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CLINICAL VIGNETTE

Review and Current Treatment of Peritoneal Carcinomatosis Due to Metastatic Gastric Cancer

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Case Report

A 25-year-old male presented to the emergency room with intermittent, colicky RLQ abdominal pain for 1 day. The pain was 5/10 intensity and seemed to localize to RLQ area. There were multiple bouts of diarrhea in the past 24 hours prior to ER presentation. There was no hematemesis or hematochezia and he noted low grade fevers at home.

Past medical history was unremarkable and he was on no medications. He did not smoke or drink. Physical examination revealed a well-developed, well-nourished muscular male. Vital signs 133/71 P 104 R 16 T 97.7. Abdominal exam showed mild tenderness in the RLQ area without rebound tenderness. There were normoactive bowel sounds. The liver and spleen were not enlarged. CBC showed a WBC 12.3 with 90% neutrophils. Comprehensive metabolic panel was unremarkable. Albumin and lipase were normal. CT of abdomen and pelvis was normal. He was discharged from the ER with diagnosis of acute diarrhea and was told to follow up with his PCP.

The patient returned to the ER 14 months later with 2-months of mild intermittent diffuse abdominal pain. The pain increased 2 weeks prior up to 9/10 in intensity. He reported losing 20 pounds in the past 4 months and had diarrhea the past 2 weeks. He saw his PCP and a RUQ ultrasound and stool tests were negative.

Physical examination revealed again a well-developed well-nourished male with stable vital signs. Abdominal exam showed minimal diffuse abdominal tenderness with normal bowel sounds.

His labs showed normal CBC and chemistries with Alb 3.9.

Repeat CT of abdomen and pelvis showed new extensive ascites, with a tubular structure that was 15 mm in diameter in the RLQ area, suspicious for appendicitis.

A laparoscopy revealed extensive whitish scaly patches and nodules throughout the peritoneal cavity. There was extensive scarring and fibrosis involving the mesentery. Small bowel mesentery was firm and "wood" like. Appendix was thickened and fibrotic with appendicolith. Omentum was shrunken and hard. Appendectomy was performed along with biopsies of omentum and peritoneal nodules.

Surgical pathology of omentum and peritoneal nodules showed poorly differentiated adenocarcinoma. The appendix also showed poorly differentiated adenocarcinoma with tumor invading the full thickness of the appendiceal wall involving the serosa. The tumor was high grade and showed signet-ring cell features.

Due to the signet ring cell findings, EGD found a 4.5 cm mass in the mid to distal body of the stomach and pathology showed poorly differentiated signet ring cell carcinoma. With these findings, it was felt that the patient initially developed gastric CA which then spread into the peritoneal cavity.

Discussion of Peritoneal Carcinomatosis Due to Primary Gastric Cancer and Due to Various Other Primaries

Non gynecologic peritoneal carcinomatosis (PC) is caused by metastatic disease from various organs including gastric, colorectal, pancreas, liver, mesothelioma and pseudomyxoma.

A large multicenter prospective French study described the natural history of PC.[1] They identified 370 cases of PC due to non-gynecologic malignancy. The primary malignancies were: gastric 125, colorectal 118, pancreatic

58, unknown 43, and miscellaneous 26. Ages ranged from 20-90 years with a mean of 67.7. PC staging ranged from stage 0 to IV. Stage 0, no macroscopic disease. Stage I, malignant granulations less than 5 mm in greatest dimension and localized in one part of abdomen. Stage II, malignant granulation less than 5 mm in greatest dimension and diffuse to the whole abdomen. Stage III, malignant granulation 5 mm to 2 cm in greatest dimensions. Stage IV, large malignant cakes (>2 cm in greatest dimension). Among PC from gastric primary tumors, 9 were stage 0, 22 were stage I, 22 were stage II, 27 were stage III, 45 were stage IV.

Seventy-eight percent (98/125) underwent resection of primary gastric cancer or underwent bypass surgery. A small percentage underwent systemic chemotherapy, 13% (17/125). The survival rates were the best for stage I, 11.2 months, but progressively worsened; Stage II, 4.5, Stage III, 3.5, and stage IV, 2.6 months. The prognosis and long term outcome with standard surgery or systemic chemotherapy is quite poor.

Since the mid-1980s, the approach to managing patients with PC has shifted. In 1973, Meyers showed cancer cells from various primaries including stomach, ovary, pancreas, and colon moved through the peritoneal cavity with great efficiency.[2] Malignant gastric cells moved from the stomach into the peritoneal cavity through the right para colic gutter. This was shown by infusing contrast (meglumine diatrizoate) into the peritoneal cavity and documenting contrast distribution in patients with different primaries. The contrast would disseminate into the rectosigmoid colon, right side of colon, and into the peritoneum overlying the bladder and pouch of douglas. Dissemination of cancer cells through the right side of colon allowed malignant gastric cells to move from the stomach into the peritoneal cavity without hematologic spread.

In the past, surgery and systemic chemotherapy were used for PC from various primaries with extremely poor results. A newer treatment method for PC has been developed after promising animal studies.

In 1980, Spatt reported hyperthermic perfusion into canine peritoneum with low adverse effects.[3] This led to human trials published in 1985. Sugarbaker and colleagues randomized IV versus intraperitoneal [heated] 5 Florouracil in patients with advanced primary colon or rectal CA.[4] In the same year, Sugarbaker and Jablonski[5] reported outcomes on patients with colorectal and appendiceal PC treated with cytoreductive surgery and intraperitoneal [heated] chemotherapy.

The current approach to managing patients with PC involves two steps: (CRS) Cytoreductive surgery and HIPEC (hyperthermic intraperitoneal chemotherapy). Cytoreductive surgery involves a specialized technique of debulking tumor in peritoneal carcinomatosis. This tedious debulking involves electro-evaporative surgery[1] using a high voltage electrosurgical tip which uses heat necrosis to remove tumor cells and makes recurrence less likely. This is followed by an extensive peritonectomy removing areas with the greatest volume of malignant visceral involvement.[2] The first to be removed is the rectosigmoid colon. Next, a complete pelvic peritonectomy is performed involving stripping of the abdominopelvic sidewalls, the peritoneum overlying the bladder, and the cul de sac of Douglas. The next area to be resected in the ileocecal valve and terminal ileum. The final area to be removed is the antrum and possibly the entire stomach.

HIPEC is innovative method of giving chemotherapy in the peritoneum to treat PC. Earlier studies reported heated chemotherapy into the peritoneum was more effective that standard systemic chemotherapy in treating PC with various primaries. Chemotherapy agents are heated to 41 C (105 F) and put into the peritoneum. This method increased penetration of the chemotherapy into malignant nodules with increased antimitotic effects on malignant cells. Enhanced antitumor effects have been reported for various drugs including oxaliplatin, mitomycin C, doxorubicin, cisplatin, paclitaxel, and irinotecan.

CRS and HIPEC has been the standard for patients with PC from appendiceal cancer due to pseudomyxoma peritonei. Pseudomyxoma peritonei is a condition characterized by peritoneum filled with gelatinous mucinous implants in the peritoneum. In a study of 69 patients[6] with appendiceal cancer with PC treated with CRS and HIPEC, the 3 year survival was 55.1 % (38/69) for appendiceal cancer with PC due to pseudomyxoma. For PC due to appendiceal cystadenocarcinoma treated with CRS and HIPEC, the 3-year survival drops off to 36.2 % (25/69) and for PC due to appendiceal adenocarcinoma treated with CRS and HIPEC, the 3-year survival was poor at 8.6% (6/69).

PC from gastric cancer is very aggressive. Peritoneal seeding is present at the time to diagnosis is 30%.[2] A meta analysis of PC due to gastric cancer included 7 prospective and 3 retrospective studies.[7] The overall median survival was 7.9 months. Four studies showed improved survival of 15 months, if there was limited peritoneal involvement after cytoreductive surgery.

Limited involvement included patients with no peritoneal seeding or tumor nodules <2.5 mm persisting after cytoreductive surgery.

Our patient underwent laparoscopy with extensive peritoneal disease. He had large metastatic nodules >5 cm and eligible for CRS and HIPEC. He underwent standard chemotherapy. Eight months after his initial diagnosis, he developed altered mental status, and was found to have metastatic disease to his brain with leptomeningeal carcinomatosis and died.

Summary

PC due to gastric cancer is a devastating and aggressive disease. Those that are diagnosed at early stage where CRS was effective to eliminate tumor nodules <2.5 mm are good candidates for HIPEC and CRS treatment; with median survival of approximately 15 months.[7] The natural history of early stage I (malignant granulations less than 5 mm in greatest dimension and localized in one part of abdomen) that where treated with surgery with or without standard chemotherapy had average survival of 11 months.[1] One can argue whether treating early stage 1 solid tumors such as gastric CA with PC with CRS and HIPEC is any better than standard treatment with surgery with or without chemotherapy. Our patient had PC from gastric CA stage IV disease (large malignant cakes (>2 cm in greatest dimension) and was not a candidate for CRS and HIPEC. He was treated with standard chemotherapy and he died 8 months after his initial diagnosis.

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