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A Clincal Study of 30 Gastric Carcinoids

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ABSTRACT

The clinical picture in 30 patients operated on for gastric carcinoids was studied retrospectively. There were 12 men and 18 women, with an age range of 32-79 years (mean 57 years). The tumours were located in the corpus area of the stomach in more than half of the patients and in one-third were relatively small ($\leq$ 1 cm). Four patients had multiple tumours. Metastases were found in eight patients, mostly those with larger primary tumours. In no case was the carcinoid syndrome present.

The patients presented symptoms simulating those of more common affections of the stomach, such as polyps, ulcer and carcinoma. Barium contrast study and gastroscopy did not reveal the true nature of the gastric disease and even biopsy of the stomach failed to give a correct preoperative diagnosis in four of five patients. Since six patients had achylia preoperatively, it is emphasized that the possibility of a gastric carcinoid, especially in the corpus area, is more likely in association with this condition.

INTRODUCTION

A gastric carcinoid is a rare type of malignant but slowly growing epithelial tumour of the stomach. It has been described in several case reports (2), but few comprehensive investigations have been made on the clinical picture of patients with this tumour (2,5). The present study was undertaken with the aim of gaining further knowledge about the age and sex distribution of the patients, the symptomalogy, and the size, location and frequency of metastases in an unselected material of gastric carcinoids.

MATERIAL AND METHODS

All available gastric carcinoids recorded in the Cancer Registry of the National Board of Health and Welfare in Sweden between 1958 and 1974 and in the local register at the Department of Pathology in Uppsala between 1975 and

1980 were collected. The tumours were all obtained at surgical resection and no autopsy material was included in the investigation. The paraffin blocks were cut into about 4 µm thick sections and stained with haematoxylin-eosin and with the Grimelius argyrophil stain (3). The findings in routinely stained sections at light microscopy and the frequency of argyrophil tumour cells were decisive in the characterization of the tumours. Only tumours with a morphology of fore-gut carcinoids (13) and with an argyrophil reaction in the majority of the tumour cells were accepted for the study. With these criteria, the material comprised a total of 30 patients with carcinoids.

The location of the tumours within the stomach was established from the morphology of the gastric mucosa bordering the tumours, the surgical records and the gastric X-ray report. Tumours in the pyloric area were all closely adjacent to Brunner's gland. These tumours were included in the study provided that at least some part of the tumour was growing in the area of the antral mucosa. The size of the tumours was given in the histopathological reports in a few cases, but otherwise was estimated by measuring the largest diameter of the tumour in the paraffin block. In four patients with multiple tumours the size of the largest tumour was noted.

Clinical information was obtained from the medical case records at the hospital in which the patient was operated upon.

RESULTS

Sex and age distribution

Of the 30 patients, 12 were men and 18 were women. The age range of the patients was 32-79 years and the mean age 57 years (M:61; F:55).

Tumour location

The different locations of the tumours among men and women are given in Table I. It is seen that most tumours were found in the corpus area of the stomach and that there was a female preponderance in all locations (except the cardia). There were no noteworthy variations in age distribution in relation to tumour location, except that the three women with multiple carcinoids in the corpus were considerably younger (range 32-41 years, mean 37 years) than the rest of the patients.

Table I. Locations of the gastric carcinoids in 30 patients, distributed by sex.

Area of stomach	Men	Women	Total
cardia	1	-	1
corpus	6	10	16[x)]
antrum	3	4	7
pylorus	2	4	6
Total	12	18	30

X) One of the men and three of the women with carcinoids located in the corpus had multiple tumours.

Tumor size

Ten of the 30 tumours were 1 cm i diameter or smaller. The largest tumours were found in the antral area. Four patients (one male and three females) presented multiple tumours (2, 3, 5 and more than 5, respectively). They were all located in the corpus of the stomach, and three of them were 1 cm or less in diameter.

Metastatic spread

Metastatic tumour growth was observed in eight of the 30 patients; all had lymph node infiltration and three of the eight also had metastases of the liver. There was a relation between the size of the primary tumour and the frequency of metastases (Table II), in that tumour spread was more common in association with larger tumours.

Table II . The occurrence of lymph node and/or liver metastases in association with gastric carcinoids of different locations in relation to tumour size.

Area of stomach	0-1 cm	1-2 cm	2-3 cm	3-5 cm	5- cm	Total
cardia	-	-	-	1/1	-	1/1
corpus	1/5	2/9	0/1	1/1	-	4/16
antrum	0/3	0/1	-	-	1/3	1/7
pylorus	0/2	1/3	-	1/1	-	2/6
	1/10	3/13	0/1	3/3	1/3	8/30

Symptomatology

The main symptoms which occurred before the operation for gastric carcinoid are given in Table III. Besides gastric pain, the most pronounced clinical signs were haematemesis and melaena. These latter symptoms could be explained by the presence of ulceration of the mucosa covering the tumour, since ulceration was observed in 18 of the 30 cases at light microscopy. Two patients underwent X-ray examination of the stomach for investigation of anaemia of unknown cause, and had no subjective gastrointestinal symptoms. Seven patients had concomitant achylia. This was diagnosed preoperatively in six patients, and half of these had an associated pernicious anaemia. The gastric carcinoids occurring in an achylic stomach were almost exlusively located in the corpus area and tended to be multiple (10). There was no clinical signs of carcinoid syndrome or other endocrine abnormality recorded in any of the patients.

Table III. Main symptoms leading to admission to hospital and further investigation of 30 patients with gastric carcinoids.

	Tumours located in:				
Symptoms	Cardia	Corpus	Antrum	Pylorus	Total
gastric pain		6	1	5	12
melaena		8	2	1	11
haematemesis		8	1		9
anaemia		5	3	1	9
vomiting		4	2	2	8
weight loss		2	2	3	7
tiredness		1	3	2	6
dyspepsia		1		3	4
diarrhoea		1	1	1	3
dysphagia	1	1			2

Preoperative investigation and diagnosis

According to information in the clinical case records, the preoperative investigations consisted mainly of X-ray examination of the stomach and gastroscopy, sometimes with a simultaneous gastric biopsy. Gastric X-ray was not performed in five patients. In three of them the reason was an emergency explorative laparotomy for a major haematemesis. In one patient gastroscopy revealed a tumour of the cardia and in one patient the gastric carcinoid was an accidental finding during operation for chronic gall bladder disease. Four patients had normal gastric radiographs. They were operated on either because of pathological findings at gastroscopy (3 patients) or because of severe haematemesis of unknown origin (one patient). Gastric biopsies were performed in five patients.

The histopathological diagnoses of the gastric tissue material were ulceration (one case), gastritis (one case), undifferentiated carcinoma (2 cases) and carcinoid (one case). After re-examination of the cases diagnosed as undifferentiated carcinoma, including Grimelius staining of the tumour, it became obvious that the specimens originated from gastric carcinoids.

A survey of the putative preoperative diagnoses arrived at from X-ray examination and/or gastroscopy, sometimes with gastric biopsy, is given in Table IV. The most common preoperative diagnosis was gastric polyp(s) (9 patients). In one of these patients multiple gastric carcinoids were subsequently disclosed and in another patient multiple adenomatous mucosal polyps were found in addition to a gastric carcinoid.

Table IV. Putative preoperative diagnosis leading to surgery in patients with gastric carcinoids.

Preoperative diagnoses	No. of patients	Comments
Polyp(s)	9	2 cases with multiple polyps
ulcer	6	
carcinoma	4	
not known	4	explorative laparotomy because of haematemesis
tumour, not specified	3	
pyloric stenosis	1	
neurinoma (?)	1	
gall stone	1	the gastric tumour was an accidental finding at operation
carcinoid	1	
Total	30	

Type of operation

The gastric carcinoids were removed by different surgical methods. Most tumours were extirpated by a Billroth I or II gastric resection, especially those located in the more distal part of the stomach. Many smaller tumours in the corpus area were removed by local resection. A subtotal or total gastrectomy was performed in some patients with large or multiple tumours.

Survival and follow-up

Two of the 30 patients died after surgery, corresponding to a post-operative mortality of 7 per cent.

Twenty-two patients were observed for one year or more. During this period three patients died from metastatic disease and one developed a local recurrence.

Of 15 patients followed for a period of five years or longer, 10 are still alive and symptom-free.

DISCUSSION

By definition, carcinoids are endocrine tumours in which the tumour cells contain endocrine secretory granules at the electron microscopic level. Since the Grimelius silver stain causes a reaction in almost all gastrointestinal endocrine cells (4), though without discriminating between them, this staining procedure was used to identify the tumours (11,12). Although the chemical background of the argyrophil reaction is unclear, it is known from ultrastructural studies that the silver stain is specific for endocrine secretory granules (4), and tumours which lack an argyrophil reaction in the majority of their cells cannot be regarded unquestionably as endocrine; for this reason a few tumours which were primarily classified as gastric carcinoids in the Swedish Cancer Registry were not accepted for the study. It is emphasized that strict criteria for the definition of endocrine tumours improves the possibility of identifying their characteristics.

Although based on a retrospective study, our findings demonstrate the difficulties in the diagnosis of gastric carcinoids. Most patients presented symptoms such as pain, haematemesis and/or melaena, anaemia, vomiting and loss of weight, which are common signs in much more frequent pathological conditions of the stomach such as ulcer disease and carcinoma. Thus, the infrequent gastric carcinoids can hardly be suspected from the clinical symptoms.

Both X-ray of the stomach and gastroscopy seem insufficient for establishing the presence of gastric carcinoids, since with these methods the tumours resemble polyps, ulceration or gastric carcinoma. The most accurate diagnostic procedure appears to be gastric biopsy, but even with this the diagnosis seems unreliable, since discrimination from undifferentiated carcinoma of the stomach, in particular, can be difficult. Additional staining of the biopsy material with the Grimelius argyrophil stain is apparently useful, but a prerequisite for the use of this procedure is, of course, that a possible diagnosis of gastric carcinoid is considered.

When the diagnosis is confirmed, carcinoids of the stomach should, if possible, be treated primarily with surgery just like carcinoids of the gastrointestinal in general (1,7,8). In gastric carcinoids less than 1 cm in diameter complete local excision may be adequate if there are no signs of invasion of the muscularis propria or lymph node involvement. Tumours larger than 1 cm should be treated by gastric resection or gastrectomy. If lymph node metastases are found, the gastric surgery should be combined with excision of all accessible nodes and such tumour cases should thus be treated as frank carcinomas.

It has been claimed that gastric carcinoids are mostly located in the antral area (6). The findings in the present study are not in agreement with this observation, as more than half of the tumours were found in the corpus of the stomach.

The carcinoid syndrome is seldom seen in association with carcinoid tumours of the stomach (14). In our series none of the patients presented symptoms indicating such a syndrome. When it does appear, the gastric carcinoid syndrome differs from the classical type. Patients with the gastric carcinoid syndrome have atypical flush, and diarrhoea is usually not a prominent symptom.

Although relatively slowly growing, carcinoids are malignant tumours with an ability to metastasize. In the present series metastases were present at the time of operation in 26% of the cases. A relation was found between tumour spread and size of tumour, in that metastases were more frequent in the larger tumours. The survival rates were also influenced by the tumour size and spread of the disease. The 5-year survival rate, as far could be estimated, was 67 per cent.

Recent investigations have shown that gastric carcinoids occur relatively frequently in association with achylia, especially those which are located in the corpus area of the stomach and tend to be multiple (9,10). It has also been suggested that gastric carcinoids which develop in an achylic stomach may have a pathogenesis similar to that proposed for carcinoma of the stomach in association with achylia and pernicious anaemi (10). These observations stress the importance of increased alertness to the possibility of a gastric carcinoid in patients with pathological findings in the stomach and an associated achylia (and pernicious anaemia).

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REFERENCES

1. Aranha, G.V. & Greenlee, H.B.: Surgical management of carcinoid tumours of the gastrointestinal tract. Am Surg aug. 429-435, 1980.
2. Christodoulopoulos, J.B. & Klotz, A.P.: Carcinoid syndrome with primary carcinoid tumour of the stomach. Gastroenterology 40, 429-440, 1961.
3. Grimelius, L.: A silver nitrate strain for A_2-cells in human pancreatic Acta Soc Med Upsaliensis 73, 243-276, 1968.
4. Grimelius, L. & Wilander, E.: Silver stains in the study of endocrine cells of the gut and pancreas. Invest Cell Pathol 3, 3-12, 1980.

5. Marks, C.: Carcinoid tumours. A clinico pathologic study. G.K. Hall & Co., cells of the gut and pancreas. Invest Cell Pathol 3, 3-12, 1980.
6. Oota, K. & Sobin, L.H.: Histological typing of gastric and oesophageal tumours. WHO. No. 18 Geneva, 1977.
7. Tilson, M.D.: Carcinoid syndrome. Surg Clin North Am 4, 409-429, 1979.
8. Welch, J.P. & Malt, R.A.: Management of carcinoid tumours of gastrointestinal tract. Surg Gynecol Obstet 145, 223-227, 1977.
9. Wilander, E.: Achylia, pernicious anaemia, ECL cells and gastric carcinoids. Virchows Arch (Pathol Anat) 387, 371-373, 1980.
10. Wilander, E.: Achylia and the development of gastric carcinoids. Virchows Arch (Pathol Anat) 394, 151-160, 1981.
11. Wilander, E., Grimelius, L., Lundqvist, G. & Skoog, V.: Polypeptide hormones in argentaffin and argyrophil gastroduodenal endocrine tumours. Am J Pathol 96, 519-530, 1979.
12. Wilander, E., Portela-Gomes, G., Grimelius, L. & Westermark, P.: Argentaffin and argyrophil reactions of human gastrointestinal carcinoids. Gastroenterology 73, 733-736, 1977.
13. Williams, E.D. & Sandler, M.: The classification of carcinoid tumours. Lancet 1:238-239, 1963.
14. Wilson, H., Cheek, R.C., Sherman, R.T. & Storez, E.H.: Carcinoid tumours. In: Current Problems in Surgery. Chicago: Year Medical Publishers 1970.

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