

Macroscopic Characteristics of Tubular Adenomas in Familial Adenomatosis Coli: The Relationship between Size, Gross Configuration and Location

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Received October 31 1994; accepted April 26 1995

Summary. 8624 tubular adenomas from 9 patients with familial adenomatosis coli were investigated to elucidate the mode of their macroscopic development. Our data indicate that most tubular adenomas remain smaller than 5 mm, suggesting that those larger than 5 mm detected clinically may already have deviated from the expected natural history of benign adenomas. Their initial macroscopic configuration appears to be the flat or sessile type, and they seem to change their macroscopic configurations to subpedunculated as they attain a size between 5 and 7 mm. Adenomas larger than 8 mm appear to take a pedunculated shape. This mode of macroscopic development may be affected by the location of adenomas, and tends to occur in adenomas of a smaller size in the rectum, sigmoid and ascending colon than in the rest of the organ.

Key words—adenoma, colon, rectum, macroscopic configuration.

INTRODUCTION

Tubular adenomas of the colon and rectum have usually been classified into sessile, subpedunculated and pedunculated types,¹⁻³⁾ and were considered to have such polypoid appearances throughout their natural history.⁴⁾ Recently, however, flat^{5,6)} and depressed^{7,8)} types have been added to the classification; they are supposed to be an initial macroscopic manifestation of adenomas.⁹⁾ Despite this, the sequence of change for the macroscopic configuration of tubular adenomas remains to be systematically described.

Several hypotheses on the mode of the macroscopic growth pattern of early colorectal carcinomas have been proposed on the basis of the adenoma-carcinoma sequence.^{1,11,12)} Yokoyama et al.¹²⁾ examined surgically and endoscopically resected colorectal carcinomas and suggested that their growth may proceed from the pedunculated type of early carcinoma to advanced carcinomas by way of the stalk invasion of carcinomas. Ushio et al.¹³⁾ carried out a retrospective observation of X-ray films of barium enemas and proposed that the main route to advanced carcinomas may be from sessile type early carcinomas. Recently Muto et al.⁵⁾ insisted that a certain number of advanced cancers may develop from small flat type adenomas.

Most of the colorectal carcinomas limited to the mucosa are "carcinomas in adenomas", so that their macroscopic characteristics are usually determined by those of the underlying adenomas. Therefore, when the macroscopic development of carcinomas (especially of intramucosal carcinomas) is discussed, one should always clarify whether one is referring to the macroscopic characteristics of the underlying adenomas or those of the carcinomas themselves.

The aim of this study was to investigate the sequence of changes in the macroscopic configuration of tubular adenomas detected in the colon and rectum of patients with familial adenomatosis coli. The data thereby obtained shall provide basic information to determine whether the macroscopic characteristics of early colorectal carcinomas are those of the underlying adenoma or reflect the development of carcinomas. Furthermore, the data may be useful to clinicians for the endoscopic differentiation of adenomas

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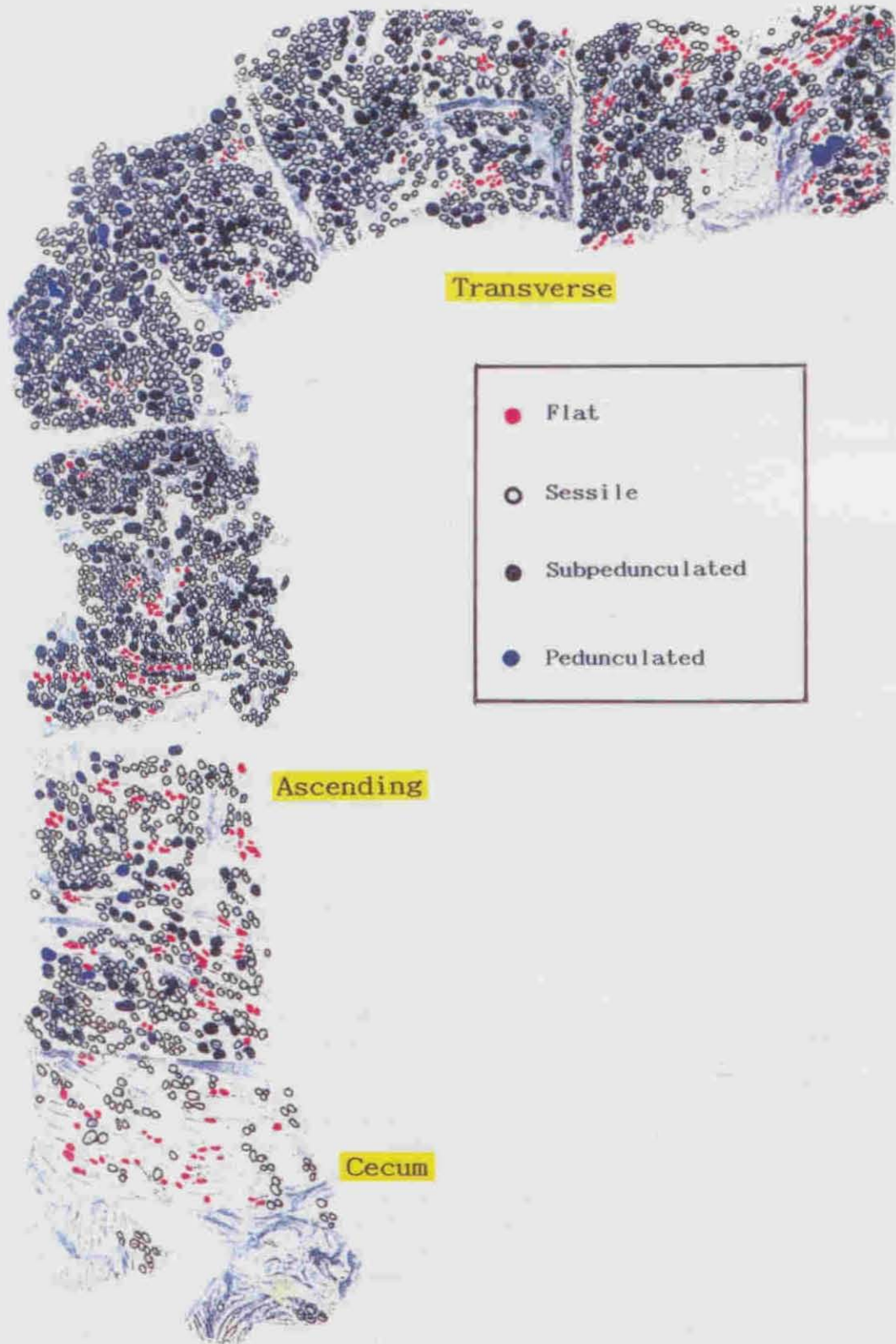


Fig. 1. A mapping of adenomas by macroscopic configuration on the color photocopy of resected specimen (NI-1117, 19yo. Female).

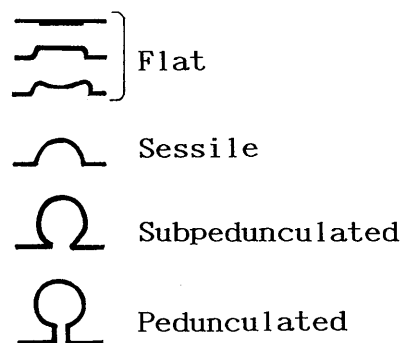


Fig. 2. Macroscopic classification of adenomas.

and carcinomas, since lesions whose macroscopic configurations deviate from the usual growth pattern of tubular adenomas are suspect for carcinoma.

MATERIALS AND METHODS

Surgically resected colonic specimens from 9 patients with documented familial adenomatosis coli were examined. The patients were 5 men and 4 women; their mean age at the time of the operation was 31.6 ± 12.5 years (ranged from 17 to 52). Informed consent was obtained from all patients. In two patients the resection included the entire colon except for the most distal portion of the rectum; in 5 patients the resected specimen consisted of the segment from the cecum to the transverse colon; in 2 patients the sigmoid colon and the proximal portion of the rectum were resected.

A color photocopy of each resected specimen was made and all grossly discernible lesions were mapped on it. Each lesion was numbered and the macroscopic configuration was determined by the naked eye and recorded in a color photocopy (Fig. 1). The macroscopic configurations of the lesions were classified into four types: flat, sessile, subpedunculated and pedunculated (Fig. 2). The flat type is defined as a plain or elevated lesion with a flat surface. Lesions with a slightly concave surface are also classified as flat types.⁹⁾ The sessile type is defined as elevated lesions with a hemispherical surface. The pedunculated type is defined as lesion with a definite stalk allowing complete mobility. Lesions with a short stalk without mobility are defined as subpedunculated. The sizes of the lesions were measured directly on the resected specimen. Lesions were assigned to a specific location (cecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum)

Table 1. Frequencies of adenomas by size

Size (mm)	No. of adenomas	Frequency
$X \leq 3$	4701	54.5%
$3 < X \leq 4$	2288	26.5%
$4 < X \leq 5$	715	8.3%
$5 < X \leq 6$	441	5.1%
$6 < X \leq 7$	251	2.9%
$7 < X \leq 8$	129	1.5%
$8 < X \leq 9$	37	0.4%
$9 < X \leq 10$	25	0.3%
$X > 10$	37	0.4%
Total	8624	100%

based on previously described anatomical criteria¹¹⁾ and accompanying clinical descriptions.

Each lesion was then individually removed, fixed in 10% formalin and embedded in paraffin. Sections (3 μ m thick) were cut, stained with hematoxylin and eosin and examined histologically to confirm their adenomatous structure.

Statistical analysis was carried out by an χ -square test. A p value of less than 0.05 was regarded as significant.

RESULTS

1. Number and size of adenomas

A total of 8624 tubular adenomas were identified in the 9 resected specimens. Size and distributions of the adenomas are shown in Table 1; 89.3% of all adenomas measured 5 mm or less and 99.6% measured 10 mm or less.

2. Macroscopic configurations of adenomas by size

More than 90% of adenomas measuring 3 mm or less were either flat (43.9%) or sessile (49.9%). As the adenomas became larger, the prevalence of these two types decreased; the subpedunculated type was the most common type among adenomas measuring between 3 and 7 mm (49.4%) and the pedunculated type represented the most common type (39.5–89.2%) of adenomas larger than 7 mm. Nearly 90% of all adenomas larger than 10 mm were of the pedunculated type (Fig. 3).

3. Relationships between size, macroscopic configuration and location of adenomas

The rectum, sigmoid colon and ascending colon were

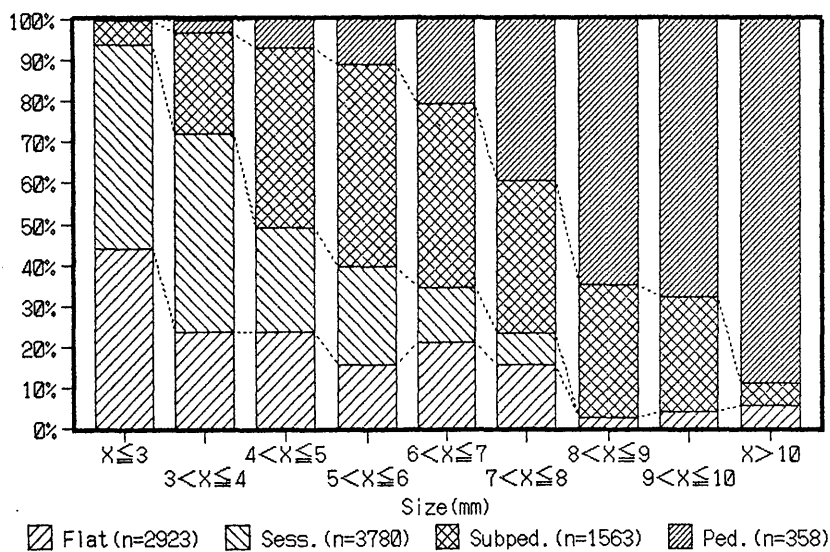


Fig. 3. Frequencies of macroscopic configurations of adenomas by size.

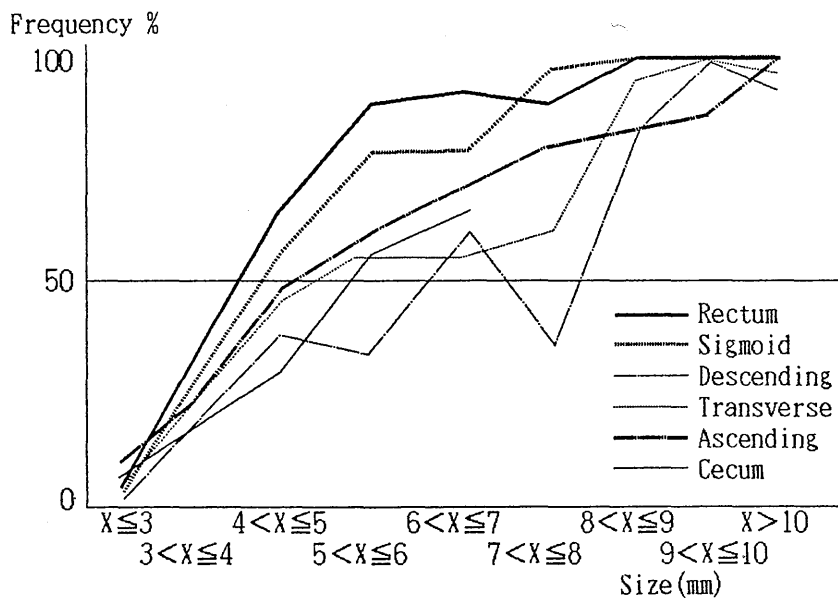


Fig. 4. Relationship between size, macroscopic configuration and location of adenomas.

the most common locations of the pedunculated and subpedunculated types (Fig. 4). For adenomas larger than 8 mm, there was essentially no relationship between the location of the adenomas and their macroscopic configuration. However, for adenomas measuring 8 mm or less, the pedunculated and subpedunculated types were significantly more prevalent in the rectum and sigmoid than in any other part of the large intestine ($p < 0.01$). As for adenomas measur-

ing between 6 mm and 8 mm, these two types were significantly more common in the ascending colon than in the transverse and descending colon and rectum ($p < 0.05$).

DISCUSSION

Based on endoscopic data, Nagasako et al.¹⁵ report-

ed 58% of tubular adenomas as being less than 5 mm in size, and in Shinya's series,¹⁶⁾ 40% measured less than 10 mm. Data obtained from autopsy series^{2,17,18)} showed a higher incidence of smaller lesions (43.7% to 69.3% for adenomas measuring less than 5 mm and 84.6% to 95.3% for those less than 10 mm). In our series, the incidence of small adenomas was even higher than in the published autopsy reports; 89.3% of the adenomas were smaller than 5 mm, and nearly all were under 10 mm.

The size and distribution of adenomas are considered to differ significantly depending on the materials available for study. It is quite possible that many minute adenomas were not detected in a series based on the endoscopic observation, and that these small lesions were difficult or impossible to discover in autopsy materials because of the extensive autolysis usually present in the intestine. Thus, the prevalence of these smaller lesions may have been underestimated in both endoscopic and autopsy studies. Our materials consisted of specimens fixed immediately after surgical resection, before any autolytic changes could occur; therefore, we believe that our data on the size and distribution of tubular adenomas in the colons of patients with familial adenomatosis coli may be regarded as more accurate than those reported so far.

According to our investigation, the majority of tubular adenomas seldom grow larger than 5 mm, and sizes over 10 mm are attained only as an exception (Table 1). Shirai et al.¹⁹⁾ also reported that 81% of adenomas smaller than 5 mm did not grow larger during a prospective observation period of 9-115 months (average of 37.2 months). Our data suggest that adenomas which are easily detected clinically may be those that have already deviated from the natural history of benign tubular adenomas, and such lesions should be carefully evaluated for the presence of accompanying carcinomas.

Based on the analysis of the data obtained concerning the relationship between size and macroscopic configuration of tubular adenomas in our series (Fig. 3), we may speculate on their mode of macroscopic development. Since more than 90% of the adenomas measuring 3 mm or less consisted of either flat or sessile types, these may represent the initial macroscopic manifestation of tubular adenomas. Adenomas maintain these macroscopic configurations (flat or sessile) until they grow larger than 3 or 4 mm. At this point, they gradually change to the subpedunculated type (size 5-7 mm) and then (over 8 mm) become pedunculated.

Focusing on the initial macroscopic configuration of adenomas, Kubota et al.⁹⁾ speculated that minute

depressed type adenomas may be an initial form of some ordinary polypoid adenomas. They reported that minute depressed type adenomas constituted approximately 15% of all adenomas less than 1.5 mm by a dissecting microscopic study of the mucosa of familial adenomatosis coli. There were no depressed type adenomas in our present investigation, and we did not speculate on the depressed type as one of the initial forms of adenomas.

As previously defined,^{20,21)} depressed type tumors are subclassified into absolutely depressed and relatively depressed types according to the height of the depressed mucosa compared with the surrounding normal mucosa (exclusive of the transitional mucosa adjacent to neoplasia). The height of the depressed mucosa of the former is lower than the surrounding normal mucosa, while that of the latter is higher and the lesion is elevated as a whole. The macroscopic distinction between relatively depressed type and flat type adenomas is sometimes difficult and subjective if the elevated lesion is accompanied by only a slight and gradual concave surface. The depressed adenomas of Kubota's series contained both absolutely and relatively depressed types (their proportion is not indicated), and judging from the schematic illustration of their paper (Fig. 1),⁹⁾ their relatively depressed type seems to be included in our flat type adenomas with a slightly concave surface. Thus, although the possibility cannot be denied that some flat or sessile types (which we speculated as the initial macroscopic manifestation of adenomas) might be derived from minute depressed type adenomas which we failed to detect by the naked eye, the adenomas initialized macroscopically as absolutely depressed are typically expected to be rare.

The mode of macroscopic development differs depending on the location of the adenomas. In the rectum, sigmoid and ascending colon, the macroscopic change from flat and sessile to subpedunculated and pedunculated occurs at a smaller size than other parts of the colon (Fig. 4). This may be explained by the free mesentery and higher mobility for the sigmoid colon,²⁾ in contrast to the higher inner pressure for evacuation found in the rectum and strong mobility of the bowel wall to send the content against the gravity which operates in the ascending colon.

On the basis of our investigation, we may conclude that: 1) most tubular adenomas do not grow larger than 5 mm; 2) tubular adenomas take the macroscopic configuration of a flat or sessile type when they do not exceed a size of 3-4 mm, and they become subpedunculated at sizes between 5 and 7 mm and pedunculated when their size exceeds 8 mm; 3) these

macroscopic changes tend to occur in adenomas of smaller size in rectum, sigmoid and ascending colon rather than in the cecum or the transverse and descending colon.

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