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Colorectal adenomas in patients presenting with inflammatory bowel disease

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ABSTRACT

Background: Adenoma is the precursor of colorectal carcinoma (CRC). Patients with longstanding active ulcerative colitis (UC) are at risk of developing CRC. Every patient with UC can also develop adenomas, which is an extra risk factor.

Aim: A large retrospective cross-sectional study was conducted to identify patients with UC and polyps.

Material and methods: All consecutive lower intestinal endoscopies carried out in a period of 16 years were searched for the presence of inflammation and concomitant polyps.

Results: Inflammatory bowel disease was diagnosed in 1029 patients. Forty-seven (4.5%) patients had concomitant polyps. The patients with polyps were divided in two groups: group 1 consisted of 34 patients in whom active inflammation was seen with coinciding polyp(s), and group 2 consisted of 12 patients in remission, in whom polyps were detected. One patient had had adenomas in the past and presented with active inflammation and a new adenoma.

In group 1, four patients had a history of active inflammation, and adenomas were seen in 29 patients, while seven patients showed hyperplastic polyps. Two patients had adenomas as well as hyperplastic polyps. In group 2 nine patients had adenomas and three had hyperplastic polyps.

Conclusion: Patients with different phenotypic expressions of inflammatory bowel disease can have concomitant adenomas in the colon. Hence, it is plausible to assume that these patients have an increased risk of developing CRC because of adenomas.

KEYWORDS

Adenoma, cancer risk, colorectal cancer, inflammatory bowel disease, ulcerative colitis

INTRODUCTION

Colorectal cancer (CRC) is one of the most prevalent cancers in the Western world. The adenoma has been established as the precursor of CRC in the general population. The adenoma-carcinoma sequence is generally accepted. Every individual has a certain, albeit unknown, risk of developing adenomas. Since detection and removal of this precursor lesion can prevent cancer developing later in life, screening colonoscopy is advocated in people above the age of 50. Initial screening in asymptomatic individuals can be done with faecal occult blood testing. The estimated increase in colonoscopy workload in normal practice is minor, given the results of a recent Dutch study.[1]

A well-known fact in the literature is that patients with longstanding active ulcerative colitis (UC) are at risk of developing CRC. Among patients with UC, dysplasia is associated with, and precedes, invasive carcinoma. Colonoscopic surveillance is recommended after eight to ten years of extensive colitis or after 15 to 20 years for left-sided colitis. Surveillance does not prolong survival.[2]

CRC in patients with UC is always thought to be the result of inflammation-associated dysplasia. Suchy *et al.* studied a series of polymorphisms in six different genes active in inflammation, and found that there are genetic changes capable of influencing risk of CRC especially in older persons.[3] Many of the molecular alterations responsible for CRC, namely chromosomal instability, microsatellite instability, and hypermethylation, also play a role in colitis-associated colon carcinogenesis.[3] Apart from this risk, every patient with UC also has the potential, just as individuals without UC, to develop adenomas. It can be hypothesised that CRC in UC can also be the result of an adenoma not associated with chronic inflammation.

Despite very many studies in the literature on adenomas and CRC, and cancer occurring in patients with UC, there is little data on the simultaneous occurrence of adenomas in patients with UC. For this reason, a large cross-sectional

retrospective study was carried out to identify patients with UC and concurrent adenomas. Also the CRCs occurring in these patients were identified.

MATERIAL AND METHODS

In this retrospective study, all consecutive lower intestinal endoscopies, sigmoidoscopies as well as colonoscopies, performed over a period of 16 years at the Department of Gastroenterology of the Zaans Medical Centre, the regional hospital for the Zaanstreek region in the Netherlands, were included.

The endoscopies were done with fibre-optic Olympus endoscopes in the beginning of the 1990s. From 1993 to 2000, the EVIS 100 system was used and after 2000 the Exera 160 and 180 systems of Olympus were used. Two experienced endoscopists performed the procedures. The result(s) of the endoscopy/endoscopies were hand-written in standardised reports. From the beginning of 2003 the Endobase™ computerised system from Olympus was used. The results of all endoscopies are entered in a prospective database system.

For the present study, all endoscopy reports in which inflammation in the colon or rectum and concomitant polyp(s) was noted, were included. The medical records of the patients were retrieved in order to obtain demographic data, as well as details on the colitis or proctitis. The histological features of the detected polyps were noted. Patients with inflammatory bowel disease and inflammatory polyps were excluded.

Statistical analysis was done with the χ^2 test for contingency tables. A value below 0.05 was considered statistically significant.

RESULTS

In 16 years, 17,780 consecutive endoscopies were performed (90.4% colonoscopies).

In 1029 patients inflammatory bowel disease was diagnosed (164 cases of Crohn's disease, 183 of ulcerative colitis, distal colitis (procto-sigmoiditis) and left-sided colitis in 231 patients, proctitis in 212, segmental colitis (inflamed small segment, usually of the sigmoid without specific signs pointing to Crohn's disease) in 44, and indeterminate colitis in 195 patients).

Forty-seven (4.5%) patients presented signs of inflammation and concomitant polyps. Biopsies and/or polypectomy specimens, for confirmation of the inflammation and type of polyps, were available from all patients.

The patients with polyps were divided in two groups: group 1 consisted of 34 patients in whom active inflammation was seen with coinciding polyp(s), and group 2 consisted of 12 patients with documented active inflammation of colon and/or rectum in the past, in whom polyps were detected during the most recent endoscopy. Finally, there was one patient in whom adenomas in the sigmoid were removed and who presented four years later, one year prior to regular follow-up, with active inflammation and a new adenoma in the sigmoid (tubulo-villous adenoma with moderate dysplasia).

In group 1, four patients had a history of active inflammation. This diagnosis was made 10 to 17 years earlier (mean 13 years). They underwent an endoscopy because of symptoms pointing to an exacerbation. During the present colonoscopy, active inflammation and concomitant polyp(s) were present.

Table 1 shows more details of the patients in both groups. In group 1 adenomas were seen in 29 patients, while seven patients showed hyperplastic polyps. Two patients had adenomas as well as hyperplastic polyps. In group 2 nine patients had adenomas and three had hyperplastic polyps. These polyps were detected during a follow-up endoscopy at a mean of 10.3 years after the endoscopy showing active inflammation (median 10 years, range 1 to 28 years).

Table 2 shows the histological classification, as well as the level of dysplasia in the polyps in both groups of patients.

Table 1. *Details on patients in the two groups*

	Group 1	Group 2
Number	34	12
Men/women	23/11	10/2
Mean age (SD)	59.7(15)	56.4(14)
Site and extent of inflammation:		
• Proctitis	5	2
• Distal colitis or left-sided colitis	16	5
• Ulcerative pancolitis	2	2
• Crohn's disease of the colon	1	3
• Indeterminate colitis	10	-
Localisation of the polyp:		
• Sigmoid	21	7
• Ascending colon/caecum	3	4
• Descending colon	1	-
• Unknown	4	-
Number of polyps	1.6	1.25
Range	1-5	1-2

Table 2. *The classification of the polyps in the two groups of patients*

	Group 1	Group 2
Hyperplastic	7	3
Tubular adenoma	25 (86%)	7 (78%)
Tubulo-villous adenoma	4 (14%)	2 (22%)
Villous adenoma	-	-
	p=ns	
Low-grade dysplasia	20 (69%)	2 (22%)
Moderate dysplasia	7 (24%)	7 (78%)
High-grade dysplasia	2(7%)	-
	p=0.03	

Moderate dysplasia was significantly more often present in the polyps of patients in group 2 (p=0.03).
Three patients with IBD developed CRC in the course of their disease (two sigmoid cancers and one rectal cancer). None of these patients had concurrent or previous adenomas.

DISCUSSION

A specific group of patients who have an increased risk of developing CRC is patients with UC. The risk increases with the duration and extent of UC. The incidence is reported to be 2% after ten years of active colitis, 8% after 20 years and 18% after 30 years.[5,6] Also in population studies, the incidence of CRC was higher when compared with a control population.[7] In more recent studies a much lower risk was calculated.[8,9] In a large population study in Italy mortality due to CRC did not appear to be different in patients with UC or patients with sporadic cancer.[10] Lutgens *et al.* assessed the time interval between onset of IBD and CRC.[11] It appeared that 22% of patients developed cancer before the recommended starting points of surveillance. They concluded that the diagnosis of CRC is delayed or missed in a substantial number of patients when conducting surveillance strictly according to formal guidelines. However, the study was done in seven university hospitals, hence investigator bias is present.
An adenoma usually precedes a sporadic cancer, while flat dysplastic lesions or dysplasia-associated lesion or mass (DALM) precedes cancer associated with UC. DALMs are a heterogeneous population of lesions with different endoscopic features (adenoma-like and non-adenoma-like).[12] Distinguishing a polyp from a mass associated with non-adenoma-like disease can be difficult. In an internet-based study significant inter-observer variability was noted between investigators.[13] An important observation is the fact that dysplasia is detected in inflamed mucosa.[14] On the other hand, dysplasia can occur because of active inflammation; it will disappear if the inflammation goes into remission. Aggressive medical treatment will result in long-standing remission and a decrease in risk of CRC.[15] The risk for development of CRC in normal non-inflamed mucosa does not appear to be higher, compared with the normal population.[16]
The present study shows that adenomas can be present in patients with either active inflammation or remission. Just as the normal population, patients with UC are also at risk of developing adenomas. Hence, it is also plausible that cancers detected in patients with UC can arise from adenomas and have nothing to do with chronic inflammation. Despite all the studies on adenomas and UC, little data are known on the occurrence of adenomas in patients with UC. Jess *et al.* studied colorectal dysplasia in inflammatory bowel disease (IBD). They used a large database of patients with documented inflammatory bowel disease. In 4% of patients, dysplasia was detected. Of these, 18 had adenoma-like lesions in regions with active inflammation, and two had an adenoma outside the region with inflammation.[8]
In another study, the prevalence of adenomas in patients with IBD was compared with local age-matched controls who participated in the national screening trial for CRC. Of 106 patients, 80 suffered from UC, 20 from Crohn's disease, and six from indeterminate colitis. Distal adenomas were found in three patients with UC compared with 67 of 749 controls (2.8 *vs* 8.9%, p=0.03). This result suggests that distal adenomatous polyps are rare in patients with IBD compared with a control population. The authors state that this finding supports the hypothesis that lesions other than polyps are important for the development of CRC in patients with IBD.[17]
Torres *et al.* studied 89 benign polypoid epithelial neoplasms from 59 patients with IBD (51 with UC, eight with Crohn's colitis). Patients were categorised arbitrarily as having a probable sporadic adenoma if the polypoid epithelial neoplasm was not located within areas of histologically proven colitis and a probable IBD-associated polypoid dysplasia if the lesion developed within an area of colitis. Sixty-six percent had active disease at the time of presentation. Nearly 70% of patients had only one polyp; the majority occurred in either the left colon or the rectum (66%). At follow-up evaluation a further neoplastic lesion developed in 20%; low-grade flat dysplasia was seen in five (12.5%), and adenocarcinoma developed in three (7.5%). However, dysplasia or adenocarcinoma did not develop in the patients who had polyps located outside areas of active colitis. Patients with probable IBD-associated polypoid dysplasia had a statistically significantly (p<0.05) longer disease duration than patients with probable sporadic adenoma.[18] However, sporadic adenomas did occur in this study.
Rubio *et al.* studied the histological phenotype of the dysplastic lesion juxtaposing colorectal carcinomas in 50 consecutive colectomy specimens of patients with inflammatory bowel disease. Adenomatous growths juxtaposing carcinomas were found in 76% (n=38) of the IBD cases: 52.3% were villous, 28.9% were serrated, 5.3% tubular and the remaining 13.2% were mixed.[19]
Given the results of the present study, patients with different phenotypic expressions of inflammatory bowel disease can have concomitant adenomas in the colon. The prevalence is according to the literature. Hence, it is plausible to assume that these patients also have an increased risk of developing CRC because of adenomas. Development of CRC in these patients is not necessarily associated with the inflammation. The presence of adenomas is irrespective of disease activity or extent.
Patients with IBD in remission should undergo screening colonoscopy, as advocated in the normal population, for detection of adenomas.

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