Carcinoma in the gastric remnant after partial gastrectomy for benign ulceration

A study of three cases illustrating the diagnostic contribution of exfoliative cytology

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EDITORIAL SYNOPSIS Three patients are described in whom cancer was found in the gastric remnants years after partial gastrectomy for benign gastric ulceration. In each case the diagnosis was established by cytological examination of gastric washings.

The occasional occurrence of carcinoma in the gastric remnant after partial gastrectomy for benign ulcer or in the stomach after gastroenterostomy is well known. Diagnosis of these growths by conventional methods may be difficult or impossible but at least two papers have stressed the difficulties and suggested that gastric cytology might be decisive. 'Although we know of no report on examination of exfoliated cells from the stomach in such cases, a finding of malignant cells in aspirated gastric contents would be most useful in establishing a diagnosis' (Freedman and Berne, 1954). 'Further experience with cytologic studies using Papanicolaou technique may also prove of value' (Berkowitz, Cooney, and Bralow, 1959).

Three patients are now reported in whom carcinoma was found in the gastric remnant at operation, and from each of whom malignant cells were recovered by means of saline washings at a time when the diagnosis was still in doubt. In two of these patients partial gastrectomy had been performed for benign ulceration respectively 11 years and 21 years before. The third patient had undergone partial gastrectomy three years before when a benign ulcer near the pylorus had been removed. At the time of operation in this patient an ulcer with surrounding induration was felt high on the lesser curve but was not included in the resection. The possibility exists that the carcinoma found in the remnant three and a half years later had been present at the time of operation and that the growth had not arisen *de novo* in the gastric stump.

CASE REPORTS

CASE 1 (L.H. 075673) The patient, Arthur S., aged 50, suffered few abdominal symptoms before 1941 when he was admitted to hospital as an emergency for surgical repair of a perforated duodenal ulcer. During the next eight years he experienced periodic bouts of epigastric pain and in January 1949, at a second hospital, partial gastrectomy with antecolic gastrojejunostomy was performed. At operation, scarring was noted in the first part of the duodenum and in the posterior wall of the body of the stomach. Afterwards he was free from symptoms, could eat normal meals, and he gained weight. In August 1959, he became aware that he was tiring easily and he was surprised to find that he had lost more than a stone in weight. By December 1959, he had become thinner, he complained of general malaise, experienced flatulence, and commented on the bulkiness and offensiveness of his stools. A routine radiograph of the chest showed infiltration in both upper lung fields and subsequent sputum cultures grew tubercle bacilli. During the next eight months he was given antituberculosis chemotherapy while observation and investigations were continued in hospital. When admitted to the London Hospital he was seen as a thin, pale man who had considerable dorsal kyphosis. At no stage of the illness could an abdominal mass be felt.

INVESTIGATIONS Haemoglobin was 48%, the mean corpuscular haemoglobin concentration (M.C.H.C.) 23%, E.S.R. (Westergren) 8 mm. The blood group was A positive. The sternal marrow was normoblastic. The serum iron level was 60 µg./100 ml. A histamine test meal (histamine 0.5 mg.) showed no free acid. Twenty out of 23 tests for faecal occult blood were positive.

Four barium meal examinations were made over a period of five months. The first barium meal was completely negative. At a second examination three weeks

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FIG. 1

FIG. 1. Near the centre of the field is a large neoplastic nucleus flanked by a superficial squamous cell on each side. The giant nucleus is hyperchromatic and chromatin is irregularly clumped. A trabecular arrangement of three neoplastic cells is seen near the lower left corner ($\times 840$).

FIG. 2

FIG. 2. Two mitotic figures are visible in a sheet of poorly differentiated cells. For confident designation of malignancy greater reliance was placed on neoplastic cells which displayed pleomorphic features ($\times 840$, enlargement $\times 2$).

later the function of the gastric remnant was described as exceptionally good. The lesser curve was irregular but the irregularity was no greater than is commonly seen along the suture line. Reports on two subsequent barium meals were indefinite. Gastroscopy was impossible because of the patient's severe kyphosis. Gastric cytology was done a week and a fortnight after the last barium meal. On both occasions blood was present in the fluid recovered from saline washings. No carcinoma cells were identified in smears made during the first examination; in the second series, individual malignant cells were identified as well as sheets of poorly differentiated neoplastic cells (Figs. 1 and 2).

At laparotomy carcinoma was found to involve the remnant extensively and extended across the stoma to the jejunum. A palliative total gastrectomy was done. The patient died three days later after rupture of the suture line.

CASE 2 (L.H. 5390/48) The patient, Dorothy G., aged 63, had undergone partial gastrectomy in 1939 when she was 41 years old. It was impossible to find out whether this was for a gastric or for a duodenal ulcer. During the 22 years that followed the operation she became recurrently

anaemic. Although she had to ascertain extent responded to treatment with courses of oral and parenteral iron, admission to hospital for blood transfusions had been necessary on several occasions. Barium meals in 1953 and 1956 were normal. In 1961 she was referred to hospital again, this time with increasing epigastric pain as well as anaemia. On examination she was a pale, thin woman with koilonychia. In the abdomen there was epigastric tenderness and the liver could be felt 2 in. below the costal margin. She had a hypochromic anaemia (Hb 50%, M.C.H.C. 29%) and tests for faecal occult blood were positive. A barium meal showed some irregularity of the lesser curve of the gastric remnant and a superficial ulcer was suspected. A further barium meal four months later failed to confirm this. Gastroscopy was not done.

Saline washings were made after introducing a rubber tube to 45 cm. The fluid recovered contained blood. Carcinoma cells were identified in four of the eight smears prepared (Figs. 3 and 4).

At laparotomy carcinoma was seen to involve the distal part of the gastric stump and appeared to originate from the lesser curve. Metastases were present in the liver.

CASE 3 (L.H. 147905) There was a story of duodenal ulcer

FIG. 3

FIG. 3. The cells forming this group contain hyperchromatic and pleomorphic nuclei. Several cells have been invaded by polymorphs but this is not a specific feature. Many similar clumps of neoplastic cells were present in smears ($\times 840$).

FIG. 4

FIG. 4. A group of four malignant cells in which secretion of mucus provides evidence of their origin from adenocarcinoma ($\times 840$).

FIG. 5

FIG. 5. On the left of the group is a large neoplastic cell of bizarre form, containing a large hyperchromatic nucleus which is surrounded by a thin rim of cytoplasm ($\times 840$).

FIG. 6

FIG. 6. A sheet of vacuolated neoplastic cells, fairly uniform in size, in which the appearances of the nuclei indicate malignancy. They are pleomorphic, hyperchromatic, bordered by dense nuclear membranes and contain giant nucleoli ($\times 840$).

attacks going back to the late twenties in George F., aged 61. In 1952 a perforated duodenal ulcer was sutured. In 1957 an emergency partial gastrectomy was done at a second hospital for a bleeding ulcer situated just proximal to the pyloric sphincter. At operation what was believed to be the scar of a healed ulcer was felt high up on the lesser curve; this indurated area apparently was not included in the partial gastrectomy. The operation was not successful, the patient continuing to suffer from attacks of epigastric pain. In 1961 he developed dysphagia and was admitted to the London Hospital. He looked pale (Hb 62%) and on abdominal palpation was tender in the epigastrium. He had not lost weight. Barium meal films tended to confirm the clinical diagnosis of carcinoma with the appearance of a soft tissue mass at the cardia extending into the fundus. No abnormality was seen on oesophagoscopy.

The centrifuge deposits made from saline gastric washings contained blood. Clumps of adenocarcinoma cells were identified in four of the eight smears prepared (Figs. 5 and 6).

At operation the growth was seen to originate near the cardia on the lesser curve and had penetrated through all layers of the stomach. The gastric remnant was removed transthoracically and an oesophagojejunal anastomosis made. The patient developed bilateral lower lobe pneumonia from which he died on the sixth postoperative day.

DISCUSSION

Considerable interest has been shown in the occurrence of carcinoma in patients who have previously undergone gastric resection or gastroenterostomy for benign peptic ulcer. Freedman and Berne (1954) studied patients with growths arising in the neighbourhood of the gastrojejunal stoma. They described three patients observed personally and provided data on 55 well-authenticated cases culled from the world literature. The subject was reviewed by Aronson and Darling (1959) and several further cases were reported by Berkowitz, Cooney, and Bralow (1959). A valuable contribution was made by Debray, Roux, Chevillotte, and Segal (1950) who were concerned particularly with growths that developed in the proximal part of the gastric remnant rather than adjacent to the stoma. De Jode (1961) reported on 19 patients who had previously undergone gastroenterostomy or partial gastrectomy and presented at the London Hospital with carcinoma of the stomach between the years 1949 and 1958. Hoffmann (1960) presented his experience of no fewer than 84 patients who developed carcinoma after operations for simple ulcers, 30 of them after gastroenterostomies and 54 after resections.

The long interval that may elapse between an operation for benign ulcer and the subsequent clinical manifestations of carcinoma in the remnant has been stressed. In 24 of the 58 patients cited by Freedman and Berne (1954), periods of 20 to 40

years elapsed between the time of operation and presentation with carcinoma. The incidence of the development of carcinoma of the remnant has been variously estimated. It was judged to be less than 1% by Freedman and Berne (1954) if those patients who were found to have carcinoma within three years of operation were excluded, on the assumption that the growths may in reality have been present in the stomach at the time of operation in these patients. Helsingen and Hillestad (1956) derived a higher figure from a follow-up study on 222 patients who had been operated on by partial gastrectomy for gastric or duodenal ulcers between 1919 and 1944. Eleven cases of carcinoma in the gastric stump developed, on average 20 years after operation. De Jode (1961) considered that there was no evidence that a preceding gastric operation predisposed towards carcinoma, or that patients who had their first operation for a gastric ulcer were more liable to carcinoma than those who had had it for a duodenal ulcer.

Whatever the true incidence of cancer in the stomach remnants, these tumours manifest certain clinical characteristics sufficiently often to allow some generalization in description. Debray *et al.* (1950) summarized important features when they commented upon '... la nécessité de songer à ces cancers quand les troubles gastriques apparaissent longtemps après la gastrectomie, sur la difficulté de leur diagnostic clinique, radiologique et gastroscopique, sur la difficulté de leur thérapeutique chirurgicale, et sur la gravité extrême de leur pronostic'. In case reports on patients such as these, the difficulty of establishing an exact diagnosis, even when suspicion is strong, is frequently reiterated. Cases 1 and 2 in the present report are typical. Although cancer of the gastric remnant was considered the likely diagnosis, uncertainty continued after months of close observation of each patient in hospital and despite repeated barium meal examinations.

Even in the intact stomach carcinoma of the upper third is relatively difficult for the radiologist to diagnose; after partial gastrectomy the difficulties are greater. Irregularities of outline are common as a result of adhesions. Distortions of the mucosal folds occur along the suture line and may be exaggerated by post-operative gastritis. Invasion of the muscular coat is readily shown in the intact stomach by failure of the involved area to stretch when the stomach is distended, whereas after partial gastrectomy it is impossible to distend the gastric remnant. Although cytological diagnosis of gastric malignancy was achieved in each of the three patients described, certain technical difficulties may sometimes be anticipated in patients who have

previously undergone gastric operations. Resting juice may not be recoverable, the tube may pass through the remnant into the stoma, washings may be contaminated with bile, and the existence of atrophic gastritis in the remnant may be responsible for shedding of atypical cells. Nevertheless, cytology is probably the only method at present available by which a precise pre-operative diagnosis of malignancy can be obtained in certain patients who have previously undergone gastric surgery.

On the basis of their experience Debray *et al.* (1950) made gloomy pronouncements on the outlook of most patients who have been found to have carcinoma in the remnant. Either the growths had extended outside the stomach by the time of laparotomy, or the patients in whom resection was possible often tolerated operation badly. The three patients now reported were no exception; one had hepatic metastases and two died in the post-operative period after resection.

When discussing the prognosis of gastric carcinomas it should be understood that the possibility of undertaking curative surgery depends largely on the presence of a type of carcinoma that gives symptoms early. Growths beginning at the cardia or pylorus may cause blockage before spread; intraluminal bleeding may arise from achlorhydric gastritis; and peptic ulceration of early superficial carcinoma may produce pain of an ulcer type. After partial gastrectomy, a wide stoma is unlikely to be blocked early by supervening carcinoma; with reduced acid production there is unlikely to be

peptic ulceration of a growth in the stump; anaemia is common and is often treated without previous investigation. It is for these reasons that cytology should not be acclaimed as a procedure that will necessarily lead to more successful treatment in many of these patients. It may, however, be regarded as a useful method of establishing a diagnosis notoriously difficult to reach by other means.

I am grateful to Dr. M. A. Floyer, Dr. J. M. Ledingham, Professor W. T. Irvine, and Mr. H. D. Ritchie for asking to have cytological examinations done on patients under their care. Dr. Denys Jennings gave me valuable advice. The photomicrographs were made by Mr. John King of the Bernhard Baron Institute of Pathology, London Hospital. Expenses were met by a grant from the London Hospital Research Fund.

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