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Adenomatous Polyps and Familial Incidence of Colorectal Cancer

H. ASTE,* S. SACCOMANNO, L. BONELLI and V. PUGLIESE
Istituto Nazionale per la Ricerca sul Cancro, Institute of Oncology, University of Genoa, Italy

Abstract—*The frequency of colonic adenomatous polyps and the incidence of colorectal cancer in close relatives were evaluated in a prospective study performed in 100 consecutive patients operated on for colorectal cancer. One hundred patients matched for age and sex, in whom double contrast enema and colonoscopy failed to show cancer, served as control group. Colorectal carcinomas in first-degree relatives were found in 11% of the surgically treated patients and 6% of the control group (the difference is not statistically significant). Solitary or discrete adenomas in patients operated on for colorectal carcinomas were significantly more frequent (32%) than in the control group (18%) ($P < 0.05$). This difference is also statistically significant when considering only those patients without relatives suffering from carcinoma; however, the same cannot be statisticaly proven with the small group of patients with a positive family history. Present findings do not indicate that single or discrete adenomas synchronous with colorectal cancer are significantly associated with a familial history of large bowel malignancy. These findings are consistent with the hypothesis of environmental factors being involved in adenoma pathogenesis.*

INTRODUCTION

COLORECTAL cancer is usually considered the result of environmental factors. A genetic component is apparent in a rather small percentage of cases as well as an increased incidence of this tumour in relatives of patients with the disease and independent of polyposis [1–3]. First-degree relatives of patients who have had colorectal cancer had a three-fold higher mortality rate from this tumour than controls [4, 5].

Present evidence supports the importance of colonic polyps as a precursor to the development of colorectal cancer [6, 7]. The frequent development of large bowel cancer in familial adenomatous polyposis and Gardner's syndrome is well known. The purpose of this study was to determine the relevance of single or discrete adenomatous polyps in patients operated on for colorectal cancer with and without familial incidence for large bowel malignancy.

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*To whom reprint requests should be addressed at: Endoscopic Service and Gastrointestinal Unit, Istituto di Oncologia, viale Benedetto XV n. 10, 16132 Genova, Italy.

MATERIALS AND METHODS

One hundred consecutive patients (63 males, 37 females; mean age 60 ± 10.5 yr) who were operated on for colorectal cancer were studied. The final diagnosis in all cases was based on histological evidence. Data were collected with regard to age, sex, site of tumour, presence of synchronous adenomatous polyps and incidence of colorectal cancer in their first-degree relatives. Polyps were assessed with the double-contrast method, colonoscopy (usually limited before resection and total after surgery) and examination of the operative specimen. Histological studies were done in polyps removed at endoscopy or on the surgical specimen.

As a control group 100 outpatients, age and sex matched (mean age 60 ± 10.2 yr), were selected at random. These patients had double-contrast radiographic studies of the colon and colonoscopy because of symptoms suggesting colorectal diseases and no colorectal cancer was detected. Polyps were removed during colonoscopy and submitted for histological examination.

Patients of both groups were questioned in detail about a history of cancer at all anatomic sites in first-degree relatives (parents, brothers and sisters). The two groups were interviewed by the

same members of the research team in the same period. Dubious or uncertain cases of familial history for colorectal cancer were considered as negatives. Patients with familial polyposis coli were excluded from this study.

The chi squared test for independent samples has been used to compare the frequency of adenomatous polyps and colorectal cancer in first-degree relatives of all cases and controls and in both groups without familial history for colorectal cancer.

Fisher's exact test has been used in comparing the presence of familiality for colorectal cancer in patients with polyps among cases and controls, and the incidence of polyps in the two groups separately with and without first-degree relatives for colorectal cancer.

RESULTS

The site of malignancy and the first-degree relatives with colorectal cancer in 100 patients operated on for adenocarcinoma of the large bowel are reported in Table 1.

In 16 cases cancer was located in the right colon (caecum, ascending and transverse portions), in 34 patients at the splenic flexure or in the descending and sigmoid colon and in 50 patients in the rectum and rectosigmoid junction. Four patients had two synchronous cancers. Single or discrete adenomatous polyps were present in eight cases in the right colon, in ten cases in the descending colon and sigmoid portion and the remaining cases in the last portions. Colorectal cancer among relatives was not found in the 16 cases of cancer of the ascending or transverse colon. Eleven subjects from the treated group and six subjects from the control group had one or more first-degree relatives with colorectal malignancies. Three cancer-operated patients and two from the control group had two first-degree relatives affected by colorectal cancer. These differences were not statistically significant. Single or discrete adenomatous polyps were detected in 32 cases operated on for cancer and in 18 of the control group. This difference is statistically significant ($P < 0.05$). Three or more polyps were detected in nine patients with colorectal cancer and in three of the control group, but this difference was not significant.

Adenomatous polyps were detected in 45% of cancer-operated patients with familial history for colorectal cancer and in 30% without familiality, and in 50 and 16% of the two control groups. These differences are not significant (see Table 2).

The difference between the prevalence of adenomatous polyps in the cancer and control groups with positive familial history was not significant, while in the absence of familiality the difference was statistically significant ($\chi^2 = 4.563$; $P < 0.05$).

Table 2. Adenomatous polyps in patients with and without familial incidence of colorectal cancer—No. of cases

Familial incidence	Cancer patients	Control group
Present	5/11 (45%)	3/6 (50%)
Absent*	27/89 (30%)	15/94 (16%)

*$\chi^2 = 4.563$; $0.05 > P > 0.025$.

DISCUSSION

A higher frequency for one or more cases of colorectal cancer in first-degree relatives of patients affected by large bowel malignancies compared to controls is shown in our study but the difference failed to reach a statistical significance, probably due to the small numbers involved. A selection bias also has to be taken into account due to the nature of the control group. These patients were highly suspected of having organic lesions and a radiological and endoscopic evaluation was mandatory. Relatives of patients with previous colorectal cancers were more sensitized to the concept of specialized medical check-ups.

Contrary to previous reports [8, 9], cancer was always located in the terminal left-side colon when family history was present, in accordance with the findings recently reported by Duncan and Kyle [10].

Adenomatous polyps were statistically more frequent in operated patients than in controls, in keeping with previous reports [6, 7, 11, 12]. They were often detected in both groups with positive

Table 1. Site of tumour, adenomatous polyps and familial incidence of colorectal cancer in 100 patients operated on for bowel malignancy

Site of tumour	No. of cases	Adenomatous polyps	Familial incidence
Ascending–transverse	16	8	0
Splenic flexure, descending–sigmoid	34	10	3
Rectum, recto-sigmoid junction	50	14	8
Total	100	32	11

familiality but failed to show a statistical difference when compared to cases without familiality. These findings are in agreement with a recent study in a reduced number of cases [10].

It is possible that in certain families a tendency to produce a few adenomas is inherited in the same way that a tendency to produce hundreds of adenomas is inherited in multiple polyposis coli [4]. Reports of so-called 'cancer families' suggest the possibility that cancer may have genetically determined solitary polyps as their basis [13–15]. However, the significant high frequency of adenomatous polyps in patients suffering from colorectal cancer without affected relatives in our study is consistent with the hypothesis of environmental factors involved in adenoma development [7].

Mechanisms other than adenomatous-cancer sequence could be indicated to explain the higher frequency of colorectal cancer in relatives of cases with the disease. Dysplastic lesions of the epithelium in a flat mucosa have been demonstrated and it has been postulated that they progress to carcinoma without developing polyps in black patients with colorectal cancer in whom adenomatous polyps are very rare [16].

Present findings do not indicate that the presence of single or discrete adenomas in a patient with colorectal tumour is significantly associated with a family history of large bowel carcinoma.

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