Villous Tumors of the Duodenum

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Nineteen cases of villous tumors of the duodenum are reported. They have a predilection for the ampullary region, tend to present with obstructive jaundice, especially if malignancy is present, and have a high prevalence of cancer (12 of 19, or 63%). Even when biopsies are available, the diagnosis of cancer is frequently missed (5 of 9 proven cancers, 56% false-negative rate), and it may be impossible to assess the presence of carcinoma *in situ* or invasive carcinoma without complete excision of the lesion. The authors' experience suggests that some small benign ampullary villous adenomas or those with carcinoma *in situ* can be excised locally but that pancreaticoduodenectomy is preferable in the fit patient for better local control both of extensive benign lesions and cancers without distant metastases.

VILLOUS TUMORS of the duodenum are relatively uncommon, about 70 cases having been previously reported.[1] The pathological categorization of villous tumors includes the designations villous adenoma, villoglandular polyp, adenomatous polyp, papillary adenoma, adenomyoma, and fibroepithelial polyp. These terms describe the different histologic elements in the tumor, but the clinical presentation and treatment of all of the variants are similar. They cause symptoms due to their location, usually near the ampulla of Vater (Fig. 1), presenting with biliary obstruction,[2] pancreatitis,[3,4] bleeding,[5,6] duodenal obstruction, vague abdominal complaints, intussusception,[7] or anemia because of chronic bleeding. These tumors are of additional importance because they, like villous adenomas of the stomach or colon, are premalignant and have a high prevalence of malignancy at the time of discovery.[5] Judgments concerning appropriate treatment have varied, in part because previous reports have been based on few cases.

We present an experience with 19 patients who had duodenal villous adenomas, the largest single series yet reported, along with our recommendations for their management.

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Methods

Records of all patients with the diagnoses of duodenal villous adenoma, duodenal tumor, and duodenal neoplasm seen at the Massachusetts General Hospital since 1972 were retrieved. Also, the office records of patients with these diagnoses were obtained from their physicians. We included only the 19 patients whose tumors were predominantly of the villous type and excluded duodenal leiomyomas, Brunner gland adenomas, and duodenal or ampullary cancers not clearly arising from a pre-existing villous tumor. Information on age, clinical presentation, diagnostic evaluation, surgical procedure, pathology, and follow-up were recorded.

Results

There were 13 females and six males with an average age of 62 years (range: 42–82) (Table 1). The tumors were located at the ampulla of Vater in 16 of 19 cases, and one case each in the second, third, and fourth portions of the duodenum. The presenting symptoms included jaundice in 12, bleeding in four (1 acute and 3 chronic), cramps and vomiting in one, vague complaints (nausea, anorexia, weight loss) in seven, acute bacterial cholangitis in two, and pancreatitis in three. The patients with malignant lesions presented with jaundice in 10 of 12 cases (all 9 with invasive cancer and 1 of 3 with carcinoma *in situ*), whereas only two of seven patients with benign tumors were jaundiced. The length of follow-up ranges from 2 months to 14 years with an average of 4 years.

The diagnosis of a duodenal tumor was not always made before operation. The upper gastrointestinal contrast study (UGI) was suggestive in six of 12 patients (Fig. 2), and a hypotonic duodenogram showed the lesion in

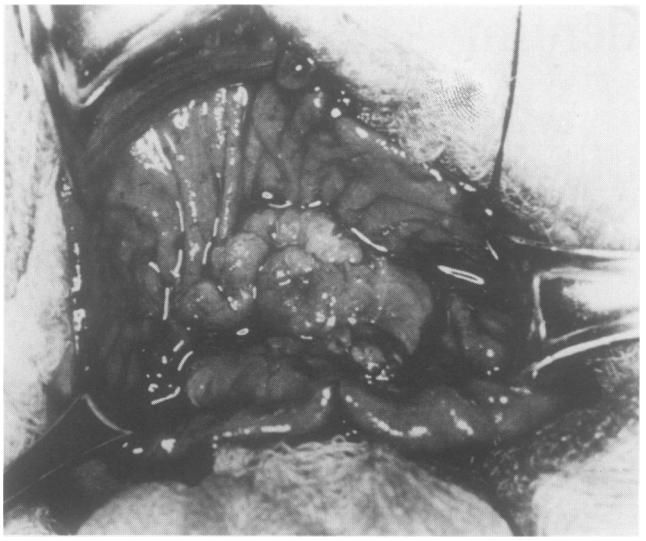

FIG. 1. Villous adenoma of ampulla, seen through the opened duodenum.

three cases when the UGI was read as normal.[8] Ultrasonography, performed in 10 patients who had jaundice or elevated serum amylase, showed dilated bile ducts in all 10 but showed a peripancreatic mass in only one. Cholangiography by either transhepatic needle or retrograde catheter demonstrated the ampullary obstruction in all 12 jaundiced patients, but transhepatic cholangiography in three of the jaundiced patients defined a duodenal mass as the cause of the obstruction in only one of them.

Endoscopic examination found the tumor in nine of 10 patients in whom it was used. Endoscopic biopsies were done in nine patients with cancer and missed the areas of malignant change in five of them (56%).[9] The biopsy from a sixth patient showed only carcinoma *in situ* (CIS), but examination of the full specimen after pancreaticoduodenectomy showed invasive cancer in the submucosa and lymphatics. One of the patients with biopsy-proven cancer had had an endoscopic examination of a villous tumor of the papilla (without surgery) 5 years before.

Of the seven benign tumors in the series, one had a biopsy with a biliary and gastric bypass because of the extent of the mass and the advanced age of the patient. One patient had a pancreaticoduodenectomy (Whipple procedure), two had local duodenal resections, and three had submucosal excision of the tumor (Fig. 3). The patient treated with the Whipple procedure had troublesome problems with diabetes after operation and died at home 17 months after the surgery.

One benign tumor recurred locally after complete surgical excision. The patient, presenting with relapsing pancreatitis, was found to have a villous adenoma on the anterior wall of the second portion of the duodenum. The mass was resected along the submucosa and a sphincteroplasty was performed. Although she remained asymptomatic, routine follow-up endoscopy and biopsy showed recurrence at 3.5 years. After pancreaticoduodenal resection, histological examination of the specimen showed

TABLE 1. *Patient Histories*

Patient	Age	Sex	Symptoms	Diagnostic tests	Surgery	Pathology	Follow-up
1	79	F	Episodic abdominal pain for 18 months, elevated LFTs	US—dilated ducts CT—dilated biliary and pancreatic ducts UGI—normal	Biopsy only; biliary and gastric bypass	Papillary adenoma	Doing well @ 18 months
2	53	F	Recurrent pancreatitis	UGI—filling defect in second part duodenum ENDO—mass @ ampulla	Submucosal excision and sphincteroplasty	Villoglandular polyp	Alive @ 4 years, recurrent at 3.5 years
Recurrence			None	ENDO—mass @ ampulla	Whipple resection	Tubulovillous adenoma	Alive @ 8 months
3	62	F	Abdominal pain, nausea, distension; morphine-Prostigmin(+)	ENDO—normal	Submucosal excision	Villoglandular Polyp	Alive @ 7 years, no recurrence
4	68	M	Chest & abdominal pain, elevated amylase	UGI—normal HD—defect @ ampulla US—dilated bile ducts ENDO—mass @ ampulla	Whipple resection	Papillary adenoma of ampulla of Vater	Died @ 17 months, many complications of Whipple, no autopsy
5	61	F	Malaise, abdominal fullness	UGI—mass in third part HD—polypoid defect in proximal third part of duodenum	Resection of duodenum with duodenojejunostomy	Villous adenoma	Alive @ 7 years, no recurrence
6	70	F	Recurrent UGI bleeding	UGI—tumor in second and third parts of duodenum	Local excision	Villoglandular polyp	Alive @ 4.5 years, no recurrence
7	65	F	Jaundice, iron deficiency anemia	UGI—normal HD—mass in duodenum	Submucosal excision	Villoglandular polyp	Died @ 4 years of respiratory failure, no recurrence @ autopsy

TABLE 1. (*Continued*)

Patient	Age	Sex	Symptoms	Diagnostic tests	Surgery	Pathology	Follow-up
8	76	M	Jaundice, anemia, weight loss	UGI—large mass in duodenal loop US—dilated bile ducts multiple liver mets ENDO—large mass in duodenal loop	None, biopsy only by endoscopy	Villous adenoma	Died of arrhythmia pre-op, no autopsy
9	70	F	Anorexia, nausea, diarrhea, jaundice	CT—pancreatic mass UGI—mass in second and third parts of duodenum THC—distal CBD obstruction due to duodenal mass	Submucosal excision	Papillary adeno-carcinoma invasive	Died @ 1 year with liver metastases
10	56	F	Jaundice, fever	US—dilated bile ducts THC—dilated ducts and mass in second part of duodenum	Whipple resection	Villous adenoma with moderately differentiated adenocarcinoma, 3 of 13 nodes (+)	Died @ 6 months with liver metastases
11	78	M	Biliary obstruction, fever, chills	US—dilated ducts ENDO—mass @ ampulla	Biliary and gastric bypass	Papillary adenoma with focal well differentiated adenocarcinoma	Died @ 5 years; low-grade GI bleeding; mass enlarging on repeat exams
12	76	F	Jaundice, weight loss, epigastric distress	THC—obstruction by stone US—stone in duct and mass by head of pancreas	Biliary and gastric bypass	Villous adenoma with focal superficial adenocarcinoma	Alive @ 18 months, chronic pain, pancreatic insufficiency
13	41	M	Jaundice, recurrent cholangitis	US—dilated ducts ENDO—mass @ ampulla biopsy benign	Biliary and gastric bypass	Villous adenoma with invasive cancer and liver metastases	Alive @ 2 months
14	59	F	Anorexia, diarrhea	UGI—duodenal mass	Whipple resection	Villous adenoma with CIS, all lymph nodes negative	Alive @ 14 years, no recurrence, multiple problems with complications of Whipple
15	63	F	Nausea, anorexia, gastric outlet obstruction	UGI—3.5 cm polyp in second part of duodenum	Endoscopic resection	Villous adenoma with CIS	Alive and well @ 2 years, repeat endo exams showed residual polyp, no cancer
16	42	M	Gardner's syndrome, biliary obstruction, chronic and recurrent pancreatitis	ENDO—mass @ ampulla, multiple gastric polyps, biopsy benign ERCP—dilated CBD and pancreatic duct	Whipple resection	Villous adenoma with CIS	Doing well @ 1 year
17	53	M	Routine exam showed obstructive LFTs	US—dilated ducts ENDO—mass @ ampulla biopsy benign UGI—normal	Whipple resection	Villous adenoma with invasive cancer, lymph nodes negative	Doing well @ 6 months
18	43	F	Juvenile polyposis, biliary obstruction, cramps, vomiting	US—dilated ducts ENDO—mass @ ampulla biopsy malignant UGI—normal	Whipple resection	Invasive adenocarcinoma arising in villous adenoma, multiple duodenal adenomas	Doing well @ 6 months
19	71	F	Jaundice, fever, 20 lb weight loss	US—dilated ducts ENDO—mass @ ampulla biopsy benign	Whipple resection	Invasive adenocarcinoma arising in a villous adenoma	Doing well @ 3 months

CBD = common bile duct; CIS = carcinoma *in situ;* CT = computerized tomography scan of abdomen; ENDO = flexible gastroduodenoscopy; ERCP = endoscopic retrograde cholangiopancreatography; HD = hypotonic duodenogram; LFT = liver function tests: serum bilirubin, alkaline phosphatase, SGOT; THC = transhepatic cholangiogram; UGI = upper gastrointestinal series; US = ultrasound.

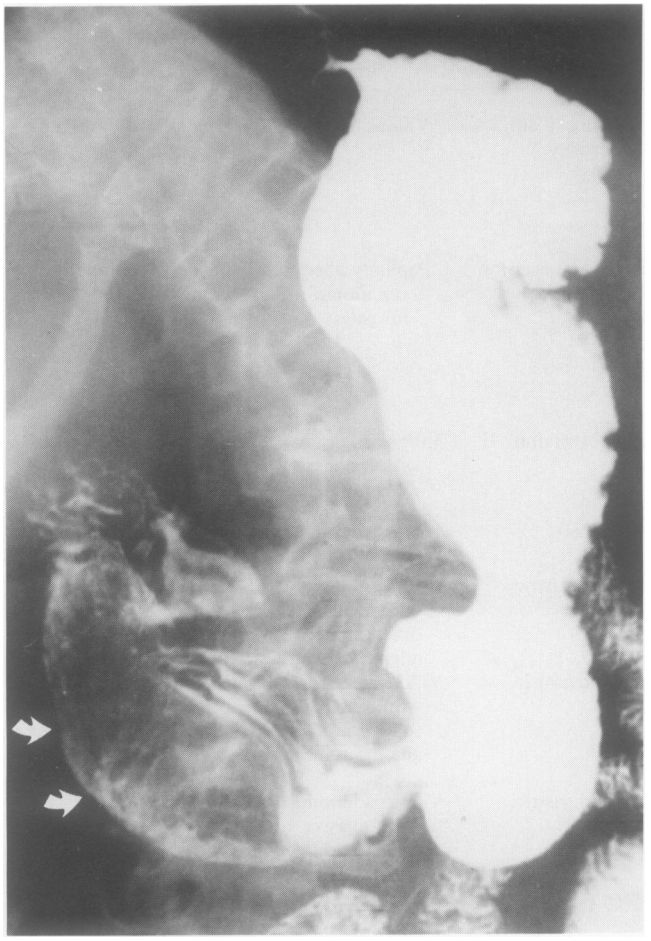

FIG. 2. Upper GI study in a patient with a large villous tumor of the duodenum.

benign villous adenoma growing into the pancreatic duct and distal common bile duct. She has been well for 8 months following the second operation.

In 12 cases, cancer was found in the villous tumor (63%), three of which were CIS. Of the latter patients, one is alive and well 14 years following a Whipple procedure. The second patient was treated originally by endoscopic removal of an ampullary polyp containing CIS, had recurrence of benign villous adenoma at 2 months, again treated by endoscopic excision, but has had no signs of carcinoma 2 years later. The third patient had Gardner's syndrome and presented with chronic pancreatitis and biliary obstruction. Although the initial biopsy showed only benign villous adenoma, examination of the complete specimen after pancreaticoduodenectomy showed CIS. This patient has been completely well for 1 year to date.

Of nine patients with invasive cancer arising from the villous adenoma, one had a biopsy of a large duodenal mass that showed only a villous adenoma but had multiple liver metastases shown by scan and borne out by his subsequent clinical course. Two others whose biopsy also showed only villous adenoma were found at operation to have invasive carcinoma, one with histologically positive lymph nodes, and one with liver metastases. The first of these died with liver and other distant metastases at 6 months, and the other was diagnosed and bypassed only recently. A fourth patient whose biopsy showed focal carcinoma in a villous adenoma was treated by gastrojejunostomy and choledochojejunostomy for palliation. At age 78, he had been judged too old for pancreaticoduodenectomy, but he survived for 5 years despite chronic low-grade bleeding from the tumor. The fifth patient had a submucosal excision of a presumed villous adenpma that was later shown to contain an invasive papillary carcinoma. This patient had multiple follow-up endoscopies that showed no local recurrence, but the patient died 12 months later with liver metastases. In the sixth case, an open biopsy showed superficial adenocarcinoma in a villous adenoma. Eighteen months after undergoing biliary and gastric bypasses, she has chronic pain and pancreatic insufficiency.

Our three most recent cases have been treated by pancreaticoduodenectomy. One had a preoperative biopsy showing carcinoma, and one showed CIS. The other had only benign elements in the biopsy specimen. Because of our accumulated experience, we judged it safer to presume cancer and opted for the definitive treatment. The resected specimen in each case (Fig. 4) showed adenocarcinoma invasive to the submucosa and in lymphatics, but all lymph nodes were negative for metastatic cancer. All three patients are well at short-term follow-up (3–6 months).

Discussion

Since 1928, when Golden published the first definitive case of a villous adenoma of the duodenum,[10] almost 70

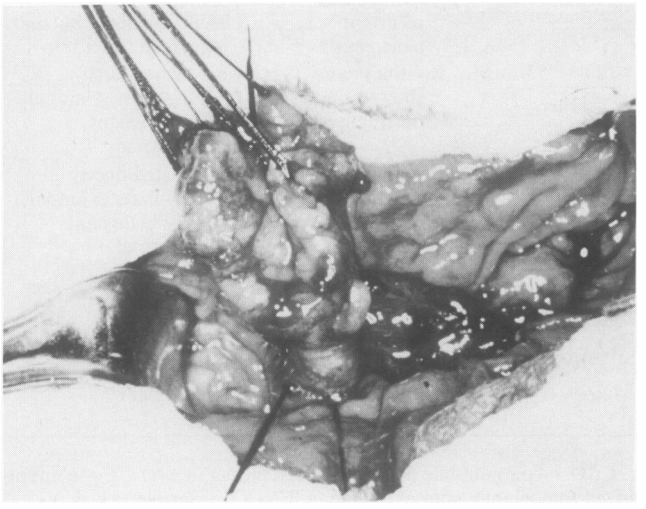

FIG. 3. Operative photograph showing the submucosal excision of a benign villous adenoma.

cases have been added to the English literature. The terminology applied to these tumors has been inconstant and confusing, with similar tumors being called papillary adenoma, papilloma, adenomatous papilloma, papillary tumor, villous adenoma, villoglandular polyp, adenomatous polyp, fibroepithelial polyp, and adenomyoma. As with villous adenomas elsewhere in the gut, it has been recognized that cancer arises with distressing frequency in duodenal villous tumors. We assume that these tumors begin as benign adenomas and undergo malignant degeneration, thereby differing intrinsically from the more common ampullary cancers that are malignant *ab initio.*

There is a markedly disproportionate proclivity for villous tumors of the duodenum to arise from or near the ampulla of Vater. The reasons for this phenomenon are only speculative. In general, epithelial tumors of the small bowel occur more in the proximal than in the distal intestine,[11] and there is a similar proximal distribution of neoplasms in rats given the carcinogen azoxymethane.[12] While similar factors have not been identified in man, it is possible that the presence of carcinogens or cocarcinogens in the bile or pancreatic secretions could explain the finding of such a large proportion of the villous tumors at the ampulla of Vater. Because the carcinogenic environment and any intrinsic susceptibility of the local mucosa are not changed by the local removal of the tumor and because local recurrence of villous adenomas is common, there is life-long need for close follow-up surveillance.

Fiberoptic endoscopy with full visualization of the duodenum was probably the most useful and accurate diagnostic tool, because it allowed both visual identification and biopsy of the tumor. Nonetheless, biopsies done through the endoscope missed areas of malignant change in five of nine patients.

The issue of malignant change of a villous tumor of the duodenum is similar to that of colonic villous adenomas but has been less well defined because of the small number of reported cases. In a large review, the prevalence of malignancy was found to be 35%,[5] and a range of 25–45% is often quoted. Many of the malignancies, perhaps 40%, are still at the stage of carcinoma *in situ* when found. In the present series, 12 of the 19 tumors (63%) contained malignant elements. Nine were frankly invasive or metastatic at initial presentation, and three had carcinoma *in situ.* To assess the presence or absence of malignancy accurately, the entire specimen must be available for examination. Smaller biopsies such as those obtained endoscopically may miss areas of malignant change or invasion,[9] as verified by our experience. Presentation with obstructive jaundice should particularly raise the suspicion of cancer; 10 of 12 jaundiced patients had cancer, and all nine invasive cancers presented in this way. It may be that the symptoms associated with early villous tumors in this region are vague and easily ignored but that malignant degeneration is then more likely to cause sufficient biliary obstruction to demand attention.

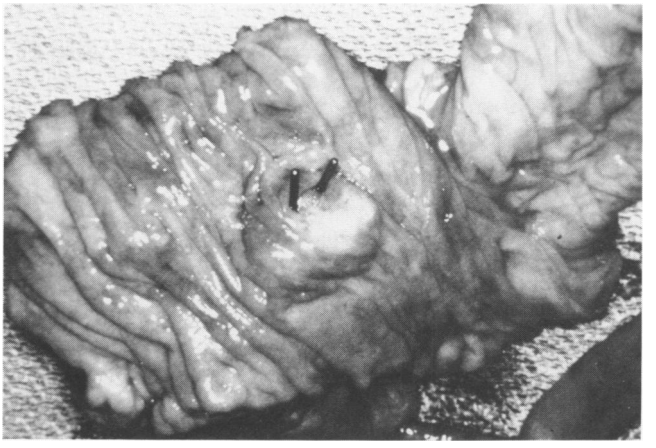

FIG. 4. Pancreaticoduodenectomy specimen in case 17. The probes exit from the orifices of the bile duct and pancreatic duct. Note the white, hard area of cancer within the larger villous structure.

The treatment of villous tumors of the duodenum can be individualized within certain limits. The presenting symptoms, location, size, and extent of the lesion, the presence and stage of carcinoma, and the medical status of the patient must all be considered.

Endoscopic removal may be a possibility for some pedunculated lesions but risks bleeding, perforation, and local complications such as pancreatitis when the tumor is close to the biliary and pancreatic ducts. Furthermore, villous tumors are usually sessile, often of a size not amenable to endoscopic removal, and tend to extend upward into the bile duct or pancreatic duct (Fig. 5).

Benign tumors located near the ampulla of Vater can sometimes be removed by submucosal excision with local reconstruction of the pancreatic and biliary ducts using a sphincteroplasty technique. This procedure has the potential to cure the lesion without the morbidity and mor-

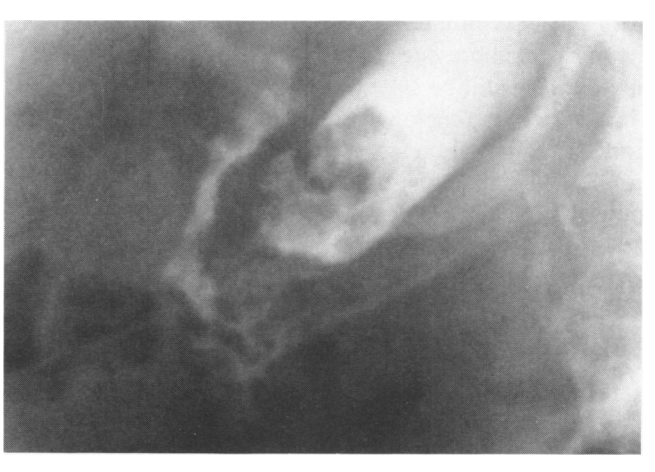

FIG. 5. Endoscopic retrograde cholangiogram in case 13. The large villous tumor of the ampulla extends well up the bile duct and partially obstructs it.

tality of a pancreaticoduodenectomy. Local recurrence after limited excision is a hazard; one of our patients had recurrence of villous adenoma after endoscopic excision and one after surgical excision. Recurrence of a benign adenoma after adequate local removal is nonetheless uncommon.[1,5]

Perhaps some patients with carcinoma *in situ* also can be treated with complete local excision alone. With the use of fiberoptic endoscopy to follow and watch for local recurrence, a more complete resection could be undertaken in the event of recurrence.

Cholecysto- or choledochoenteric bypass have been recommended by some[13,14] as an alternative to excision and sphincteroplasty. The choice may depend on the size of the tumor and the size of the pancreatic and common bile ducts. However, the tumor, if left in place, remains a potential threat for bleeding.

Patients with invasive carcinoma without evident metastases can be predicted to have the same results from a pancreaticoduodenal resection as any other patient with duodenal or nonpancreatic periampullary carcinomas—approximately 30% 5-year survival.[5,15,16] The presence of regional lymph node metastases substantially reduces the chance of cure, and, of course, the finding of distant metastases indicates that the fate of the patient is already determined.

Sixty-three per cent of the patients in this series harbored cancer in the villous tumor, often not proven by tissue diagnosis until complete excision and examination of the entire tumor. For this reason alone, the case can be made for pancreaticoduodenectomy on presumption of cancer in any patient who is physically fit for the larger operation. In addition, presentation with jaundice or the finding of hard areas within the tumor on palpation at operation are strong specific indices of cancer. Large tumors and those that spread up along the biliary and pancreatic duct epithelium may not be removable except by pancreaticoduodenectomy. In those cases in which the histological examination of a locally excised tumor reveals the unexpected presence of an invasive cancer, the patient may perhaps still be salvaged by reoperation to perform a more adequate regional resection. Today the expected mortality from pancreaticoduodenectomy should be well under 5%,[17] safe enough that a curative operation should not be denied to most patients. Eight patients in this series had a pancreaticoduodenal resection, with no operative deaths.

There is a very high incidence of duodenal adenomas[18,19] and an increased incidence of periampullary carcinoma[20] in patients with polyposis syndromes. Yao et al.,[19] reviewing 29 cases of duodenal tumors in patients with familial polyposis of the colon, found cancer in eight of 14 with Gardner's syndrome and four of 15 with familial polyposis coli. The duodenal tumors in these cases were usually large and symptomatic at the time of diagnosis, in contrast to the small, asymptomatic polyps found on routine endoscopy in the majority of patients with Gardner's symdrome and familial polyposis coli. Periodic upper GI endoscopy is probably warranted in all patients with polyposis syndromes in order to monitor the duodenum for changes suggestive of carcinoma and to facilitate earlier treatment.

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