 1965.¹⁴ This more recent study includes over 700 patients. The 5-year survival rate in Dukes' C patients was the same in both groups, with a slight advantage in the group which did not receive preoperative radiation therapy—47 vs. 40%. Whether this reversal of experience in this more recent series means that we have improved our surgical attack, or that it is due to the altered technique of radiotherapeutic administration, is not known. In the older study, 250 kv had been used through multiple ports, whereas, in the newer series, radiocobalt was used through singular, anterior and posterior ports.

At present, the feeling among members of the Colon and Rectal Staff is to use preoperative irradiation only in patients who are particularly young or particularly old, and in whom the tumor appears to be bulky, infected, or is of borderline operability.

Although we have not been able to corroborate our earlier findings by the current randomized study, the initial report has stimulated other investigators to pursue this problem.

From the separate studies of experimental tumor systems in animals (mice, rats, and rabbits) by O'Brien et al.,⁷ Smalley and Das Gupta,¹² and Whiteley et al.,¹⁷ it seems that preoperative irradiation definitely lends a beneficial effect on animals so treated prior to surgery, as compared with the control group who received surgery alone.

Dwight et al.⁶ analyzed their randomized study of 700 patients assembled from a cooper-

ative effort of different Veterans Administration hospitals in which they tried to duplicate the low dosage preoperative administration of radiation therapy, originally described by us. They found there was no apparent difference in surgical complication or mortality between the experimental and control group of patients.⁶ Furthermore, lymph node involvement in resected specimen of treated patients was less (27%) than in those of the control group (40%), and the expected 5-year survival of the treated group was significantly better in those having abdominoperineal resection (45%), as compared with 30% for the control group.

A study by Allen and Fletcher¹ conducted for 8½ years includes 52 patients who received a cancericidal dose of 5000 to 6000 rads administered to the tumor site via a 2 Mev Van de Graaff or cobalt-60 machine. Surgery was performed 4 to 6 weeks after completion of radiotherapy. Surgical complication rate was considered within reason. (One patient experienced peritonitis from tumor perforation, one patient became totally obstructed, and the one patient receiving 6000 rads had delayed wound healing.) Their preliminary results were encouraging for the Dukes' C group, in that 6 out of 10 patients survived 9 to 57 months (60%). Ten of the 52 tumors after irradiation showed either no residual cancer (five patients) or conversion into in-situ cancer (five patients). So far, no clinical evidence of local recurrence has been found. These authors are encouraged to proceed with further enlargement of this program.

A pilot study from the New Haven Department of Radiology, headed by Tepper and Kligerman,¹⁵ also uses large doses of radiotherapy which is directed to the abdomen and pelvis roughly in the shape of an inverted T; 4500 rads are delivered to opposing anterior and posterior ports via a 6 Mev linear accelerator in 4½ weeks. This is followed by subsequent surgery, and the results are compared with a control group of patients who had surgery only. Of the 19 patients thus treated with preoperative radiotherapy, only five showed positive lymph node metastasis, whereas seven of nine patients in the control group exhibited lymph node spread of the disease. These authors feel that their application of radiotherapy must be responsible for sterilizing some of the regional lymph nodes, and they are enthusiastic in continuing their study.

CURATIVE IRRADIATION

There is no argument that surgery is the modality of choice in the curative treatment for cancer of the colon and rectum, but as I have intimated, there are occasions when radiotherapy is used instead in patients who are very poor surgical risks, when advanced tumors are considered inoperable, or when a combination of both conditions exists. Binkley had reported remarkable results in small tumors in a highly selected series. Williams, at St. Bartholomew's Hospital in London, described his experience with the 1 Mev machine in the treatment of 220 patients and reported that 29% of these patients survived 2 years and 5.5% survived 5 years.¹⁸ More recently, Wang¹⁶ cited seven patients who survived from 4 to 15 years without disease, following the administration of 3500 to 5500 rads to their cancer in the rectum or rectosigmoid.

Using a special Philips-Vanderplatts tube via an endoscope, Papillon, since 1948, has been able to apply contact irradiation to carefully selected patients with cancers of the rectum which were under 5 cm in size, soft to palpation, and located in the distal 14 cm of the rectum. In a recent summary of 100 patients so treated, and followed for over 5 years, he reports a 67% 5-year overall cure rate.^{8,9} Included in this figure are four patients who required subsequent surgery for a cure. Of the 33 patients who died, 16 succumbed to other causes without evidence of cancer, 10 from metastases, and 7 from local recurrence of disease.

PALLIATIVE IRRADIATION

We believe that radiotherapy can afford a maximum of palliation with a minimum of discomfort to the patient.

The resection of localized disease in the perineum, liver, lung, abdominal wall, or anastomotic sites has yielded an additional 10% 5-year survival. We do not hesitate to excise gross metastases particularly in the omentum and ovaries, and to relieve intestinal obstruction surgically in face of nonresectable disease. However, the patients with recurrent cancer amenable to additional surgical attack are relatively rare, compared to the majority of them who suffer from nonresectable disease. It is in this group that radiotherapy can constitute an important mode of therapy.

Recently, we have completed an analysis on

165 patients who were suffering from recurrent cancer of the colon and rectum.¹⁷ All patients were seen at weekly intervals during the treatment and at monthly intervals during their post-treatment evaluation until their death. The findings of these examinations and assessment of their symptoms and the patient's response were recorded on work sheets kept current on each patient. An objective evaluation of the individual's work quotient or performance status was also made. His ability to perform different tasks and his need for medication, etc., were evaluated.

The patients were separated into four groups depending on the extent and concentration of their recurrence.

Local disease pattern: Most of these patients had intrapelvic disease and were in pain due to pressure on the bladder, bowel, or sciatic nerve. Nonresectable perineal recurrences were also found in these patients. One hundred and three patients, or 62%, of the entire study group fell in this category.

Hepatic pattern: These patients had disease progression characterized by massive liver enlargement. Pain was a prominent symptom. Pressure on the stomach, diaphragm, or abdominal wall was noted, as were nausea and anorexia. Asymptomatic liver metastasis was not treated by radiation therapy. Jaundice was not a contraindication to treatment unless accompanied by hepatocellular damage with marked liver failure. There were 22 patients (13.3%) in this group.

Intra-abdominal pattern: This group consisted of 27 patients (16%) whose disease was characterized by diffuse gross or miliary implants within the large or small bowel mesentery. Radiation therapy was directed to the site of predominant symptom causation. Ascites and pressure symptoms secondary to the fluid accumulation were not felt to be amenable to external radiation therapy.

General pattern: This group consisted of 13 patients (8%) of the whole group whose major manifestation was that of generalized disease, particularly metastatic involvement of the lung, brain, or bone. Good local effect was obtained from radiation therapy to the painful bone lesions.

Most patients were treated by the telecobalt-60 source. A few were irradiated by 250 kv x-ray. The treatment fields were individualized according to the clinical site and extent of the disease. In the case of localized pelvic disease, anterior and posterior 20 × 20 cm

fields were used as well as a perineal cone if indicated. Hepatic irradiation was either to the whole liver or sections which were obviously involved with disease. Cancericidal radiotherapy was not the objective in this study. Approximately 2000 to 2500 rads only were delivered in 8 to 12 consecutive treatment days. Recognizable side effects included malaise, anorexia, and nausea which were mostly temporary. The patient was usually ambulatory. Occasionally, those patients receiving total liver irradiation required hospitalization.

In the evaluation of treatment results, a graded format was used according to strict criteria: *Grade I*, excellent response, objective regression of palpable disease, complete pain relief, return to normal duties, and definite increase in performance status; *Grade II*, good response, objective regression of palpable disease, pain relief but requiring some medication, ability to care for self, and increase in performance status; *Grades III or IV*, no objective regression of disease, pain relief but requiring regular medication, assistance in care, and no increase in performance status, and *Grade IV*, no response or treatment failure.

In the local disease group, over one quarter of the patients had an excellent response, one half had good response, and all but 5% received some benefit from radiation therapy. The average life of the patient after treatment in this group was 18 months, and 30 months for those who had excellent response to treatment.

Twelve of the 22 patients in the hepatic pattern benefited from irradiation to the liver. Seven of these patients received more than one course of irradiation to the liver, and the average life span after treatment was about one year.

Sixteen of 27 patients with intra-abdominal pattern received excellent or good palliation. The average life expectancy after irradiation in this group was 11 months.

In patients with a general pattern of metas-

tasis, only 1 out of 13 had an excellent response, and five had a good response. Since few patients with generalized disease have a major symptom which lends itself to localized irradiation, chemotherapy is more often the modality of choice. The average post-therapy life expectancy was only 8 months in these patients.

SUMMARY AND CONCLUSIONS

The value of preoperative radiotherapy for cancer of the rectum remains questionable. Although the experience from our retrospective study seemed to indicate that patients with Dukes' C lesions benefited greatly from a 5- and 10-year survival assessment, we have not been able to reconfirm this in a more recent prospective randomized study. The clinically highly malignant lesion of borderline operability probably warrants a course of radiotherapy prior to surgery nevertheless. However, the final figures on this, as well as other studies in other clinics using varying techniques of preoperative administration, are not finalized and remain to be objectively appraised when such studies are completed. The recent VA study does estimate a projected increase in 5-year survival at 15 patients per 100 patients who received abdominoperineal resection. Radiation therapy for the curative treatment of cancer of the rectum and colon is possible but falls short of surgical method of treatment in effectiveness, and is only warranted when a tumor is too far advanced to be considered operable, when the patient is of extremely poor surgical risk, or both.

Palliative management of recurrent cancer of the colon and rectum, if and when beyond surgical help, with moderate dosages of radiotherapy (2000 to 2500 rads), is recommended, and is expected to obtain relief of symptoms in more than 50% of such patients in the final months of survival.

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