Carcinoid Tumors of the Gastrointestinal Tract

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The charts of 135 patients with gastrointestinal carcinoid tumors diagnosed over a 22-year period at 2 hospitals are reviewed and the clinical and pathological aspects discussed. Carcinoids occur most commonly in the appendix, jejunoileum, and rectum. Those smaller than 1 cm in diameter provide evidence of malignant potential only occasionally; lesions in the 1–1.9 cm range do this quite variably, and tumors 2 cm and larger are almost always invasive or metastatic or both. All gastrointestinal carcinoids except those of the appendix enlarge, invade, and metastasize predictably if given sufficient time. Most carcinoids except those of the rectum have already been adequately treated surgically when diagnosed by the pathologist. Local excision is effective treatment for noninvasive rectal carcinoids smaller than 2 cm in diameter, but those that have invaded or grown to 2 cm should undergo more radical resection. In general, gastrointestinal carcinoids carry better prognoses than do adenocarcinomata, and even in the presence of distant metastases long-term survival occurs in a significant number of patients. The frequent concomitance of associated malignant diseases accounts for as many or more deaths in these patients than the carcinoids themselves.

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SINCE THE FIRST DESCRIPTION by Lubarsch in 1888[3] and Oberndorfer's[9] synthesis in 1909 of the term "carcinoid," 3,718 cases of carcinoid tumors have been described.

The carcinoid tumor or argentaffinoma is thus an uncommon tumor which contains a rich store of the tissue hormone 5-hydroxytryptamine (serotonin) which is produced by the argentaffine or Kulchitsky cells of the gastrointestinal tract. Carcinoids have been described in the stomach, duodenum, gallbladder, pancreas, in the lung, and in ovarian and testicular teratomata as well as at all levels of the gastrointestinal tract. The appendix is one of the common sites where the tumor presents as a yellowish mass at the appendicular tip, and though the tumor at this site may show local invasion histologically, it is generally benign in its course.

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Carcinoids may be incidental findings at laparotomy or at autopsy. In the gastrointestinal tract, the tumor commences in the submucosa and extends outwards gradually involving the serosa, subsequently extending into the mesentery and adjacent structures. The tumor grows very slowly so that even with distant metastases many patients survive for long periods of time. The overlying mucosa usually remains intact, although occasional ulceration may occur. Only rarely does the tumorous mass encroach on the lumen, but annular constricting lesions may occur resulting in obstruction.

A review of our experience with carcinoids of the gastrointestinal tract provides 135 cases for study.

Materials and Methods

One hundred and sixty-one patients with carcinoid tumors of the gastrointestinal tract were seen at Charity Hospital and the Veterans Administration Hospital in New Orleans from 1948 to 1970. Five patients were excluded from analysis because of insufficient information. Twenty-one patients represented carcinoid-islet cell tumors of the duodenum that had been previously and separately studied[14] and were not further considered. The resulting 135 cases were composed of 115 from Charity Hospital and 20 from the Veterans Administration Hospital.

To determine the natural history of carcinoid tumors at specific sites in the gastrointestinal tract, the carcinoids were grouped according to location and mode of discovery as shown in Table 1. Included in this series are 35 patients with rectal carcinoids upon which a previous report was based.[2] We found no patient with carcinoids

TABLE 1. *Location and Method of Discovery of 135 Carciniod Tumors of the Gastrointestinal Tract*

Location	Clinical	Autopsy	Total
Rectum	37	0	37
Appendix	27	2	29
Jejuno-ileum	18	19	37
Duodenum	8	4	12
Stomach	8	2	10
Colon	8	2	10
Total	106	29	135

of the esophagus, gallbladder, pancreas, or Meckel's diverticulum.

Attention was directed mainly to the charts of the 106 patients whose carcinoids were diagnosed clinically, and symptoms, method of diagnosis, treatment, pathologic features, and coexisting diseases were noted. The 29 carcinoid tumors discovered at postmortem examination were incidental findings and had produced no clinical symptoms. These cases were included only when pathologic features and the presence of coexisting disease were considered.

The carcinoid tumors were categorized according to size under one of three headings: 1) Less than 1 cm; 2) One to 1.9 cm; and 3) Two cm or larger.

The appropriate size of tumor was obtained from the description recorded by clinicians, surgeons or pathologists. The definition of size appeared important, and a search was made for correlation between tumor size, the presence of symptoms and extent of the disease process.

Followup information was available for 102 of the 106 clinical patients and was provided by outpatient clinic reports or Tumor Registries.

Results

Age and Sex

The average age of patients with appendicular carcinoids was 26 years, but ranged 45–55 years of age for the remainder of the 106 patients. There were no significant sex differences, the slight variations encountered being related rather to the composition of the patient populations of the two hospitals or by the nature of the operative procedures leading to the diagnosis.

Symptoms, Diagnosis and Treatment

Rectum. Symptoms referable to the rectum were present in 23 of the 37 patients with rectal carcinoids. These symptoms were caused by carcinoids in only 10 of the patients and were related to tumor size and extent as shown in Table 2. None of the 25 patients with carcinoid tumors smaller than 1 cm had symptoms attributable to their tumors.

TABLE 2. *Symptoms and Tumor Characteristics in the 12 Patients with Rectal Carcinoids One Centimeter in Diameter or Larger*

Symptoms	No.	Tumor Characteristics
Decreased stool calibre	4	Large proliferative masses
Rectal bleeding	3	Ulcerative lesions
Rectal pain	3	Infiltrating tumor
None	2	Small, no ulcerations or invasions

TABLE 3. *Treatment for the 37 Patients with Rectal Carcinoids*

Treatment	
Biopsy only	19
Biopsy with fulguration	4
Local excision	3
Anterior resection	1
A-P resection	10
	37

Rectal carcinoids were palpable on digital examination in 22 (59%) patients and visualized sigmoidoscopically in 34 (92%). In three patients with small lesions the tumors were undetected by either means. A microscopic diagnosis of carcinoid was made on 29 biopsy specimens, four of these confirming tentative clinical diagnoses. The carcinoid tumors were typically described by examiners as firm, smooth, yellowish submucosal nodules. An erroneous microscopic diagnosis of carcinoma was made on biopsies from 5 patients so that rectal carcinoids were either missed or mis-diagnosed in 8 patients (22%).

The modes of therapy applied to the 37 patients with rectal carcinoids are demonstrated in Table 3. Abdominoperineal resections were carried out in 10 patients and in 5 the original histologic diagnosis had been that of carcinoma. They were subsequently re-classified as carcinoids after completion of the operation. In four patients the presence of synchronous concomitant anorectal carcinoma determined the need for abdominoperineal resection. In only one patient was an abdominoperineal resection carried out for the specifically stated purpose of curing a carcinoid tumor of the rectum.

Jejuno-ileum. Symptoms in the 18 surgical patients with carcinoid tumors of the jejunum or ileum are categorized in Table 4. None of the patients presented with symptoms of the carcinoid syndrome. Abdominal masses were noted clinically in 6 patients who underwent operation. Three of these were attributable to intussusception and in 2 the masses were due to the matting of bowel loops. In only

TABLE 4. *Signs and Symptoms in 18 Surgical Patients with Jejunoileal Carcinoids*

Intestinal Obstruction		12
Acute:	5	
Chronic:	7	
Palpable mass:		6
GI bleeding		2
Asymptomatic		4
Total		18

1 patient was the primary tumor itself large enough to be clinically palpable.

An accurate preoperative diagnosis of acute intestinal obstruction was made in 5 patients. In the 7 patients with chronic partial obstruction vague abdominal complaints were of minimal diagnostic aid and a preoperative diagnosis of an underlying bowel tumor was not made in any of these cases. X-ray studies with contrast media were positive for intestinal obstruction in 2 patients but did not provide an accurate diagnosis of the underlying carcinoid tumor.

In the 12 patients with varying degrees of obstruction only one carcinoid was larger than 2.5 cm in diameter and this represented the only palpable primary tumor. This was a 6 cm tumor arising in the terminal ileum and invading the cecum. Luminal occlusion by the bulk of the primary lesion was not apparent in any of the other 11 patients with obstruction. In three patients the mechanism of obstruction was attributable to intussusception. The mechanism of obstruction was not overtly related to the primary lesion in the other eight patients in whom large mesenteric metastases, the presence of mesenteric fibrosis, or kinking and matting of bowel loops provided the pathogenetic basis for the intestinal obstruction (Fig. 1).

Resection of small bowel and mesentery was carried out in all 18 surgical patients. In 6 patients the right colon was resected en-masse with the terminal ileum. In 14 cases the operating surgeon was unaware that a carcinoid tumor was present in the resected specimen, while in the other 4 patients frozen sections were obtained and provided immediate and accurate diagnosis.

Stomach and Duodenum. There was 8 patients with gastric and 8 patients with duodenal carcinoids providing a total of 16 with gastroduodenal carcinoids who underwent surgical therapy. Upper gastrointestinal bleeding was a prominent feature in all 8 patients with gastric tumors and occurred in 4 patients with duodenal lesions. In each of these 12 patients, either an ulcer or an ulcerative mass was found. The gastroduodenal symptoms were usually attributable to coexisting disease, i.e. peptic ulcer or gastric carcinoma, rather than to the carcinoid tumor per se. There were associated gastric ulcers in 4 patients and duodenal ulcers in 7, the carcinoid being found in the base of the ulcer crater in most.

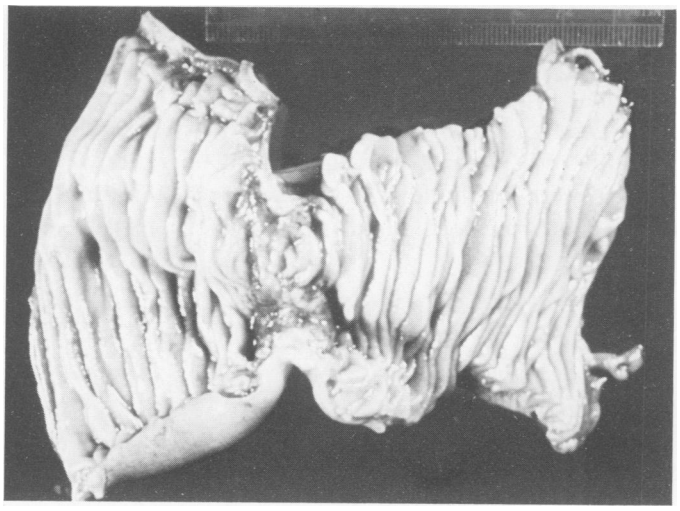

FIG. 1. Carcinoid of jejunum with narrowing of lumen induced by fibrosis causing subacute obstruction.

Gastric analysis was performed in 3 patients and in none was hyperchlorhydria present. Endoscopy and barium contrast studies were accurate in establishing the presence of associated pathologic processes, but the carcinoid tumors were diagnosed preoperatively in only 2 patients with polypoid lesions.

Treatment consisted of 14 gastric resections for ulcer or carcinoma, actual or suspected; one pancreatoduodenectomy for an invasive tumor of the second portion of the duodenum; and one local excision of a polypoid tumor of the duodenal bulb. This latter case represented the only carcinoid tumor diagnosed intraoperatively.

Colon. Carcinoid tumors of the colon occurred in 8 surgical patients, 6 of whom were symptomatic. The symptoms are categorized in Table 5 and strongly resemble those attributable to the more commonly encountered adenocarcinoma. Palpable lesions were present in 2 patients. Four tumors were demonstrated preoperatively, 1 by proctoscopy and 3 by barium enema. Four were first discovered at laparotomy, 2 for obstruction, 1 for perforation, and 1 during an elective cholecystectomy. All the tumors were thought clinically or operatively to be carcinomatous except the one within reach of the sigmoidoscope. Appropriate resections of right or left colon were performed.

Appendix. In 27 patients the diagnosis of carcinoid tumor was made after appendectomy. The procedure was performed for appendicitis in 17 patients and as an incidental procedure in 10. In 6 cases the tumors were located in the proximal half of the appendix in patients who presented with appendicitis and it is conceivable that the tumor was of etiologic importance in causing the symptoms. In the other 21 patients the distal location of the tumors excluded a role in the pathogenesis of appendicitis nor could any symptoms be attributed to them.

Appendectomy alone was the treatment for appendiceal carcinoids in all but two patients. One underwent a subsequent negative "second-look" laparotomy, and a right hemi-colectomy was performed in the other. Neither residual tumor nor metastasis was found in the resected specimen.

Surgical extirpation was the sole mode of therapy in the 106 patients in the clinical series. None received adjuvant chemotherapy or palliative irradiation for carcinoid tu-

mor. A palliative hepatic resection was performed in 1 of the 2 patients who developed the malignant carcinoid syndrome. These two patients did not manifest symptoms attributable to the syndrome when the intial diagnosis of a carcinoid tumor was made and surgical treatment instituted, but presented with symptoms and biochemical findings of the carcinoid syndrome 5 or more years after treatment of the primary lesion.

TABLE 5. *Symptoms in 8 Surgical Patients with Carcinoid Tumors of the Colon*

Anemia	1	
Weight loss	1	
Large bowel obstruction	3	
Acute:		2
Chronic:		1
Perforation	1	
Asymptomatic	2	
Total	8	

Extent of Disease

The relationships between extent of disease in terms of local invasion as well as nodal and distant metastases in 135 patients with carcinoid tumors in this series are categorized in Table 6. The tumor size at each affected level of the gastrointestinal tract is appropriately tabulated. A tumor was considered invasive when it had infiltrated to or beyond the muscularis propria. The liver was involved in all patients who had distant metastases, and tumor implants were frequently found also in the parietal peritoneum, omentum, mediastinum, or spinal cord. No metastases to lung, brain, or bone were encountered in this series.

It is noteworthy that among the 37 patients with rectal carcinoids there were two patients with carcinoids smaller than 1 cm in diameter who presented with metastases to the regional nodes in the absence of muscularis invasion. These two cases have been previously recorded and considered by Genre *et al.*,[2] but it is necessary to explain the apparent paradox of patients in the rectal group having more distant than regional nodal metastases. This is attributable to the fact that resection was not performed in several patients whose distant metastases were discovered at exploration so that the status of regional nodes was unknown.

We have classified carcinoid tumors as being malignant when either muscular invasion and/or metastases were found. Fifty of the series of 135 cases (37%) were thus defined as being malignant carcinoids. Of the 106 patients in the clinical group, 43 (41%) had carcinoids which qualified for malignant status, in distinction to the autopsy series where only 7 (24%) were malignant.

It was apparent in this study that the larger the tumor the more likely its malignant propensity. At each level of the gastrointestinal tract there was a correlative relationship between those lesions that were 1 cm in diameter or larger and the presence of malignant characteristics. This relationship is demonstrated in Table 7.

TABLE 6. *Extent of Disease in 135 Patients with Gastrointestinal Carcinoids*

			Overt Malignancy			Pathologic Features: Metastases	
Location	Size	No.	No.	%	Invasive	Nodes	Distant
Rectum	Less than 1 cm	25	3	12%	1	2	0
	1–1.9 cm	6	3	50%	2	0	2
	2 cm or larger	6	5	83%	5	1	4
	Total	37	11	30%	8	3	6
Jejuno-ileum	Less than 1 cm	20	6	30%	6	1	0
	1–1.9 cm	12	12	100%	12	8	2
	2 cm. or larger	5	5	100%	5	5	5
	Total	37	23	62%	23	14	7
Stomach	Less than 2 cm	5	0	0%	0	0	0
	2 cm or larger	5	5	100%	5	5	3
	Total	10	5	50%	5	5	3
Duodenum	Less than 2 cm	10	0	0%	0	0	0
	2 cm or larger	2	2	100%	2	2	1
	Total	12	2	17%	2	2	1
Colon	Less than 1 cm	1	0	0%	0	0	0
	1–1.9 cm	2	2	100%	2	1	1
	2 cm or larger	7	7	100%	7	7	6
	Total	10	9	90%	9	8	7
Appendix	Less than 1 cm	29	10	34%	10	0	0

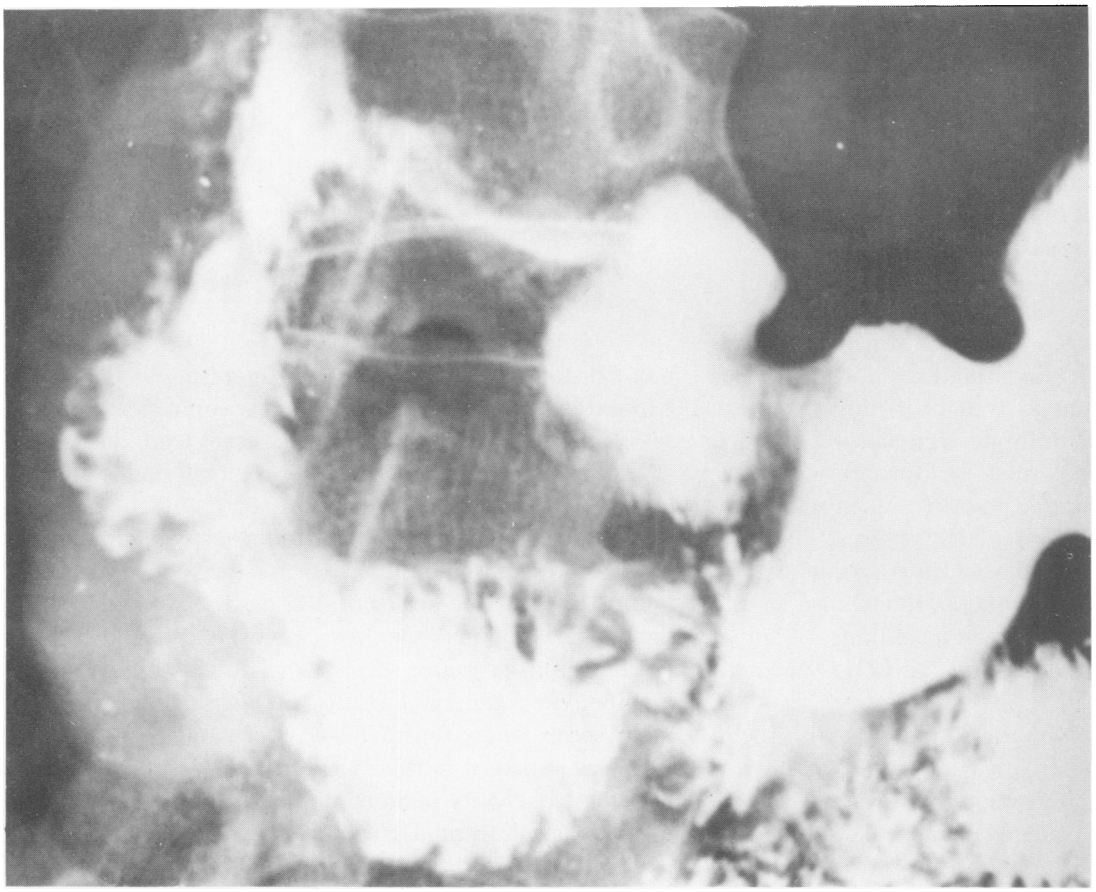

FIG. 2. Gastric filling defect discernible on barium study due to gastric carcinoid.

Site Distribution

The distribution of carcinoid tumors within their respective locales in the gastrointestinal tract is shown in Tables 8 and 9. It is of interest that the middle third of the rectum, i.e. 5–8 cm from the anal verge, provided the locus for 57% of the rectal carcinoids, and 50% of this group demonstrated malignant features. Forty three percent of the rectal carcinoids were sited in the proximal and distal thirds of the rectum, but malignant features were present in only 7% of this group.

Multicentricity

Carcinoids were found to be multiple in 40% of patients with jejunoileal tumors and in 8% of patients with rectal lesions. Multiplicity was not a feature of carcinoids in other locations.

TABLE 7. *Variable Effect of Size on Malignant Propensities (Tumors Greater than 1 Cm)*

Location	No.	Tumor: 1 cm + No.	%	Overt Malignancy No.	%
Colon	10	9	90%	9	90%
Jejuno-ileum	37	17	46%	23	62%
Stomach	10	6	60%	5	50%
Rectum	37	12	32%	11	30%
Duodenum	12	3	25%	2	17%

Associated Malignant Neoplasms

It is noteworthy that although patients with colon carcinoids did not have associated malignant neoplasms, such an association occurred at every other site (Table 10).

The Carcinoid Syndrome

Significant elevations of urinary 5-hydroxyindoleacetic acid were found in 1 of 4 patients with hepatic spread from gastric carcinoids, in 2 of 6 patients with rectal carcinoids metastatic to liver, and in 2 of 7 patients with

TABLE 8. *Rectal Carcinoids: Level of Involvement*

Level (cm)	No.	Malignant Features
11	1	0
10	5	1
9	3	0
8	3	2
7	6	4
6	7	2
5	4	2
4	3	0
3	1	0
2	2	0
Unspecified	2	0
	—	—
Total	37	11

TABLE 9. *Extra-Rectal Carcinoids: Site Distribution*

Jejuno-ileum (37)	
Jejunum	5
Ileum	29
Jejunum & Ileum	3
Stomach (10)	
Antrum	10
Duodenum (12)	
1st portion	10
2nd portion	2
Colon (10)	
Cecum	5
Descending colon	1
Sigmoid	4
Appendix (29)	
Base	2
Mid	4
Tip	23

hepatic metastases from jejunoileal carcinoids. The latter 2 were the only patients in the entire series manifesting the malignant carcinoid syndrome.

High levels of urinary 5-HIAA were also noted in one patient with a localized duodenal carcinoid. After excision of the duodenal carcinoid the level of 5-HIAA returned to normal.

Elevations of 5-HIAA were not seen in any of 9 patients with liver metastases from duodenal and colon carcinoids.

Survival

Of the 106 patients in the clinical series, 102 were followed. There was 5-year followup for 85 (83%) of the 102, the other 17 being alive and free of clinical disease less than 5 years. Ten-year data were available for 70 patients, and both the 5-year and 10-year survival figures are shown in Table 11.

It is interesting that all 18 patients in the jejunoileal group had tumors with malignant characteristics. Of the 11 patients whose rectal carcinoids were designated as malignant, 9 qualified for 5-year followup, only 2, or 22%, surviving 5 years or more. Two of the 6 patients dying of metastatic rectal carcinoid had tumors in the 1–1.9 cm range.

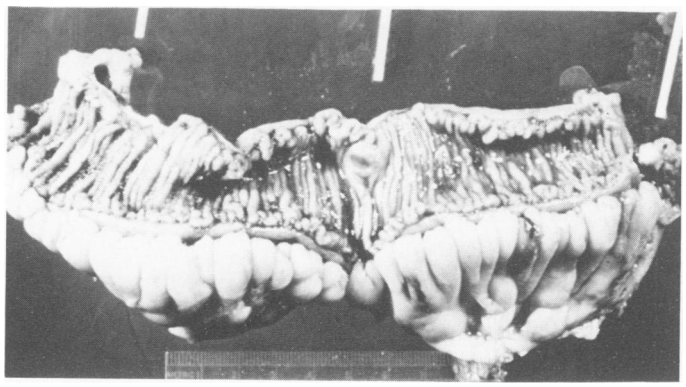

FIG. 3. Multiple carcinoid tumors within single jejuno-ileal segment.

TABLE 10. *Associated Malignant Neoplasms*

Site	No.	%
Rectum (37)	12	32
Jejuno-ileum (37)	14	37
Stomach (10)	2	20
Duodenum (12)	3	25
Colon (10)	0	0
Appendix (29)	4	13
Total (135)	35	26

Of the 24 patients with carcinoids metastatic to liver, 5 (21%) survived 5 years and 4 of these survived 10 years. The primary tumors were jejunoileal in 3 and of colon origin in 2. None of the 6 patients with hepatic metastases from rectal carcinoids survived 5 years.

No patient with an appendiceal carcinoid died of the disease and none developed evidence of recurrence or metastasis.

Discussion

Pathology

Lubarsch[3] demonstrated by serial sections that carcinoid tumors begin in the mucosal crypts of Lieberkuhn, and more specifically, Masson,[4] using silver staining techniques, showed their origin to be from the Kulchitsky cell. The affinity for silver stains led to the term argentaffin tumors but this histochemical phenomenon is neither specific for carcinoids nor consistently present, and is not necessary for their identification.

Many carcinoids are the size of a match head, most are no larger than a dime,[1] while a few exceed a diameter of 2 cm. They appear grossly and microscopically in a submucosal position even though they originate in the mucosa. They are composed of small cells, uniform in size and occurring in various patterns,[1] but neither cellular morphology nor histologic pattern can be used to distinguish the aggressive lesions.

Their expansion is usually horizontally within the submucosa as well as away from the lumen. The more aggressive lesions, having penetrated the wall of the viscus of origin, can invade mesentery, parietal peritoneum, and other organs. Metastases, when present, are usually to regional lymph nodes and liver and only occasionally to other distant sites such as lung, brain, and bone.

Lubarsch[8] thought these tumors to be malignant and called them "little carcinomas" to differentiate them from the ordinary adenocarcinoma. By 1907, however, most of the few discovered lesions had been found to be localized, and Oberndorfer[9] confidently emphasized their benign and harmless character and coined the term "carcinoid." In 1949, Pearson and Fitzgerald[11] reviewed the first large series of gastrointestinal carcinoids and found metastases in 38% of non-appendiceal cases and recommended that all carcinoids be considered malignant.

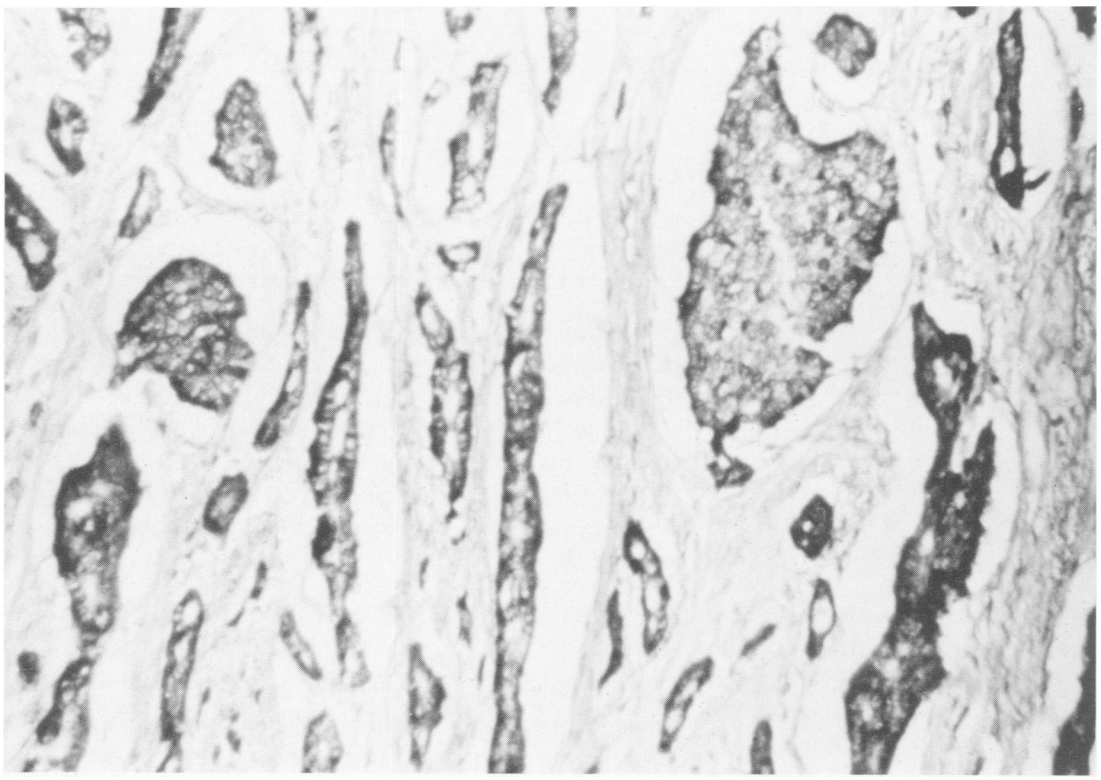

FIG. 4. Microscopic appearance of carcinoid with wavy strands and argentaffin positive columns of cell (×240).

McDonald[5] in 1956 was the first to propose an index of malignancy exclusive of known metastases. In a classic paper describing a large series of gastrointestinal carcinoids, he noted muscular invasion in all but one case of those extra-appendiceal carcinoids that had metastasized and suggested that carcinoids be reported by pathologists in terms of invasiveness. Peskin and Orloff[12] and Orloff,[10] in their study of rectal carcinoids, demonstrated a striking correlation between size and malignant behavior. They noted a 4% incidence of metastasis (and invasion) for tumors less than 2 cm in diameter in contrast to 80% (invasion, 93%) for lesions 2 cm or larger. Our findings (Table 6) support such a relation between size or invasiveness on the one hand and the occurrence of metastases on the other for all extra-appendiceal carcinoids. Furthermore, according to our data, the aggressiveness of those extra-appendiceal tumors in the 1–2 cm range approaches or equals that of the larger lesions.

Symptoms

Carcinoid tumors of the stomach, duodenum, appendix, and rectum are usually asymptomatic, symptoms related to associated diseases often leading to their incidental discovery.

Carcinoids of the large and small intestine usually provide symptoms, although for each the complaints may vary from vague and longstanding to dramatic and acute. Symptoms of colon carcinoids are indistinguishable from those of adenocarcinoma, and those beyond the reach of the sigmoidoscope will usually be diagnosed as carcinoma by barium enema or at laparotomy.

Symptomatic jeunoileal carcinoids cause acute or chronic intestinal obstruction. A small intramural jejunal or ileal carcinoid does not readily obstruct the bowel lumen but may serve as an intussusceptum. More commonly, the bowel may be kinked by neoplastic or fibrotic distortion of the mesentery, the primary tumor itself being

TABLE 11. *Survival of 85 Patients with Carcinoid Tumors*

		5 Year Data			10 Year Data			
Site	No.	Qualify	Survival	Per cent	Qualify	Survival	Per cent	Dead of Carcinoid
Rectum	37	30	14	46%	25	9	35%	6
Jejuno-ileum	18	14	8	57%	11	5	45%	4
Stomach	8	8	4	50%	7	3	43%	3
Duodenum	8	6	4	66%	4	2	50%	1
Colon	8	6	2	33%	6	2	33%	4
Appendix	27	21	17	80%	17	13	76%	0
Total	106	85	49	58%	70	34	49%	18

inconspicuous. McNeal[6] postulated that a carcinoid, by continued intramural lateral expansion after invasion and attachment to the muscularis, causes serosal indentation, kinking of the bowel, and apposition of adjacent serosal surfaces. Later, the fibrotic reaction commonly accompanying carcinoid tumors completes the adhesive and obstructive process.

Diagnosis and Treatment

Carcinoid tumors of the stomach, duodenum, jejunoileum, and colon are usually first defined as carcinoids by the pathologist a day or two after an operation in which significant and appropriate portions of the involved organ and its lymphatic drainage routes have been resected for other disease, real or suspected. Consequently, surgeons rarely plan therapy for these lesions and are willing to accept what has been done as adequate, and justifiably so.

For appendiceal and rectal carcinoids, however, a different situation is presented. Carcinoids of the appendix are also diagnosed postoperatively by the pathologist, but in this case the surgeon is confronted with the question of advisability of re-operation. There are contemporary proponents of an aggressive approach in the treatment of appendiceal carcinoids, but the most conservative and seemingly the most authoritative opinion is given by Moertel *et al.*[7] in their definitive paper based on the study of 144 cases. All had invaded muscularis, lymphatic invasion was present in 98%, and the serosa was involved in most. Despite this consistent local invasiveness, they found metastases in only 2 of the 3 lesions 2 cm or larger in diameter. Their categoric statement that simple appendectomy is adequate for all lesions except those with gross evidence of invasion or those greater than 2 cm in diameter reflects our view.

The rectal carcinoid is the only carcinoid which can be seen, felt, and diagnosed without a major surgical procedure. In most instances the therapeutic alternatives, as in the case of villous adenoma, are simple local excision or the more formidable abdominoperineal resection.

Peskin and Orloff,[2] in 1959, first proposed criteria for the choice of treatment in patients with rectal carcinoids. They emphasized the importance of obtaining a specimen, by biopsy or excision, adequate for microscopic examination for muscular invasion. In the presence of such invasion radical resection was recommended, while in its absence local excision would be deemed sufficient. Because of their observation of a precipitous increase in the incidence of muscular invasion and/or metastasis when rectal carcinoids attained a size of 2 cm or greater, they suggested that radical resection be seriously considered for these larger lesions even if invasive features were absent. Recently Orloff[10] re-affirmed these criteria and reported a 76% 5-year survival rate resulting from the application of these therapeutic principles.

Associated Malignant Neoplasms

The high incidence of associated malignant neoplasms in patients with carcinoid tumors has been known since Pearson and Fitzgerald's discovery of this occurrence in 23% of autopsy cases.[11] This association was more frequent in our patients than is usually reported,[1,10] particularly in the rectal group, for which we found an incidence of 32%. Another interesting finding in our series was that the associated malignant diseases were responsible for more deaths than the carcinoids.

Survival

Carcinoid tumors of the appendix carry an excellent prognosis, while the outlook is poorest for patients with colon carcinoids. The prognosis for patients with other gastrointestinal carcinoids is reasonably good, the 5-year survival rates in our series varying from 46% to 66%.

Shorb and McCune[13] referred to the long-term survival that can be expected in patients with gastrointestinal carcinoids, even in the presence of recurrence or metastases, and they emphasized the value of palliative resections for these patients. Wilson[15] has reported the benefits of palliative hepatic resection for symptomatic metastatic carcinoids, and, of our 24 patients with hepatic metastases, 2 underwent successful hepatic resections, and 21% of the total survived 5 years.

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