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Late development of a second primary carcinoma of the stomach

*Report of five cases**

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MULTICENTRIC cancer of the stomach has been long recognized[1] and is not rare. The development of a second primary cancer many years after the original gastric resection has received less attention in the literature and presumably occurs only rarely. As the number of long-term survivors of successfully treated cancer of the stomach increases, one may expect an increase in the number in whom a second cancer develops. Such patients will never be numerically great, but their existence at all will alert the physician to such a possibility, and lead to prompt surgical exploration and a possible second 'cure.'

Our study is based upon a small group of patients who seemed to qualify according to four criteria designed to minimize the possibility that the supposed second primary growth was actually a recurrence of the original carcinoma (*Table 1*). These criteria are:

(1) *The original gastric resection must seem to be curative;* i.e., there was no evidence of preoperative or postoperative metastatic spread beyond the limits of the resection; all visible or palpable tumor was removed; and the pathologist found the lines of resection free of tumor.

(2) *Sufficient time must have elapsed from the original gastric resection.* There is no absolute number of years postoperatively in which to exclude recurrence of any cancer. For cancer of the stomach, most patients destined to die of the disease will succumb within three years, but recurrences as late as 16 years after gastrectomy have been observed by one of us (S.O.H.). Five years without evidence of recurrence is the commonly accepted interval (for statistical purposes) to denote 'cures' of cancer.

Morganstern[2] reviewed a series of 11 patients in each of whom a second gastric malignancy developed subsequent to a gastrectomy for malignant disease. The time interval between the two tumors in all cases was at least

* *One case previously reported in reference 1.*

Table 1.—Data of five patients, each of whom had late development of a second primary carcinoma of the stomach

Case no.	Sex	At first operation: Age of patient, yr	At first operation: Type of primary tumor	At first operation: Tumor in regional nodes	Time interval, yr	At second operation: Age of patient, yr	At second operation: Type of primary tumor	At second operation: Tumor in regional nodes	Survival time after second operation
1	M	53	Adenocarcinoma	No	27	80	Adenocarcinoma	(?)	7 months
2	M	57	Adenocarcinoma with mucin	Yes	7½	65	Adenocarcinoma without mucin	No	10 yr*
3	F	49	Adenocarcinoma	No	6½	56	Colloid carcinoma	Yes	10 months
4	M	42	Adenocarcinoma	No	23	65	Adenocarcinoma	No	9 months
5	F	50	Adenocarcinoma	Yes	9	59	Undifferentiated adenocarcinoma	(?)	4 months

* Patient died of myocardial infarction. All others died of carcinoma.

seven years. In Morganstern's own experience with two patients, 23 years and 32 years had elapsed.

(3) *The second primary growth must not occur in the line of previous resection* (the line of the anastomosis).

(4) *The cell type of the second carcinoma must be sufficiently different from the first one to permit the pathologist to infer that they are separate tumors.*

Five cases are reported here briefly: in each of four patients it is thought that two independent, successive, primary carcinomas of the stomach developed; and in one patient there possibly was a late recurrence.

Report of cases

Case 1. A 53-year-old Caucasian man underwent partial gastrectomy with gastrojejunostomy in 1935, for adenocarcinoma. The neoplasm lay in the distal portion of the stomach, and was 5 cm by 9 cm. Histopathologic examination showed the lesion to be limited to the mucosal layers; nodes were not affected.

The patient remained in good health until January 1963, 27 years later, when at the age of 80 years he had pain in the lower abdomen, weakness, constipation, weight loss, and tarry stools. Studies showed no source of the bleeding, and he responded favorably to blood transfusion and an ulcer regimen. Recurrence of bleeding in December 1963 led to discovery, by means of gastroscopic examination, of an ulcerating bleeding nodule thought to represent cancer in the gastric remnant. At operation a neoplasm was found in the gastric remnant just proximal to the site of the prior gastrojejunostomy. It was not a favorable type of lesion and a palliative resection was performed. Histopathologic examination of the lesion showed a poorly differentiated adenocarcinoma, involving stomach and jejunum, extending locally into fat, and present in the lines of resection. The condition of the patient progressively worsened and he died seven months after the second operation.

Comment. The long time interval (27 years) between the initial operation and the second one seems to exclude the possibility that the second lesion was a recurrence of the original cancer.

Case 2.* A 57-year-old Caucasian man underwent partial gastrectomy with gastrojejunostomy in April 1941, for a mucin-producing adenocarcinoma that invaded the transverse mesocolon and four nodes in the greater omentum. In January 1949, seven and one-half years after the initial operation, the patient experienced gastrointestinal symptoms, but diagnosis could not be made from roentgenograms. Persistence of symptoms led to further roentgenography in July 1949; a tumor of the lower esophagus and fundus of the stomach was demonstrated. An esophagogastrectomy was performed (eight years after the initial gastrectomy) when the patient was 65 years old, for a fungating tumor that was an adenocarcinoma, without mucin, encircling the cardioesophageal opening. No nodes were affected.

In the summer of 1959, after a 10-year-interval of good health, at the age of 75 years the patient died suddenly of a heart attack.

Comment. The two cancers were histopathologically different, and the first one had metastasized to lymph nodes whereas the second had not. (The patient survived the first cancer despite involvement of lymph nodes for 18 years.) This patient had the unique distinction of being cured according to conventional standards of two separate cancers of the stomach.

Case 3. A 49-year-old Caucasian woman had undergone several biopsies and a wide V-shaped resection of a scarred region of the lesser curvature of the stomach in March 1955.

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* *Previously reported by Brown and Moots.*[1]

The tissue specimens showed only scarring on frozen section, but permanent sections showed the presence of adenocarcinoma. Nine days later, subtotal gastrectomy and gastrojejunostomy was performed; the resected stomach showed no further evidence of malignant lesions.

In November 1961, six and one-half years later, when the patient was 56 years of age, anorexia and weight loss developed; roentgenograms of the stomach showed an abnormal mucosal pattern along the lesser curvature, and a gastric cytologic study showed tumor cells. A large, infiltrating tumor of the cardia and lower esophagus was resected, including 3 in. of esophagus, proximal jejunum, and tail of the pancreas. Histopathologically, the tumor proved to be a signet-ring adenocarcinoma ("colloid" carcinoma) and 9 of 20 lymph nodes showed cancer. There was no tumor present at the previous line of anastomosis, but there was microscopic cancer in the new esophageal line of resection. In September 1962, less than a year after she had undergone the second operation, the patient died of cancer.

Comment. Although before the second operation it was believed that the patient had a recurrence of the original tumor, the pathologic findings strongly support the view that the neoplasm was a second primary cancer.

Case 4. A 42-year-old Caucasian man underwent partial gastrectomy and gastrojejunostomy on April 9, 1942, for an adenocarcinoma limited to the mucosa and not affecting lymph nodes.

In November 1965, 23 years after the initial operation, at the age of 65 years, the patient was examined because of constant periumbilical burning pain radiating through to the back, anorexia, weight loss, nausea, and vomiting. Roentgenographic studies showed a filling defect in the fundus of the gastric remnant, and gastric cytologic studies showed abnormal cells consistent with malignancy. The patient underwent a palliative esophagogastrectomy for a tumor affecting the entire gastric remnant. Histopathologic study showed a poorly differentiated adenocarcinoma with no involvement of resected nodes. The patient died nine months postoperatively.

Comment. The postoperative elapsed time of 23 years strongly favors the diagnosis of a new primary carcinoma in this patient.

Case 5. A 50-year-old Caucasian woman underwent subtotal gastrectomy and gastrojejunostomy in November 1954, at another hospital, for diffuse adenocarcinoma of the antrum with involvement of two perigastric lymph nodes. In July 1963, she was first examined at the Cleveland Clinic because of continuing nausea, vomiting, and severe loss in weight. Various studies were ambiguous, but laparotomy was performed on December 23, 1963, nine years after the first operation. Carcinomatosis involving peritoneal surfaces was found, and also a possible primary (or massive recurrence) in the gastric remnant. A biopsy specimen showed undifferentiated adenocarcinoma. A palliative anterior gastrojejunostomy was performed, but the patient lived only four months postoperatively.

Comment. The diagnosis could not be resolved: either this was a new primary carcinoma or it was a recurrence nine years after resection of the initial tumor.

Discussion

In each of four of these five patients, there seems little doubt that a second primary cancer of the stomach developed in the gastric remnant after an interval of some years following a gastric resection for an initial primary cancer of the stomach. In one patient it is thought that a new primary neoplasm developed nine years after the initial treatment for cancer of the stomach, although the possibility cannot be excluded that it was a long-delayed recurrence.

The practical importance of recognizing that a new primary cancer may develop many years after an operation for primary cancer of the stomach is exemplified by case 2: the patient was apparently cured not only of a first cancer but also of a second cancer! It has long been recognized that in patients who have survived one cancer of the colon, others may well develop, and they are monitored by their medical attendants with this in mind. It seems that the same possibility exists for survivors of cancer of the stomach.

Summary and conclusions

Five cases are reported with probable or possible development of a second primary cancer of the stomach after an apparent cure of a first primary cancer of the stomach. Criteria for differentiating a new primary neoplasm from a recurrence of a previously treated cancer of the stomach are: (1) Original gastrectomy should have been regarded as curative; (2) sufficient time should have elapsed (at least five years); (3) the second primary neoplasm is not in the old anastomotic line; (4) histopathologic characteristics of the two tumors should differ.

One of the five patients survived 18 years after excision of the first primary cancer of the stomach and 10 years after excision of the second primary cancer, before succumbing to a heart attack at the age of 75 years.

Although it is rare, the clinician should realize that a second cancer may develop in the gastric remnant. The development of new symptoms referable to the stomach in a patient who has undergone gastric resection for cancer should alert the clinician to a possible new neoplasm. As in case 2, a second cure can be possible if appropriate surgery is performed.

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