

Is Biopsy Necessary if Colonoscopy is Normal?

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Multiple endoscopic biopsies were taken from 100 consecutive patients who had a macroscopically normal colon at colonoscopy. Of these, 78 were regarded as histologically normal; 13 cases of melanosis coli, 7 cases of intestinal spirochetosis, and 2 cases of collagenous colitis were identified. In no cases was there histologic evidence of inflammatory bowel disease. Histologic abnormality could not be predicted by retrospective analysis of various clinical, hematologic and biochemical data. In individual subjects the microscopic abnormality was present to a varying degree in all biopsies, except in intestinal spirochetosis where patchy distribution occurred in some subjects. It is therefore concluded that significant pathology may be missed without biopsy of the apparently normal colon, but in order to reduce the workload of pathology departments and shorten the duration of the examination two biopsies from the hepatic flexure and sigmoid colon may be adequate.

KEY WORDS: colonoscopy; biopsy.

Many patients present to gastroenterological clinics with symptoms requiring large-bowel investigation. Our experience has shown that radiologic examination may fail to detect early inflammatory bowel disease, small neoplasms, and colonic polyps. It has therefore become the policy of our unit to perform colonoscopy in preference to barium enema. However, this results in a significant number of normal examinations being undertaken, and raises the question of whether biopsy is necessary in a macroscopically normal colon. If multiple biopsies are taken routinely, not only does this lengthen the time of the procedure, but it also significantly increases the workload of histology departments.

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In inflammatory bowel disease it is generally accepted that rectal biopsy may be useful even if the mucosal appearances are normal (1-6) and a similar situation has been reported at colonoscopy in such patients (7). The mucosa may also appear normal in microscopic colitis (8-10) and collagenous colitis (11-14), and these disorders would be missed without routine biopsy. It was the purpose of this study to determine what proportion of apparently normal colons were histologically abnormal, to see whether any clinical or laboratory parameters could be used as predictors of abnormality and to formulate guidelines for colonoscopists on the need for biopsy in the face of a normal examination.

MATERIALS AND METHODS

Of a total of 313 patients presenting for colonoscopy over a 12-month period, 100 subjects in whom no macroscopic abnormality was detected were studied. The group consisted of 64 females and 36 males, age range 16-86. A

TABLE 1. PATIENT DETAILS

Finding	Number	Presenting symptoms (number of patients)					Abnormal laboratory results (number of patients)*			
		Abdominal pain	Diarrhea	Constipation	Bleeding	Mucus	↓ HB	↑ ESR	↓ ALB	↓ K ⁺
Collagenous colitis	2	0	2	0	0	0	0	0	0	0
Intestinal spirochetosis	7	4	6	1	2	4	2	1	1	0
Melanosis coli	13	11	2	4	7	4	0	0	2	2
Normal	78	58	43	7	24	21	7	4	1	0

* ↓ HB—hemoglobin < 11.5 g/dl; ↑ ESR—ESR > 20 mm/hr; ↓ ALB—albumin < 35 g/l; ↓ K⁺—potassium < 3.5 mmol/l.

previous rigid sigmoidoscopy and rectal biopsy was not performed in all subjects as it was not the purpose of the study to compare this technique with colonoscopy. A full examination was obtained in 98%, and in the remaining patients the hepatic flexure was reached. Two biopsies each were taken from the cecum, hepatic and splenic flexures, and rectosigmoid junction. All colonoscopies were performed by P.J.W. and all histologic assessments by A.M.L. The biopsies were examined at the time of colonoscopy and then reviewed several months later, at the end of the study. Presenting symptoms and biochemical and hematologic data were also recorded.

RESULTS

Histologic examination revealed collagenous colitis in two subjects, intestinal spirochetosis in seven, melanosis coli of varying degree in 13, and normal appearances in the remainder. No cases of inflammatory bowel disease or microscopic colitis were identified. No symptom pattern or laboratory result predicted any particular histologic finding (Table 1).

It is noteworthy that patients with melanosis coli did not all report laxative usage. When a histologic abnormality was found, it was present in all specimens in collagenous colitis and melanosis coli. Intestinal spirochetosis was noted throughout the colon in only three of seven patients. In one patient it was observed only in the rectosigmoid biopsies, and in three patients it was absent in the rectosigmoid but present at other sites (Table 2).

In the normal cases there was a tendency for the cecal biopsy to show apparently more chronic inflammatory cells in the lamina propria than those of other sites.

DISCUSSION

This study shows that a significant number of histologic abnormalities can be detected in a colon judged normal at colonoscopy. However, in assessing the need for routine biopsy of the apparently "normal," mucosa the most salient question is whether knowledge of these abnormalities may assist in the diagnosis and subsequent management of the patient.

Collagenous colitis is a recently described condition (11–14) characterized by a thick subepithelial band of collagen. It appears to be associated with a history of chronic watery diarrhea and is thought to be rare, although there are no data of its incidence. It is of interest that we found two cases in 100 examinations, indicating that the condition may not be as uncommon as previously considered.

Spiral bacteria have been known to occur in the large bowel for many years (15), and recent interest has focussed on their prevalence and possible pathogenicity. In patients presenting for sigmoidoscopy, the prevalence noted in previous studies has ranged between 5 and 10% (16–18) (compared with 7% in the present study) but is as high as 36%

TABLE 2. POSITIVE HISTOLOGY RELATED TO SITE OF BIOPSY

Histologic finding	Total cases	Positive biopsies			
		Rectosigmoid	Splenic flexure	Hepatic flexure	Cecum
Melanosis coli	13	13	13	13	13
Spirochetosis*	7	4	6	6	6
Collagenous colitis	2	2	2	2	2

*Spirochetosis: present at all biopsy sites in 3/7 patients; present in rectosigmoid biopsy alone in 1/7 patients; present in all biopsy sites except rectosigmoid in 3/7 patients.

in homosexual males (19). Controversy exists as to whether these organisms can cause abdominal pain, diarrhea, and rectal bleeding, and reports of symptomatic improvement following elimination of spirochetes with antibiotics (16, 20) have not been confirmed in larger series (17). The finding of spirochetosis at biopsy may therefore be useful information, both as a possible marker for other sexually transmitted diseases in the homosexual male and as a cause of otherwise inexplicable large-bowel symptoms.

Melanosis coli was noted histologically in 13 patients in whom the mucosa had been regarded as normal macroscopically. None of these cases reported regular laxative use, although it is of interest that in seven the final diagnosis was of functional bowel disorder with diarrhea predominating in two. Laxative abuse is seldom freely reported by patients, and the presence of melanosis coli on biopsy, particularly in patients complaining of diarrhea should lead the clinician to strongly suspect this as a possible diagnosis.

Sigmoidoscopy and rectal biopsy was not performed in all patients prior to colonoscopy as it was felt that even if these were normal, further large-bowel investigation would still be necessary. In Crohn's disease the incidence of characteristic histology in macroscopically normal rectal mucosa lies between 0 and 4% in most series (1, 5, 21) although it has been reported as being 18% by one center (2, 4). The diagnostic yield from rectal biopsy alone is therefore low, although it may be increased by multiple biopsies and serial sectioning (6) and, even if a positive result were obtained, further investigation to assess the extent of disease would be required. We noted that spirochetosis was predominant in the right side of the colon, and in three cases it would not have been detected by distal colonic biopsy alone. A recent report has also indicated that collagenous colitis may exhibit minimal rectal involvement and may be missed on rectal biopsy (22). Although not performed routinely as part of the present study, it is probably wise to perform a lower rectal biopsy to exclude pathology limited to this area. However, biopsies from this site may exhibit artifacts resulting from rectal catheterization if this is used during the preparative process.

Our department has a special interest in the medical management of inflammatory bowel disease (IBD), and thus many patients presenting for colonoscopy are suspected to be suffering from this condition. During the period of the present study,

129 patients were found to have IBD at colonoscopy. It is of interest that in no case in which this diagnosis had been excluded macroscopically, was it found histologically. We also detected no cases of microscopic colitis (8–10) in this series. This may be due to differences between endoscopists in the classification of a "normal" mucosa or could be a reflection of the rarity of the condition.

Our results show that many normal specimens would result if a policy of routine biopsy at colonoscopy was adopted, and we were unable to identify a pattern of clinical or laboratory data which would consistently predict a particular histological abnormality. With the exception of four cases of intestinal spirochetosis, the microscopic lesions were present at all biopsy sites. Interestingly, even in otherwise normal patients there appeared to be an increased concentration of chronic inflammatory cells within the lamina propria of the cecal biopsies. These were classified as within normal limits if all other sets of biopsies were normal. It was thought that one possible explanation for this appearance was that the mucosa was noted to be thinner in the cecum, leading to crowding of the cells within it. However, no attempt was made to quantify this subjective observation which probably merits further investigation.

Thus, in making a recommendation concerning the location and number of biopsies taken during a "normal" colonoscopy, a cecal biopsy alone may be misleading and lead to a false positive diagnosis of nonspecific colonic inflammation, and a sigmoid biopsy appears to miss some cases of intestinal spirochetosis. Therefore based on the results of this study, biopsies from the sigmoid colon and hepatic flexure are the minimum required to ensure detection of all histologic abnormalities, and this has now become the policy of our unit.

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