Radiation Damage to the Small Intestine

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Although radiation therapy has proven effective in both cancer control and cure, grave side effects may occur. Among the most serious treatment complications encountered by a patient with malignant disease is that of radiation injury to the small intestine. Patients with gynecologic malignancies are most often found to have these problems of therapy. The etiology of radiation damage at the cellular level is mostly molecular damage resulting in lethal cellular injuries. Accompanying vascular and connective tissue may also be altered and cause later complications. Because of the complex nature of the patient's malignant disease and treatment, diagnosis of radiation injury to the small bowel and other pelvic structures can be most difficult to determine. The management of acute manifestations of enteric radiation injury includes diet modification and drugs that affect intestinal motility. Long-term manifestations of enteric radiation injury present more serious difficulties. Initially, the patient must be stabilized to reverse the effects of chronic malnutrition, sepsis, and electrolyte imbalance. Immediate surgery may be necessary in patients with suspected perforation. Most patients, however, require further studies for complete assessment of clinical damage. In patients with enteric fistulas, an operation is always necessary for fistula control. Complete enteric bypass utilizing minimally affected intestine is mandatory to ensure the least morbidity and mortality. Prevention of enteric radiation injury requires efforts to minimize postoperative adhesions, avoidance of excessive therapy to segments of fixed small bowel, and dosimetry alteration when complications arise during initial therapy.

Ionizing radiation was introduced in 1894 as an effective method of cancer therapy. Since that time, various techniques of administering radiation therapy such as teletherapy and/or brachytherapy have been developed. Although these improved techniques of irradiation are effective in both cancer control and cure, certain side effects and complications have been encountered which limit the amount of effective radiation that can be administered.

Radiation therapy has been found to be most effective in the primary therapy of such cancers as squamous cell carcinoma of the cervix, carcinoma of the intrinsic larynx, and certain testicular malignancies. Radiation therapy forms a part of the treatment regimen in other curable tumors such as squamous cell carcinoma of the oral cavity, adenocarcinoma of the endometrium, carcinoma of the breast, and certain forms of lymphoma and pediatric tumors. In addition, radiation therapy is frequently applied in the palliative management of incurable cancers in several locations. Although many cancer patients have benefited by the increased use of radiation therapy for their curative and palliative care, others have encountered significant complications. In some instances, these complications have outweighed the problems presented by the original cancer in terms of morbidity and mortality.

Among the most serious complications of radiation therapy encountered by a patient with malignant disease is that of radiation injury to the small intestine. Acute-phase symptoms may quickly pass with conservative management, yet long-term complications can present serious obstacles to the enjoyment of a cancer-free cure. Although radiation injury to the small bowel can be seen in patients with many types of malignancies, the patient with gynecologic malignancy is most often encountered [1–5].

Mechanism of Injury

Radiation therapy may affect tissues through long-term transformation such as point mutations. How-
ever, most of the radiation effect results in immediate molecular damage. Energy dissipated from ionizing radiation generates a series of biochemical events inside of the cell. Free radicals, produced from intercellular water, interact with DNA to prevent replication, transcription, and protein synthesis. Although some injuries may be repaired by intracellular repair mechanisms, lethal injuries also occur. The relative sensitivity of various cells to ionizing radiation accounts for the wide range in timing of clinical manifestations. Rapidly proliferating cells such as intestinal mucosa are most sensitive to ionizing radiation and are, therefore, at greatest risk for injury. However, accompanying vascular and interstitial connective tissue may undergo radiation damage. The alterations in vascular and interstitial connective tissue are slowly progressive and, therefore, present later in the clinical course [6]. Concomitant cardiovascular disease, atherosclerosis, and diabetes may increase the incidence of these late complications initiated by radiation therapy [1].

Radiation injury to any tissue is basically dose dependent. To assess the radiation dosage to any point, one must consider the energy level of the radiation, the portal size and location, the fractional amount, and the frequency of radiation exposure [2–4, 7, 8]. Calculations of dosage absorbed at different points may vary even in a single portal. In consideration of the tolerance of small bowel to radiation therapy, one assumes that the small bowel is a continuously moving organ. Areas of small bowel fixation such as the duodenum, the terminal ileum, and areas of small bowel that have become fixed by adhesions from a primary malignant process or from a prior abdominal operation have been shown to be particularly susceptible to the effects of ionizing radiation.

Clinical Manifestations

The clinical manifestations of radiation damage to small bowel can be divided into 2 groups according to the time of appearance (Table 1). Acute enteral complications of radiation therapy are defined as those complications that occur either during or immediately following a course of radiation therapy. Nausea, vomiting, cramps, and intermittent diarrhea are all symptoms of acute radiation enteritis. Such symptoms are probably caused by a breakdown in the intestinal mucosa which is no longer able to absorb the usual fluids and nutrients. The mucosa is also unable to prevent the efflux of fluids from the underlying supporting stroma. These changes in the intestinal epithelium result in disorders of motility and transport of fluid and solutes.

Table 1. Clinical manifestations of radiation injury to the small bowel.

<table>
<thead>
<tr>
<th>Acute</th>
<th>Long-term</th>
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</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Obstruction, partial or complete</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Perforation</td>
</tr>
<tr>
<td>Cramps</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Intermittent diarrhea</td>
<td>Malabsorption</td>
</tr>
<tr>
<td></td>
<td>Fistulas</td>
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</tbody>
</table>

Long-term complications of radiation therapy are usually manifestations of progressive vasculitis and interstitial fibrosis initiated by radiation therapy, often delivered many years before clinical signs develop [9]. Partial or complete intestinal obstruction, intestinal perforation, gastrointestinal bleeding, malabsorption, and enteric fistulas are all long-term enteral complications of patients treated with abdominal or pelvic radiation therapy.

Establishing the Diagnosis

Because of the complex nature of the patient’s intrinsic malignant disease and the multimodal nature of many cancer therapies, it is often difficult to implicate radiation as the sole cause of gastrointestinal complaints. Symptoms of nausea, vomiting, or bloody diarrhea may be direct manifestations of underlying gastritis or proctitis which may or may not be related to recently administered radiation therapy. For this reason, the etiology of specific complications among patients treated with radiation therapy may be difficult to assess.

In patients with obvious obstruction or fistulas, the location of the complication is demonstrated by either physical examination or x-ray studies. Partial small bowel obstruction can be more difficult to diagnose. The patient’s symptoms may be limited to transient late postprandial cramps and distention. On physical examination, positive findings frequently may be absent. Small bowel barium studies are notoriously inexact; extensive narrowing may be present with normal radiological findings.

In patients with chronic weight loss, specific tests of small bowel absorption have been applied to define the presence of and the exact nature of the absorptive defect [10]. Significant hypocalcemia and hypoproteinemia may often accompany the malabsorptive state. When radiation injury of the small bowel is encountered, similar injury to other pelvic structures must also be investigated [11, 12]. Especially with gynecologic malignancies, injuries to the rectum, fixed sigmoid loops, or the urinary