
Family Practice Grand Rounds

Inoperable Rectal Cancer

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DR. GLENYS O. WILLIAMS (*Assistant Professor, Department of Family Practice*): In Grand Rounds today we will present the case of an elderly lady with inoperable rectal cancer. Our purpose is twofold: first, to hear about the chemotherapy of this disease from Dr. David Brown; and second, to talk about the effect of the disease on the immediate family and how this was managed.

Mrs. N. T. was the bright, feisty, 88-year-old widow of a small-town grocery store owner. When she was found to have carcinoma of the rectum, surgery was considered. Abdominoperineal re-

section with permanent colostomy is the operation of choice; it reduces the risk of local recurrence, but mortality rates are very high in the elderly. This particular tumor, however, was thought to be inoperable, and electrocoagulation¹ or cryosurgery was considered, but Mrs. T. refused to have any local therapy. Dr. Brown will now discuss the remaining available treatment, chemotherapy.

DR. DAVID BROWN (*Clinical Pharmacist, Williamsburg Family Practice Office*): Several antineoplastic agents have been investigated clinically for their activity against colorectal cancer. The subjects of these clinical trials fall into two groups: (1) the tumor has been surgically removed, or (2) the tumor is inoperable because of tissue invasion or metastasis. Without chemotherapy, the median survival time is approximately five years for the first group and approximately seven months for the second group. Approximately 70 percent of surgically "cured" patients eventually develop tumor recurrence or metastasis.² The

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goals of chemotherapeutic research are to improve survival time and to reduce the rate of recurrence in surgically "cured" patients.

Antineoplastic drugs are selected for research protocols on the basis of tumor responsiveness. In this context, "tumor response" means "at least a 50 percent decrease in measurable area occupied by the tumor."³ About a dozen drugs have been studied individually for their effects on colorectal tumors. Unfortunately, only 8 to 21 percent of patients obtain a tumor response to these agents.² Fluorouracil (5-FU) and cyclophosphamide are the best single agents found. When either drug is given in an optimum dosing regimen, only 21 percent of the patients obtain a tumor response. Cyclophosphamide can be given orally, but it is unpopular because of the high incidence of side effects and toxicity. Fluorouracil must be given intravenously on a weekly basis and is usually well tolerated by the patient during the maintenance phase of treatment.

Various regimens involving combinations of antineoplastic agents have been found to have superior tumor responses when compared to the individual agents. Tumor responses of 17 to 43 percent have been observed with some of these combination regimens.^{2,4} The best tumor response has been obtained by a combination of 5-FU and Methyl CCNU. The latter drug is available only for investigation in approved centers with approved protocols. The combination regimens generally have a higher incidence of intolerable side effects than the single drug regimens.

These studies have evaluated only "tumor response," not patient response. It seems logical to infer that a decrease in tumor size should reduce or delay the patient's symptoms associated with tumor size. Unfortunately, this inference has not been documented in any of the reviews of clinical studies that I have read. Furthermore, the "tumor response" to these agents is transient. The median duration of colorectal tumor response to these chemotherapeutic regimens is only about five months.^{2,3}

Regimens that have demonstrated tumor responses have also been investigated in large-scale clinical trials. These trials have examined the effect of chemotherapy on patient survival. Early trials showed promising results. Various 5-FU regimens significantly improved the five-year survival of patients with Duke's stage B and C cancers.² A

few studies have shown slight improvements in median survival times. The test of these found a median survival time of 9.7 months compared to survival of 5 to 7 months in historical controls.² These studies have been criticized for using historical controls (retrospectively selected cases) because this method fails to account for possible effects of changes in surgical techniques over the years. Three subsequent studies using prospective randomly selected treatment and control groups found no significant difference in five-year survival with 5-FU vs placebo.³

At this time, the balance of scientific evidence does not support the routine use of chemotherapy for colorectal cancer. Continuing research may eventually discover more effective regimens. For that reason, patients should be offered an opportunity to participate in organized clinical trials. Those who cannot or will not participate in such trials may wish to try 5-FU therapy with the understanding that it probably will *not* improve survival. At best, 5-FU offers about a 20 percent chance that the colon tumor will shrink by at least 50 percent in size. The only possible goal of this therapy would be the hope of reducing or delaying symptoms, but this effect has not been documented.

If 5-FU therapy is used, the following regimen should be given:

1. Calculate dose according to patient's ideal body weight
2. Check white blood count prior to each dose. Do not administer 5-FU if white blood count is below 3,500
3. Check other signs of toxicity: stomatitis, vomiting, or diarrhea
4. Initial regimen: 12 mg/kg (max 800 mg) intravenously daily for four doses, then 6 mg/kg intravenously every *other* day for four doses, then proceed to maintenance therapy
5. If toxicity occurs during initial therapy, discontinue therapy and proceed to maintenance therapy starting one week after toxicity subsides
6. Maintenance regimen: 10 to 15 mg/kg (maximum 1,000 mg) intravenously each week
7. If toxicity develops during maintenance regimen, hold therapy until one week after toxicity subsides, then resume therapy with a lower dose

Best tumor size reduction results are obtained by initiating therapy with a mildly toxic regimen and then maintaining the response with a reduced dose.³ A white blood count of 1,500 to 3,500/cu

mm, stomatitis, or diarrhea demonstrate an adequate degree of initial toxicity. Maintenance therapy should allow a white blood cell count near the lower limit of normal and an absence of intolerable side effects. Occasional nausea within a few days of each weekly dose is common and is not grounds for discontinuing therapy. This regimen has a documented tumor response in 21 percent of patients. Less aggressive regimens have at best only a 10 percent tumor response.

It may often be impractical to administer the initial regimen because of the frequency of intravenous injections. An alternative approach is to start with weekly maintenance therapy, increase the dose until the "mild toxicity" occurs, then continue maintenance at a reduced dose.

Mrs. T. was started on a conservative 5-FU regimen of 11.5 mg/kg per week.

DR. WILLIAMS: Every week for 18 months her niece took time from work to bring Mrs. T. to the Family Practice Office for 5-FU injections and white blood counts.

At this time the tumor was easily palpable on rectal examination; it was large, hard, irregular, bled to touch, and became fixed in the pelvis. The symptoms were distressing, and progressed from frequent small bowel movements, which were sometimes bloodstained and offensive flatulence, to complete fecal incontinence. There was no pain, but there were increasing vague discomfort, weakness, and fatigue. Most of Mrs. T.'s energy was used in coping with the incontinence and frequent changes of pads and clothing.

DR. BROWN: After four weeks without toxicity, the dose of 5-FU was increased to 19 mg/kg each week. After three weekly doses of this high-dose regimen, her white blood count dropped to 2,500/cu mm, and she developed severe diarrhea. This is the desired "mildly toxic" response that is associated with better effectiveness. The drug was withheld for three weeks until the patient was ready to try again. She was then maintained on 11.5 mg/kg per week for 13 months. During this time, the drug was withheld on only four occasions for episodes of malaise, nausea, or diarrhea. Her white blood count hovered around 5,000 throughout this period. The 5-FU was discontinued at the patient's request when she was too weak to come to the office.

DR. WILLIAMS: When Mrs. T. chose to stop chemotherapy, we visited her at home regularly.

The aims of treatment after discontinuing chemotherapy were (1) to keep the patient comfortable, (2) to keep the stool firm enough to minimize incontinence, and soft enough to minimize the risk of obstruction,^{5,6} and (3) to help the patient come to terms with her increasing weakness and approaching death. Acetaminophen proved adequate for pain relief and Metamucil (psyllium hydrophilic mucilloid) for stool control. Mrs. T. was given the opportunity to discuss death, but she did not; she did say firmly that she would never go to a nursing home. Ms. Pamela Miller visited the family several times. She will give us some family background and explain how help at home was organized.

MS. PAMELA MILLER (*Family Service Specialist, Department of Family Practice*): Mrs. T. lived in a duplex, and her mildly retarded twin sister Millie lived in the other half; there was a connecting door. Millie did the cooking for herself and her sister, but rarely went out. Their niece and her husband, now retired, lived two blocks away.

When determining patients' needs, it is necessary to consider their finances, and how much help they need in performing the activities of daily living: feeding, bathing, toileting, transferring, continence, and mobility. It is also necessary to evaluate the cost difference between in-home health services and institutionalization. Of course it is difficult, if not impossible, to put a dollar amount on the cost of friends, family, and society as a whole.

The niece visited several times a day and did the food shopping and the laundry. Millie was asked to provide frequent, small, nutritious meals and drinks between meals, and she was enthusiastic about her job.

Mrs. T. needed help with bathing, cooking, toileting, and continence, and her mobility decreased as she became weaker. Her mental status changed also; some days she was clearer than others. Financial help was not needed, but the bill for disposable diapers and sanitary pads every week was considerable. The public health nurse organized the nursing care plan and visited once a week. The home health aide bathed Mrs. T. twice a week. A homemaker relieved them of some household chores. Many neighbors dropped in every day, and the community pharmacist delivered their prescriptions. Mrs. T. was utilizing all available resources for a home health care plan.

The home care system worked well until Mrs. T. began to get more confused, especially at night, and two frightening episodes occurred. First, she left the gas stove turned up high and nearly started a fire; then one night she wandered down to the basement and was too weak to climb back up the stairs. Safety precautions must be instituted for some elderly people, just as for young children. These problems were met by disconnecting the stove on Mrs. T.'s side of the duplex and putting a bolt on the basement door too high for her to reach. Tensions between the sisters built up, and Mrs. T. complained about Millie, her constant offerings of food, and her shouting.

The home care plan was no longer meeting the patient or family needs.

Problems leading to institutionalization can be divided into three categories: (1) patient's behavioral patterns, (2) family or supporter's limitations, and (3) environmental or social conditions. First, patient behavior can deteriorate in several areas. Their sleep may be disturbed, and they get up during the night while the family is getting its needed rest. Next, the patient can develop incontinence of feces or urine, which can be difficult for a family to cope with. Problems arise if the patient's ability to move without help decreases. Another point to consider, as happened in this case, is the danger of a patient's irresponsibility, exemplified by Mrs. T. nearly starting a fire. Second, the family's limitations are quite important to consider.⁷ Do the family members work? Are they already overloaded with family responsibilities? Are they anxious or depressed? Do they have sufficient physical strength to care for the patient? Third, there are many social factors to consider. How much will the social life of the provider or family be affected? Will they be able to leave the house at all? Can they take a vacation? What are the finances of this family? Can they afford private help? And last, what is the physical layout of the house in which the patient will live? Are there stairs? Is the bathroom accessible?

I realize that many areas have been only superficially covered, but my point is to show the complicating factors involved in making a decision whether to keep a family member at home or placed in a nursing home.

DR. WILLIAMS: In 1975 Sanford⁸ studied the stress factors that led to institutionalization of old people and identified the types of problems least

Table 1. Stress Factors

Problem	Tolerance (Percent of Supporters Able to Tolerate Problems)
Incontinence of urine	81
Inability to dress	77
Restriction of social life	54
Personality conflicts	52
Inability to communicate	50
Inability to get on/off commode unaided	22
Sleep disturbance	16
Inability to walk at all	13

Adapted from and reprinted with permission from British Medical Journal (Sanford JRA: Tolerance of disability in elderly dependents by supporters at home: Its significance for hospital practice. Br Med J 3:471, 1975)

tolerated by their supporters (Table 1). Mrs. T.'s family were being asked to tolerate fecal incontinence, sleep disturbance, personality conflicts, and restriction of social life; they had reached their limit.

DR. JEFFREY MILKS (*Second year family practice resident*): Were there any other family members who could have helped, so that Mrs. T. could stay at home?

MS. MILLER: There was another younger sister, in California, but she thought that Mrs. T. and Millie should both go into a retirement home.

It is an extremely sensitive, emotional time and many families will turn to their physician for help.

DR. WILLIAMS: The niece's husband, Mr. M., came to the Family Practice Office demanding that Mrs. T. be removed to a nursing home at once because his wife could not stand the strain any longer. He wanted me to tell Mrs. T. that she had to go. A great-niece called long distance with the

same request. Nobody in the family had been willing to discuss it with the patient or was willing to do so now. A crisis had been reached.

A family conference was set up, but first I talked with Mrs. T. alone. She was cachectic and slightly confused, but she said that it would be good to get away from her sister and their fights. She wanted "to get some peace" and was willing to try the nursing home for a few days' rest. This was reported at the family conference, but since no nursing home bed was available immediately, and there was no home hospice service, some relief had to be found for the family in the meantime.

MS. MILLER: Temporary respite care for Mrs. T. in a geriatric hospital or nursing home would have been possibilities for relieving Millie and the niece, but none of these were available in this rural community. A "sitter" was another possibility, but few sitters have nursing skills, and at \$3 per hour they were too expensive. Church members were willing to provide relief by day, but not at night. A commercial laundry or hospital based incontinence service with home delivery and pickup were not available. But the home health aide was able to increase her visits to once every day, and some tension was eased by arranging for Millie to be taken out of the house to a congregate meal site twice a week.

DR. WILLIAMS: In the end, Mrs. T. was admitted to a nursing home, where she developed liver metastases and fungating inguinal nodes. She died six months later, 30 months after starting treatment. Her mental state remained confused after admission, and she did not complain. It was as though mental confusion was a protective mechanism to help her cope with the reality of being in the nursing home. However, her niece was the only relative she seemed unable to recognize, as though she blamed her that she was not at home.

DR. BROWN: Chemotherapy does not yet offer documented benefits to the patient with colorectal cancer. It does offer the hypothetical, but unproved, hope of reduced symptoms by reducing tumor size in a minority of patients. If chemotherapy is chosen, the regimen should have demonstrated tumor shrinking effects with minimum toxicity and inconvenience. Therapy should be discontinued when it becomes evident that symptoms are not controlled or when the patient will no longer tolerate the regimen.

DR. WILLIAMS: For the professionals who had worked hard to meet Mrs. T.'s wishes and make home care possible to the end, it was a disappointing result. But the level of stress experienced by family members cannot always be appreciated by an outsider. Treatment by chemotherapy may have given Mrs. T. a few more comfortable months, but the answer to inoperable rectal cancer has not yet been found.

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