

Original article

Total Colectomy with Mucosectomy and Ileal Pouch-Anal Anastomosis in Patients with Familial Adenomatous Polyposis

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SUMMARY

Purpose: The aim of this study was to present our experience in the treatment of patients with familial adenomatous polyposis (FAP) and their families.

Materials and methods: The material comprises 36 patients with FAP who had undergone prophylactic colorectal surgery, including those operated on because of colorectal cancer (CRC). Anal continence preserving surgery was performed on 34 patients: 30 had ileal-pouch anal anastomosis as primary surgery, 4 had ileal-pouch anal anastomosis as secondary operation after ileorectal anastomosis. Total proctocolectomy was performed on 2 patients with FAP and rectal cancer. Two patients with desmoid tumours were detected. Surgical outcome was assessed on the basis of hospital records. A questionnaire was used to evaluate the postoperative functional outcome. Finally, most family members had blood samples taken for detection of mutation of the APC gene.

Results: The histology of the specimen retrieved from these patients showed in four a malignant tumour which had not been suspected preoperatively: two rectal adenocarcinomas (one in the ileorectal group), and two carcinomas in situ. One of these patients accepted the option for pouch excision and permanent ileostomy but the other refused. Surgical outcome was very good, without any major early or late postoperative complications. Functional results after ileal-pouch anal anastomosis are satisfactory. All pouches are in place and functional.

Conclusions: Preventive surgery is indicated in patients with FAP. Total colectomy, anal mucosectomy and ileal-pouch anal anastomosis, when possible, is preferred over ileorectal anastomosis or total colectomy with permanent ileostomy. The coexistence of cancer, the age of the patient, the development of desmoid tumours or extracolonic neoplastic tumours are factors that influence the choice of the operation and the outcome.

Key words: Familial adenomatous polyposis; ileal pouch-anal anastomosis; adenomas; colorectal cancer; desmoid tumours

INTRODUCTION

The hallmark of familial adenomatous polyposis (FAP) is the growth of hundreds of adenomatous polyps throughout the colon and rectum by young adulthood. Without intervention almost all patients develop colorectal cancer by age 40. FAP is inherited, in an autosomal dominant manner and is responsible for about 0,5-1 percent of CRC, affecting 1 in 8000 individuals in the US. The predisposing adenomatous polyposis coli (APC) gene map to chromosome 5q21, was cloned in 1991, and encodes a 2483-amino acid protein. Germline (i.e. inherited from generation to generation) mutations in the APC gene result in FAP. Nearly all APC mutations causing FAP yield a shortened or truncated protein. Mutations in APC can also predispose to related clinical entities that are sometimes distinguishable, including Gardner syndrome, attenuated adenomatous polyposis coli (AAPC), and the majority of kindreds with Turcot syndrome. Mutations in APC found in the colon and rectum but not in the germline also occur as very early events in sporadic (without a significant family history) CRC.

The diagnosis of FAP is usually based on the presence

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of >100 colorectal adenomatous polyps on examination of the presenting patient (proband or index case). In autosomal dominant inheritance, on average 50 percent of the patient's first-degree relatives (parents, siblings, and offspring) will be at risk. Subsequently, clinical approach to FAP involves both patients and their family members and can be divided into three steps: identification, surveillance and therapeutic management. The main aim of treatment in FAP is to stop the progression of one or more colorectal adenomas to cancer, as in over 80%, the cause of death is CRC. Therefore preventive surgical treatment is required. The aim of this retrospective study is to define our approach in management of these patients.

PATIENTS AND METHODS

Records of 36 patients, 21 males and 15 females with a mean age of 31.8 years (range 17 to 56 years) were studied with respect to preoperative, peroperative and postoperative data. Thirty-two patients were referred to our department for their first operation and four had been already treated elsewhere by ileorectal anastomosis. In the first group of patients preoperative workout revealed an adenocarcinoma in the rectum in two patients, an adenocarcinoma of the transverse colon in a third, and high degree dysplastic lesions in five other patients. In the second group, the indication for surgery was inability to control recurring adenomas after fulguration.

The two patients with rectal adenocarcinoma were treated by total proctocolectomy and permanent ileostomy. In the remaining 34 patients, including those with previous ileorectal anastomosis and the patient with the adenocarcinoma of the transverse colon, a total colectomy with preservation of the anal sphincter, anal mucosectomy and ileal pouch-anal anastomosis was performed (IPAA). (Table 1)

The histology of the specimens retrieved from these 34 patients showed a malignant tumour which was not suspected preoperatively in four of them: two rectal adenocarcinomas (one in the ileorectal group) and two carcinomas in situ.

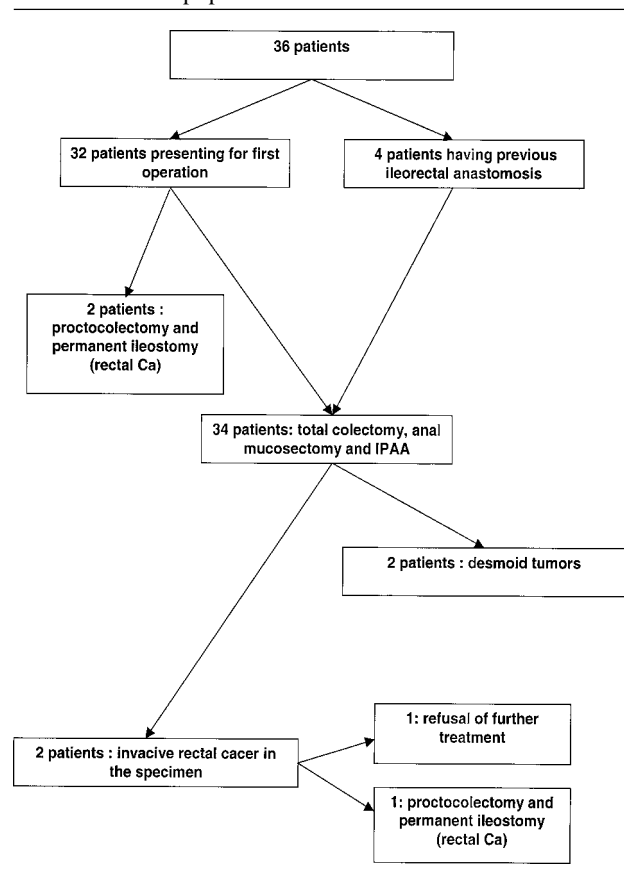
In the two patients found to have infiltrating carcinomas, a reoperation consisting in pouch excision with permanent ileostomy was proposed. One of these accepted this option, but died from brain tumour seven years later. The second, who refused the permanent stoma, died 9 months later from progressive disease.

All patients were put in a surveillance programme including:

- Regular evaluation of the functional results of the restorative proctocolectomy.
- Annual gastroscopy for detection of polyps in the upper gastrointestinal tract and in particular in the second part of the duodenum and the periampullary region.
- "Pouchoscopies", every year for early detection of reappearance of polyps at the site of anastomosis and in the pouch itself.
- Regular clinical examination and upper and lower abdominal and parietal ultrasound for detection of possible development of a desmoid tumour or other malignant tumour, intraabdominally or in the abdominal wall.

In two patients (one of the proctocolectomy and one of the ileal-pouch anal anastomosis group) desmoid tumours were detected: in the first patient the tumour

Table 1. Patient population



was intrabdominal and in the second the CT scan revealed two desmoid tumours in the abdominal wall at the rectus sheath at the site of the surgical scar. (figure 1)

The first patient had his tumour excised, but died with recurrence of the desmoid tumour 22 months later. The second patient was operated on, and the desmoid tumours of the abdominal wall were removed. During the exploratory laparotomy of this patient, three other intraabdominal desmoid tumours were found. (figure 2) These tumours were undetected by the preoperative CT scan.

One patient developed a cystic mass originating from the pancreas, which was removed by laparotomy. Histology showed it to be a neoplastic tumour originating from pancreatic stem cells with potentially both endocrine and exocrine differentiation and was considered to be a

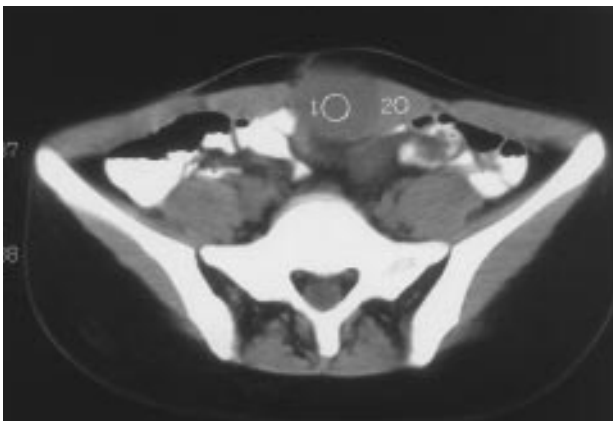


Figure 1. CT scan: desmoid tumours in the abdominal wall

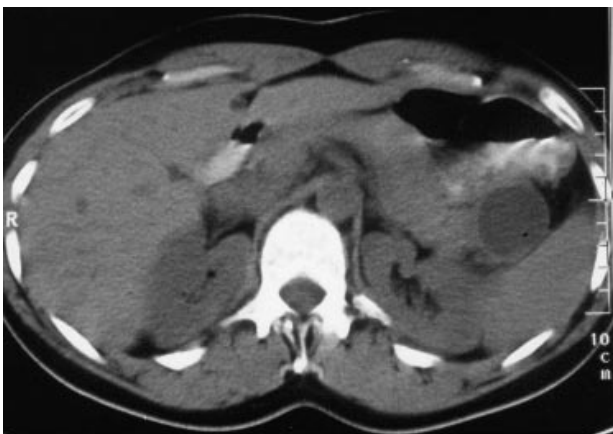


Figure 2. Operative specimen: Desmoid tumour in the mesentery of the small intestine

carcinoma with potential low grade malignancy (figure 3).

Most of family members had blood samples taken for detection of mutation of APC gene, in an effort to establish a registry of such patients, and to encourage the immediate family and other branches of the families of patients, to come forward for genetic counseling.

Two subjects had ophthalmic examination for detection of CHPRE (Congenital Hypertrophy of the Retinal Pigmental Epithelium). Two other patients were found to be eterozygotic for the pathological mutation 2601delGA which, up to to now, has not be described in the international literature.

Functional results after IPAA are satisfactory. All pouches are in place and functional. The mean number of stools are 2,9 per day. Stools at night vary from none to 4 per week, with a mean of 0.8 stools per night per week. The majority of patients are perfectly continent. Only two reported occasional spotting during the day. Nocturnal continence is perfect in all patients. The time for a complete, normal evacuation of the pouch ranges from 3 to 15 minutes, with a median of 5.4 minutes and the ability to defer defecation for 30 minutes to more than an hour, with a mean value of 36 minutes. Perineal skin irritation has been described by one patient, and two patients reported dietary restriction and occasional use of antidiarrhoic drugs. No patient reported restriction of his or her social and professional activities as a result of the operation.

DISCUSSION

When a patient is diagnosed with FAP, one of the

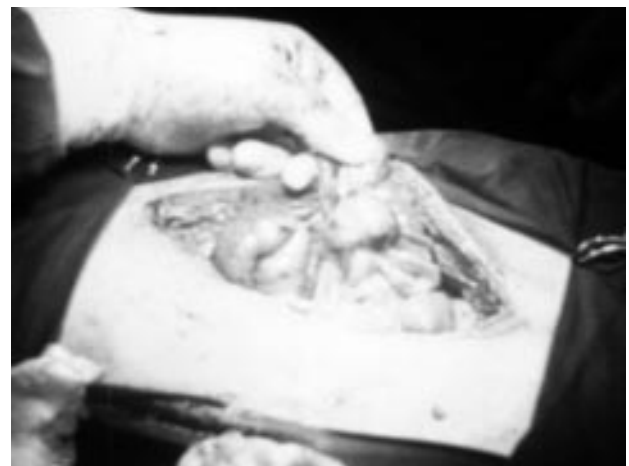


Figure 3. CT scan: Cystic tumour arising from the pancreas

most important decisions to be made is the choice of prophylactic surgery. Of the three options (colectomy with ileorectal anastomosis (IRA), proctocolectomy with ileal pouch-anal anastomosis ((IPAA), and proctocolectomy with end ileostomy), ileorectal anastomosis is the simplest and least complicated, with least disturbance in bowel function.¹

In a large series, patients who underwent IRA scored significantly better for daytime and nighttime stool frequency, soiling, occasional passive incontinence, flatus and feces discrimination, stool consistency, and need for antidiarrheal medication. There was no difference with regard to perianal irritation, episodes of bowel discomfort, or dietary restrictions and IRA might still be considered in patients with a mild phenotypic expression of the disease in the rectum, but does not protect the patient from the development of cancer in the rectum and necessitates regular endoscopic surveillance.² Patients with rectal cancer at presentation, and patients at high risk for developing rectal cancer after IRA should have a proctocolectomy as their initial procedure. Factors that help define rectal cancer risk after IRA include colon cancer at diagnosis and >1000 polyps in the colon at the time of colectomy. Recent studies have shown that some mutations are associated with more aggressive polyposis, and, probably, these patients are better served with a pelvic pouch as their initial operation.^{3,13} These observations are in agreement with our material, where four patients with IRA were treated by rectal excision and IPAA, because of the development of numerous polyps uncontrollable by fulguration in the retained rectum. The case of the patient in this group carrying an unsuspected rectal adenocarcinoma, emphasizes the fact that this type of operation should be reserved for reliable individuals who are capable of following an intensive surveillance programme.

IPAA is a more complex procedure and is more likely to affect the patient's lifestyle, but some authorities recommend it for all FAP patients because it eradicates the risk of cancer. In expert hands, IPAA has a fair need for reoperation, fecal leakage, pouch frequency, ability to defer evacuation, pouchitis, and offers a good overall quality of life.⁴ Controversy exists over the technique of pouch-anal anastomosis. The double-stapled technique invariably preserves the anal transitional zone and a small amount of mucosa and may result in better postoperative anal function. This should be balanced against a 28% percent incidence of adenomas in the anal transitional zone. Conversely, a mucosectomy potentially removes all rectal mucosa, hence theoretically eliminating all cancer

risk.⁴ It is mainly for this reason that in our practice, IPAA with anal mucosectomy is preferred over stapled IPAA. Anal mucosectomy should be complete as development of invasive rectal cancer originating from retained islets of mucosa has been reported.⁵

On the other hand, there is evidence that formation of an ileal pouch does not eliminate the risk of polyp formation. Several authors have implicated colonic metaplasia (villous atrophy, crypt hyperplasia, and increase in sulfated mucin) as the reason for the development of ileal adenomas, or even carcinomas in the pouch of patients with FAP. (%) Surveillance is necessary at three-year to four-year intervals, with endoscopic removal of larger polyps (>5mm). If polyps appear early in the pouch, or if carpeting by polyps or larger polyps are present, more frequent follow-up, or even surgical intervention may be necessary.^{6,7,8}

Advances in the treatment of FAP with associated reduction in mortality from colorectal carcinoma make extracolonic manifestations of the disease more common and life-long surveillance mandatory. The most life-threatening extracolonic manifestations of FAP are periampullary carcinoma and desmoid tumours.

The upper gastrointestinal tract should be monitored endoscopically at the time of diagnosis and assessed regularly thereafter. Gastric polyps are less frequent, with a very low malignant potential, but prevalence of duodenal adenomatosis among FAP patients varies from 50% to greater than 90%, and some patients (3-5%) develop duodenal cancer. Periampullary adenomas seem to carry a high risk of malignant transformation. Duodenal adenomas should be resected so as to avoid the devastating effects of invasive periampullary carcinoma.⁹ In our series, duodenal tumours were not detected. On the other hand, three of our patients had numerous hyperplastic polyps of the stomach.

Additionally, the development of desmoid tumours needs to be monitored (by CT or MRI) to avoid the severe complications of local invasion.

Desmoid tumour is an uncommon locally invasive non-metastasizing neoplastic lesion. The etiology of this tumour is unknown and its treatment is controversial. Desmoid tumours are histologically benign but due to their infiltration and compression of surrounding structures are potentially life-threatening. The annual incidence rate is 2-4 per million people. The mesenteric variant constitutes about 10% of all desmoid tumours, although in familial adenomatous polyposis (FAP)

patients this may be up to 70%. As depicted in our series, complete surgical removal of desmoid tumours is sometimes difficult. Due to the small number of patients with mesenteric desmoids the therapy reported in the literature is mainly empirical. The value of short- and long-term treatment (up to 6 years) with the anti-oestrogenic agent toremifene in combination with sulindac, a N.S.A.I.D., in such patients is at present unclear.^{10,11}

A subset of patients present with fewer colorectal polyps, later age of onset of polyps and cancer, and a predilection toward involvement of the proximal colon. This variant of familial adenomatous polyposis is known as attenuated familial adenomatous polyposis. Polyps are diagnosed at a mean age of 44 years, with cancer diagnosed at a mean age of 56 years. Frequent involvement of the proximal colon necessitates the use of colonoscopy for surveillance, and infrequent involvement of the rectum supports the role of a total abdominal colectomy and ileorectal anastomosis. Attenuated familial adenomatous polyposis is transmitted in an autosomal dominant fashion. Several distinct mutations within the APC gene have been associated with an attenuated phenotype, but variability of disease expression within families possessing identical mutations makes classification difficult. Although currently recognized as a distinct clinical entity, attenuated familial adenomatous polyposis may be part of a spectrum of disease that includes familial adenomatous polyposis and is caused by different mutations within the APC gene. Because of its unique characteristics, yet apparent overlap with familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, increased awareness of attenuated familial adenomatous polyposis should improve diagnosis, surveillance, and treatment strategies.¹²

FAP is rare disorder and is associated with less than 1% of CRCs, but CRC risk in patients with FAP if this condition is left untreated, approximates to 100%. Since FAP is a potentially preventable cause of CRC clinicians should have an adequate knowledge of it to identify the disease and to manage the patient and family. Children of an affected individual are at 50% risk of inheriting the predisposing gene. After the identification of an index patient, genetic testing in combination with the detection of extra-colonic manifestations allows more accurate identification of family members likely to have the faulty gene, enabling the targeting of screening and preventive surgery only to those at risk.

Several studies have attempted to correlate genotype with phenotype in patients with FAP. Mutations have

been reported through the 15 exons of the APC gene, with the exception of exons 1 and 2. Mutations occurring in the 5' end of the gene (particularly exons 3 and 4) are associated with the attenuated form of FAP. In contrast, a region of exon 15 is invariably associated with severe polyposis and includes the most frequent APC mutation at codon 1309. Therefore, when a FAP family has a known mutation, the implications of the site of the mutation should be considered when making decisions about screening and surgery. For example, endoscopic screening must begin before the usual age of 10 to 15 years of age, and in such patients total proctocolectomy and IPAA should be strongly considered at the time of initial surgery.^{1,13,14}

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