

# Villous adenomas and carcinoma of the duodenum in Gardner's syndrome

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**Summary:** Patients with Gardner's syndrome are increasingly found to have polyps on routine upper gastrointestinal endoscopy, and their risk of developing periampullary carcinoma is between 3–12%. We report a 45 year old man with Gardner's syndrome who presented with periampullary carcinoma 5 years after colectomy. Review of the literature amassed another 21 cases of periampullary carcinoma in patients with Gardner's syndrome.

## Introduction

Familial adenomatous polyposis (FAP, also known as familial polyposis coli) and related syndromes, such as Gardner's syndrome, are genetically determined growth disorders that predispose to tumours in various parts of the body.<sup>1</sup> The mode of inheritance is autosomal dominant, and the FAP gene has been localized to chromosome 5.<sup>2</sup> The association of polyposis coli, soft tissue tumours and osteomas was originally described by Gardner in 1951.<sup>3</sup> With the increasing availability of fiberoptic endoscopy, gastric and duodenal polyps have been found in 46% of patients with FAP and Gardner's syndrome,<sup>4</sup> although polyps in up to 100% of Japanese patients have been reported.<sup>5</sup> Periampullary carcinoma was described as a complication of Gardner's syndrome in 1967.<sup>6</sup> Since that time we have found 21 examples of this association in the world literature, to which we now add a further case.

## Case report

A 45 year old man presented in 1987 with a short history of painless obstructive jaundice. Six years earlier Gardner's syndrome had been diagnosed on the basis of an osteoma at each angle of the mandible (Figure 1), soft tissue tumours in the scalp and on the dorsum of both feet and multiple colonic polyps. He had undergone abdominal colectomy with ileorectal anastomosis in 1982 and was followed up with annual proctoscopy and rectal

fulguration. Multiple small gastric and duodenal polyps were diagnosed endoscopically in 1985. There was no previous family history, but his 17 year old son also has Gardner's syndrome.

Ultrasound examination showed a dilated common bile duct and gallbladder with a small mass in the region of the ampulla. At endoscopy there were multiple tiny polyps carpeting the stomach and numerous polyps throughout the duodenum. A larger ulcerated tumour was observed at the papilla; biopsies showed villous adenoma. ERCP (Figure 2) showed gross dilatation of the biliary and pancreatic ducts. Hypotonic duodenography confirmed a 4 cm periampullary mass, and at least two more sizeable polyps were seen in the proximal jejunum.

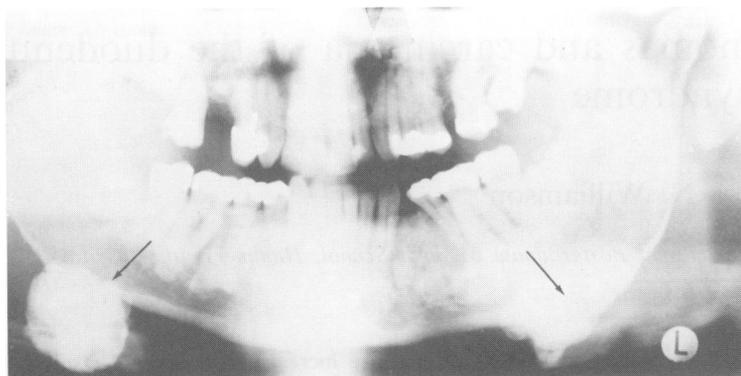
The patient was submitted to conservative proximal pancreatectomy,<sup>7</sup> preserving the stomach, pylorus and first 5 cm of the duodenum. Besides the obstructing tumour in the descending duodenum, a second soft polypoid lesion was palpable just distal to the duodenojejunal flexure and was included in the resection specimen. Recovery was uneventful and the patient was discharged at 12 days. Polyps were seen throughout the excised segment of small intestine, and all those sampled proved to be villous adenomas. The larger lesion at the papilla showed early invasive adenocarcinoma.

## Discussion

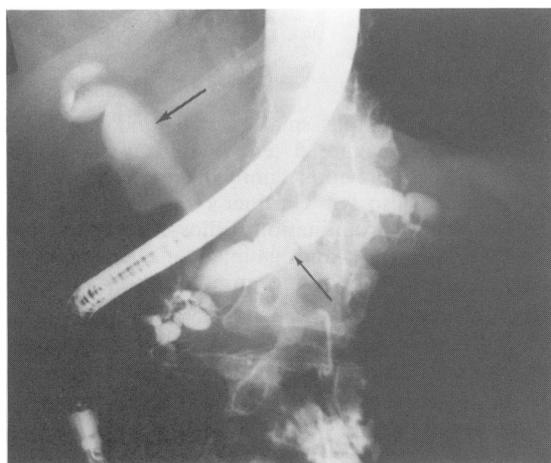
The genetic and premalignant nature of familial adenomatous polyposis has been recognized since Cripps<sup>8</sup> described two members of the same family

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**Figure 1** Radiograph of the mandible showing an osteoma at each angle (arrowed).



**Figure 2** Endoscopic retrograde cholangiopancreatogram showing dilatation of the bile duct (broad arrow) and pancreatic duct (narrow arrow) behind a duodenal tumour obstructing the papilla.

with rectal polyps in 1882 and Handford<sup>9</sup> noted an association with carcinoma of the colon in 1890. It is increasingly apparent that the polyposis syndromes can affect not just the large bowel but the entire gastrointestinal tract, and extraintestinal manifestations are frequently present as well. The incidence of periampullary tumours in Gardner's syndrome has been estimated at between 3–12%.<sup>10,11</sup> Patients with Gardner's syndrome may have a 100-to 200-fold increased risk of developing periampullary carcinoma compared with the general population.<sup>10</sup>

The clinical features of the 22 patients unearthed by our review of the literature are shown in Table I. Interestingly, there is a male predominance (70%), even though the mode of inheritance of

Gardner's syndrome is autosomal dominant and not sex-linked, but the number of patients is small. The interval between diagnosis of colorectal polyps and periampullary carcinoma ranges between 0–30 years (median 15 years; mean 14.2 years). In 16 of 20 cases other duodenal polyps were stated to be present. Only 9 of these 16 case reports described the type of polyp, *viz.* 8 adenomas and 1 hamartoma. The type of adenoma was classified in 4 of the 8 cases, and all 4 were villous (papillary) adenomas. Adenocarcinomas are known to develop more frequently in villous adenomas than in other adenomas of the small intestine.<sup>12</sup> Adenocarcinomas of the small bowel are rare, being 100–160 times less prevalent than carcinomas of the stomach or large intestine, but when they do occur they have a marked proximal distribution: over 40% arise within the duodenum, and no less than 80–90% within the duodenum and proximal jejunum.<sup>12,13</sup> Gastric polyps found in patients with FAP and Gardner's syndrome are of the fundic gland type, and gastric adenomas are extremely uncommon.<sup>4</sup>

Surgical management of periampullary carcinoma in Gardner's syndrome presents a dilemma because of the extent of gut actually or potentially affected. Our patient had already undergone colectomy and had additional polyps in the stomach and jejunum, for which radical resection seemed impractical. Hence a conservative pancreatotomy was performed, preserving the pylorus and proximal duodenum (which was clear of polyps) together with the jejunum-ileum, but fortunately removing a large polyp in the region of the duodeno-jejunal flexure. The advantages of conservative pancreatotomy over the traditional Whipple's operation are avoidance of the post-gastrectomy syndromes and marginal ulceration, return of normal gastric function and improved postoperative weight gain.<sup>7</sup>

**Table I** Periampullary carcinoma in patients with Gardner's syndrome

Case	(reference)	Sex	Age at diagnosis		Associated stigmata of Gardner's syndrome		
			of colonic polyps	of periampullary tumour	Osteomas	Soft tissue tumour	Supernumerary teeth
1	(16)	M	36 (PM)	36 (PM)	+	+	-
2	(6)	M	24	44	+	+	+
3	(6)	F	37	38 (PM)	+	-	-
4	(17)	F	35	36	+	+	-
5	(18)	M	33	40	+	+	+
6	(19)	M	29	49	+	+	-
7	(19)	U	U	U	U	U	U
8	(19)	U	U	U	U	U	U
9	(20)	M	31	45	+	+	-
10	(21)	M	23	40	+	+	+
11	(22)	M	37	63	+	+	-
12	(22)	F	26	39	-	+	-
13	(23)	M	47	49	-	+	+
14	(24)	M	44	60	+	-	-
15	(25)	M	22	50	-	+	-
16	(10)	M	35	59	+	+	+
17	(10)	M	68	68	-	-	-
18	(15)	M	29	48	+	+	-
19	(26)	F	25	55	-	+	-
20	(27)	F	29	56	-	+	-
21	(28)	F	29	41	-	-	+
22	(this report)	M	39	45	+	+	+

U = unstated; PM = diagnosed post-mortem.

Periampullary carcinoma is the second commonest neoplasm and cause of death in patients with FAP.<sup>14,15</sup> Indeed, in one series of patients with FAP undergoing colectomy and ileorectal anastomosis at the Cleveland Clinic over the last 25 years, more patients have died of periampullary carcinoma than of rectal carcinoma.<sup>1</sup> The need for routine upper gastrointestinal endoscopy in patients with FAP and Gardner's syndrome is clearly appar-

ent,<sup>4,10,15</sup> with a high index of suspicion for those polyps found to be villous adenomas.

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