Surgical Management of Peritoneal Carcinosis: Diagnosis, Prevention and Treatment

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Summary. Gastrointestinal and ovarian malignancies frequently recur with metastatic disease limited to the abdominal cavity. Due to full thickness penetration of tumor through bowel wall, spillage of tumor from lymphatic channels by surgical trauma or perforation of the tumor through the ovarian capsule, tumor cells are disseminated throughout the peritoneal surfaces either prior to or at the time of surgical removal of the primary tumor. In the past, diagnosis of recurrent cancer was difficult because no sensitive diagnostic test was available by which to image a small tumor volume present on peritoneal surfaces. Computerized tomography with intraperitoneal infusion of contrast can demonstrate tumor nodules not otherwise detectable. Intraperitoneal installation of I-131 labeled monoclonal antibody has allowed visualization of mucinous tumor on peritoneal surfaces not seen by any other radiologic test. Intraperitoneal chemotherapy has been shown to provide palliation in patients with small volume disease confined to peritoneal surfaces. Because of limited penetration of chemotherapy into large tumor nodules this treatment strategy has not been effective for bulky intraabdominal recurrent cancer. Cytoreductive surgery utilizing high voltage electrocautery and CO2 laser evaporation of tumor can make patients relatively disease free. These surgical technologies combined with postoperative intraperitoneal chemotherapy have been shown to be of benefit for selected patients with recurrent intraabdominal cancer. The wider application of these intraperitoneal chemotherapy treatments for patients in an adjuvant setting may be of value in preventing the occurrence of peritoneal carcinosis and in improving survival.

Key words: Peritoneal carcinosis – Colon cancer – Ovarian cancer – Gastric cancer – Pancreas cancer – Intraperitoneal chemotherapy – Intraperitoneal immunotherapy – 5-Fluorouracil – Mitomycin-C.

A New Hypothesis Regarding the Mechanism of Gastrointestinal and Ovarian Cancer Recurrence

The natural history of recurrent gastrointestinal and ovarian malignancy is such that a large proportion of patients recur with metastatic disease at the resection site and on peritoneal surfaces. The explanation of this pattern of spread has not been provided in the past. With ovarian cancer tumor penetrates through the capsule, seeds malignant cells throughout the peritoneal surfaces and in the absence of effective chemotherapy eventually results in death from tumor progression. The same phenomenon occurs frequently with gastrointestinal malignancy. Not infrequently, colon cancer will penetrate full thickness through the bowel wall and result in peritoneal implants in the area of the tumor on the serosal surface. The same full thickness tumor penetration of the stomach wall is frequently encountered with gastric cancer. This may not be the only cause for peritoneal carcinosis. At the time of surgical removal of the primary tumor, multiple lymphatic channels must be transected. In a large proportion of patients these lymphatics channels are contaminated by tumor microemboli. These free tumor cells are disseminated at the time of surgery or leak retrograde from severed lymphatic channels in the immediate postopera-
tive period. The resection site presents to the tumor cells the ideal setting in which to implant and grow. Presumably, this is why local recurrence is so frequent in gastric cancer and in pancreas cancer, especially if lymph nodes are involved by malignancy. In these two diseases a wide resection, as is seen in colon cancer with its long mesentery, is usually not possible. Transection of lymphatics containing viable tumor cells may occur in a majority of patients. The presence of free intraperitoneal tumor cells from the margins of surgical resection is postulated to be the major course for disease recurrence in these malignancies.

Diagnosis of Recurrent Cancer on Peritoneal Surfaces

Traditionally recurrent cancer on peritoneal surfaces has been difficult to confirm. Frequently, before there is radiologic evidence of recurrent cancer a rise in the plasma CEA level is detected. It is not unusual for every radiologic test to be normal even though there is gross intraabdominal disease recurrence. The radiologic test that most clinicians use is the abdominal-pelvic computerized tomogram. A positive CT scan is shown in Fig. 1. Complete opacification of all bowel loops with oral contrast material is of great value when one attempts to discriminate between normal loops of bowel and tumor masses.

The accuracy of the abdominal-pelvic CT scan in detecting intraabdominal malignancy is surprisingly low [11]. Tumor masses that surround the liver may be noted because they indent Glisson's capsule and resemble an intrahepatic filling defect [6]. In other parts of the abdomen tumor masses even 4 cms and above are routinely missed. Tumor within the pelvis is especially difficult to accurately visualize [11].

An improvement in the diagnostic accuracy of the abdominal-pelvic CT scan is available. If soluble contrast material is introduced in a large volume of fluid into the peritoneal cavity, the parietal peritoneal surfaces are well-visualized on a CT scan. Even small tumor deposits down to 1 cm in size can be readily demonstrated. Pelvic tumor masses may be seen using this technique but missed by routine CT scan. If oral contrast is used along with the intraperitoneal contrast the thickness of the wall of the large and small bowel loops can be readily determined. Thickened bowel loops often mean that there is a diffuse spread of tumor over the visceral peritoneal surfaces. Figure 2 shows an abdominal cut on a CT scan with intraperitoneal contrast. No abnormalities are noted but the parietal peritoneal surface is clearly visualized. Figure 3 shows a pelvic CT scan with the intraperitoneal infusion of soluble contrast in 2 liters of fluid. Obvious tumor masses are visualized.

Recently, a new technique has been described to visualize intraperitoneal deposits of mucinous adenocarcinoma. In grade I mucinous adenocarcinoma of colon or ovarian origin, copious amounts of free intraabdominal mucin is frequently present. This will readily bind to the intraperitoneal administration of I-131 labeled monoclonal antibody. Using a whole body gamma camera the deposits of mucinous tumor can be accurately visualized. Figure 4 shows the radionuclide scan obtained after an intraperitoneal installation of I-131 labeled monoclonal antibody B72.3. In this patient all diagnostic tests were negative except for the monoclonal antibody scan. This technology may be of value in the future for accurately detecting and quantitating mucinous tumor present on peritoneal surfaces [2].

Rationale for Intraperitoneal Chemotherapy

Regional cancer treatments may be more beneficial to patients than systemic therapies if three criteria are met. 1) The systemic benefits of treatment are not sacrificed because adequate doses of drug are administered locally so that therapeutic amounts are present within the peripheral circulation. 2) Higher levels of effective chemotherapeutic agents are present local-regionally so that increased local anticancer effects are present. 3) The local and systemic toxic side effects are no greater than when the drugs are administered by the intravenous route. These criteria are met with several effective anticancer agents used intraperitoneally for the treatment of gastrointestinal malignancy.

The rate at which a drug leaves the peritoneal cavity is, in large part, dependent upon its molecular weight. Table 1 shows the correlation of the absorption of a drug with its molecular weight [7]. The larger the molecular weight the slower the absorption. If a drug of the proper size is selected and if that drug is administered in a large volume of fluid into the peritoneal cavity, high concentrations of drug will remain in the peritoneal cavity for an extended time period with a slow release