

# Adenocarcinoma Of The Stomach: A Plea For Early Diagnosis

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**Abstract:** In the United States, early diagnosis and cure of gastric carcinoma remain elusive. Patients with this disease commonly have gastrointestinal symptoms that often go unexplained. Physicians give gastric carcinoma a low priority in their differential diagnosis and are unaware of the risk factors patients may have. Patients may have a normal upper gastrointestinal series, and fiberoptic gastroscopy is delayed.

Patients with unexplained indigestion and abdominal pain, coupled with such risk factors for gastric carcinoma as national origin, diet, heredity, and previous subtotal gastrectomy for gastric ulcers, should be given the opportunity of esophagogastroduodenoscopy. (J Am Board Fam Pract 1991; 4:171-4.)

According to recent statistics, there were nearly 25,000 new cases of stomach cancer in 1988 and approximately 14,400 deaths resulting from this disease.<sup>1</sup> Even though the frequency of gastric carcinoma is decreasing in the United States, only 10 to 16 percent of patients treated with gastric resection survive more than 5 years. Stomach cancer ranks eighth in incidence and sixth in mortality for all malignant disease. Age distribution is wide, with most cases occurring in patients who are in their sixth to eighth decades. Gastric carcinoma occurs in twice as many men as it does women. Stomach cancer is eight times more frequent in Japan than in the United States. In Japan, where esophagogastroduodenoscopy (EGD) procedures are liberally offered, more than 50 percent of patients are 5-year survivors.<sup>2</sup>

Factors implicated in the development of gastric cancer are culture; heredity; a high ingestion of salt, nitrates, and complex carbohydrates; and a low intake of fat, protein, green leafy vegetables, and fresh fruit. Countries that report a high rate of gastric cancer are Japan, Chile, Costa Rica, Scandinavia, China, and Iceland.<sup>3</sup> Native white American men are at low risk, whereas Hispanic, Hawaiian, American Indian, and black men appear to be at high risk.

To determine the incidence of stomach cancer, Lundegardh and associates<sup>4</sup> followed 6459 patients for 25 to 33 years. All patients had undergone partial gastrectomy for benign ulcer disease.

Their overall risk for stomach cancer was no different than that found among sex- and age-matched controls. When the patients were classified according to the duration of follow-up after surgery, sex, surgical procedure, and diagnosis at the time of operation, however, differences in risk were observed among subgroups. Groups that were noted to be at high risk were women; those patients who had undergone a Billroth II anastomosis compared with those who had had a Billroth I anastomosis; those operated on for treatment of gastric ulcer compared with those operated on for treatment of duodenal ulcer; and patients operated upon at a younger age according to the following subgroups: younger than 39 years, 40 to 49 years, 50 to 59 years, and older than 60 years of age.

## Case History

On 30 September 1988, a 72-year-old man came to the office complaining of crampy abdominal pain that was made worse by eating and that often awakened him from sleep at night. The patient had otherwise been in good health for most of his life. He was a second-generation Irish American who was born and raised in a New England seaport community. The patient's family ate home-grown vegetables from a garden in which human manure from an outhouse was used as fertilizer. The father had died of stomach cancer. The patient had worked primarily in industrial settings, and exposure to industrial chemicals, including phenol, soda ash, and triphosphate sodium, was noted; however, he denied exposure to asbestos. His diet consisted of seafood two to three times

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each week (mackerel, halibut, shrimp, clams, lobster, mussels, and smoked herring). There was no history of ingestion of raw fish, fava beans, cabbage, or compounds containing nitrates. There were no known allergies; alcohol was consumed in moderation, and the patient did not use tobacco. The following is an account of the patient's recent medical history:

On 11 August 1987, the patient was seen by a physician for nausea, vomiting, anorexia, and vague abdominal pain. His physical examination disclosed no masses, and a stool test for occult blood was negative. The symptoms resolved spontaneously. On 24 February 1988, the patient visited a second physician at a tertiary care center. He again complained of crampy abdominal pain, which had been present for 1 month. The pain was associated with constipation but without fever, nausea, vomiting, or rectal bleeding. The physician's impression was irritable bowel syndrome or an occult tumor. A bulk laxative (Metamucile) was prescribed. The examination included an abdominal roentgenogram, which showed slight dilation of small bowel loops in the left upper quadrant, suggesting a localized ileus; a barium enema showed a single diverticulum but no signs of polyps or colon carcinoma; and a normal upper gastrointestinal series was reported. On 14 March 1988, the patient, complaining of crampy abdominal pain, was again seen by the second physician. Abdominal ultrasonography showed gallstones but no other pathologic condition.

On 26 April 1988, the patient was seen by a third physician at the same tertiary care center. The patient complained of gaseous abdominal pain, which often awakened him from sleep at night. An anticholinergic-antispasmodic medication (Donnatal™) and an antacid (Mylanta™) were prescribed. Stool tests for ova and parasites were negative. On 14 May 1988, computed tomography of the abdomen disclosed prostatic enlargement and para-aortic lymphadenopathy extending from below the renal vein down to the aortic bifurcation. The radiologist believed it to be either a metastatic disease or a lymphoma.

Consultations with a urologist for a cystoscopy and prostatic biopsy and with a hematologist for a lymph node biopsy were recommended. The patient was subsequently seen by a urologist at a community hospital, who prescribed sul-

famethoxazole and trimethoprim for a presumed urinary tract infection and naproxen for his abdominal pain. The patient, distraught with his present medical condition, was subsequently referred to us by another patient.

A review of systems disclosed nausea, heartburn, indigestion, excessive flatus, and an 11-kg weight loss. Positive physical findings included an enlarged right lobe of the prostate and a very strong positive reaction to a stool test for occult blood. Rigid proctosigmoidoscopy to 20 cm disclosed no abnormalities. Laboratory values were the following: hemoglobin, 120 g/L (11.7 gm/dL) (normal, 111–156 g/L); hematocrit, 0.35 (35 percent) (normal, 0.33–0.47); and carcinoembryonic antigen, 53.4 ng/mL (normal, < 5.0 ng/mL). An electrocardiogram showed diffuse ST segment elevation consistent with early repolarization and Q waves in leads 2, 3, and aVF. Because of indigestion, chest pressure, and abnormal findings on an electrocardiogram, the patient had a stress test, but it was considered nondiagnostic because of positionally induced electrocardiographic changes. A stress echocardiogram was then performed, and no abnormal wall motion was detected, making the diagnosis of coronary artery disease unlikely. Because of his long history of abdominal pain and indigestion and the normal upper gastrointestinal series, on 4 October 1988, the patient, sedated intravenously, underwent an office-based esophagogastroduodenoscopy performed with a video gastroscope. A large, friable, erythematous, gastric ulcer with raised edges was noted in the fundus of the stomach. Seven samples obtained by retroversion of the gastroscope were collected for biopsy. Brush biopsies were also performed for gastric cytology. Histologic examination showed a class 5 adenocarcinoma, and histopathologic studies showed an adenocarcinoma arising in atrophic gastritis.

The patient was referred to a second tertiary care center where he had a subtotal gastrectomy for palliative purposes. He underwent several courses of chemotherapy, but he died of metastatic gastric cancer 15 months after it was diagnosed.

## Discussion

### *Esophagogastroduodenoscopy versus Upper Gastrointestinal Series*

Both advantages and disadvantages of EGD have been shown by Winamer, et al.,<sup>5</sup> who studied

75 patients with both exophytic and infiltrative types of gastric carcinoma. When EGD with biopsies and brush biopsies was done on exophytic lesions, the diagnostic accuracy increased to 92 percent; however, the diagnostic accuracy of infiltrative gastric carcinoma decreased to 50 percent with similar biopsy techniques.

Bemvenuti and colleagues<sup>6</sup> found that the gastric cardia and antrum behind the incisura proved to be the most difficult areas to access for biopsy. They had better results with brush biopsy (72.4 percent) than with biopsy (66.7 percent) in making the correct diagnosis.

Graham, et al.<sup>7</sup> assessed the number of biopsies that would accurately yield a correct diagnosis in patients with esophageal cancer and gastric carcinoma. The first biopsy yielded a diagnosis in 70 percent of cases of gastric carcinoma and in 98 percent of cases of esophageal cancer; three additional biopsies increased the yield to more than 95 percent; seven biopsies resulted in an accuracy in more than 98 percent; and when biopsies and cell studies were coupled, the diagnosis was established in 100 percent of the patients. The importance of using both modalities cannot be overemphasized.

Green and associates<sup>8</sup> retrospectively reviewed radiologists' reports of findings on upper gastrointestinal films in 27 of 28 patients with surgically proven gastric carcinoma. In 19 percent, no lesions were seen, malignancy was suspected or diagnosed in 44 percent, and in 37 percent, benign lesions were diagnosed. It became evident that reliance on an upper gastrointestinal examination proved fatal for some patients.

Along a similar vein, Nelson and colleagues<sup>9</sup> reported the superiority of endoscopy over radiology in differentiating benign from malignant gastric ulcer. A cohort of 123 patients were followed for more than a 5-year period during which 109 proved to have benign ulcers, and 14 had malignant ulcers. Endoscopy established a correct diagnosis in 106 of 109 cases of benign ulcers and in 11 of 14 cases of malignant ulcers; radiologic studies of the upper gastrointestinal tract demonstrated 91 of 109 benign ulcers of which 7 were incorrectly called carcinoma; 6 of 14 malignant ulcers were correctly identified, although 5 of 6 were called benign. The authors concluded that a combination of gross appearance

and biopsy was 97.7 percent accurate, whereas upper gastrointestinal studies were only 70 percent accurate.

### Cancer Types

Approximately 50 percent of gastric cancers arise within the antralpyloric area, causing symptoms of gastric outflow obstruction. Proximal gastric lesions usually cause dysphagia. Tumors in the body and fundus (25 percent) are often asymptomatic until extension or ulceration is prominent. The classic morphologic classification separates gastric carcinoma into five types: (1) fungating, 35 percent; (2) ulcerating, 25 percent; (3) diffuse or linitis plastica, 26 percent; (4) polypoid, 7 percent; and (5) superficial, 6 percent.<sup>10</sup> A newer classification based on the cellular behavior of the tumors has been suggested. This classification differentiates the lesions into two groups: (1) expanding type, which has a centralized cohesive, enlarging tumor mass; and (2) infiltrating type, which widely infiltrates through tissue planes rather than forming a large mass. Nearly all of the polypoid, superficial, and fungating types are expanding, and nearly all of the diffuse types are infiltrating. The ulcerative forms are divided between the two types.<sup>11</sup> The description of the infiltrating type of tumor relates to the principal mode of metastatic spread, i.e., through the submucosal lymphatic plexus. Maingot<sup>12</sup> describes eight mechanisms of metastatic spread: (1) within the stomach wall, (2) within the esophageal and duodenal wall, (3) through regional lymphatic drainage, (4) by direct extension to the neighboring organs, (5) by venous invasion and circulatory dispersion, (6) by peritoneal seeding, (7) by transplantation (iatrogenic), and (8) by transluminal implantation. Spread in the submucosal lymphatics of the stomach, especially cephalad into the esophagus, and regional nodal metastases to the omentum, celiac nodes, and paraortic nodes are the most common distribution patterns of metastatic disease.

### Recommendations

Certain factors in this case history, such as continued abdominal pain despite normal findings on an upper gastrointestinal examination, the family history of stomach cancer, and the ingestion of smoked herring, could have alerted the physician to gastric carcinoma. It would

appear that the time to have offered gastroscopy was in March 1988, when symptoms persisted despite normal findings on the upper gastrointestinal series. Gastroscopy could have resulted in an earlier diagnosis. If gastroscopy is recommended only after the patient has an abdominal mass, anemia, weight loss, or an elevated carcinoembryonic antigen, the probability of detecting localized disease remedial to surgical resection will be limited.

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