Large Bowel Adenomas

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The primary purpose of screening the large bowel is to detect invasive cancer early. Screening also can reveal the presence of large bowel adenomas, which most pathologists and clinicians with expertise in this field regard as precursors of colorectal cancer. Two clinical trials are now under way to confirm the preliminary evidence that removal of colorectal adenomas can reduce the incidence of subsequent large bowel cancer. The available evidence is sufficient to justify the development of diagnostic and treatment strategies for detecting and removing colorectal adenomas.

Polyps are visible growths that protrude from the mucosa of the large bowel. Of the several types of polyps that may arise in this tissue, only one—the neoplastic adenoma— is strongly associated with risk for transformation to invasive cancer. Adenomas, particularly if multiple, also are associated with an increased risk that invasive cancer may be present elsewhere in the large bowel.

Some colorectal adenomas are completely benign (Fig. 1); others contain in situ (Fig. 2), intramucosal (Fig. 3), or invasive cancer (Fig. 4). In situ and intramucosal cancer are limited by, and external to, the muscularis mucosa of the adenoma and carry no risk of lymphatic or hematogenous dissemination. However, contiguous spread of intramucosal cancer into the deeper substance of the adenoma can occur, in which case the adenoma is said to contain invasive cancer. This progression, sometimes referred to as the adenoma-cancer sequence, is the current explanation for the pathogenesis of most colorectal cancers.

The risk of invasive cancer’s being present within an adenoma correlates with interactive morphologic characteristics. The risk increases directly with increasing size of the polyp and becomes notably higher when an adenoma reaches about 1.5 cm in diameter. Invasive cancer also is more likely to be present if the adenoma is sessile, has a villous morphology, or contains severe dysplasia. An adenoma containing invasive cancer is referred to as a malignant colorectal polyp. The very small polyp, less than six mm in diameter, often has adenomatous elements, but seldom if ever contains an invasive cancer. There are, however, reports of small, non-ulcerated, invasive colorectal cancers measuring one cm in diameter.

The natural history of colorectal adenomas is not well understood. Statements
regarding the frequency and histology of adenomas have been clouded by imprecise terminology, and estimates of incidence have been marred by unrecognized prevalent adenomas.

Colorectal adenomas usually follow a course of slow growth. An adenoma may take an estimated 10 years to double in diameter. Some small adenomas may regress spontaneously.

Identification of patients who are at high risk for colorectal adenomas and cancer depends on historical, physical, and morphologic risk factors. The importance of dysplasia and the utility of cytology merit further investigation. Current studies of cytogenetics, proto-oncogenes, and DNA flow cytometry in adenomas may lead to new, clinically useful insights.6–9

**Diagnosis and Treatment**

Most colorectal adenomas can be both identified and removed endoscopically. Although an air-contrast, barium enema examination can reveal polyps as small as five mm in diameter, endoscopy may be therapeutic as well as diagnostic. Accurate assessment of the risk status of the individual patient for the future development of adenomas and/or colorectal cancer depends on the pathologic examination of all colorectal polyps present in the colon. All colorectal polyps should be endoscopically removed and recovered if possible. When it is not possible to remove a polyp completely, endoscopic biopsy specimens from the lesion may be of some assistance in the pathologic evaluation of the lesion, but information derived from biopsies must be interpreted with caution because the specimens are small and may not be representative of the overall histopathology of the lesion. For example, carcinoma within a polyp is usually focal, often centrally depressed, and generally impossible to detect if it is not present in the biopsy material.

In patients with an identified adenoma, it is essential that the entire colon be examined, because adenomas are often multiple and because finding one adenoma increases the likelihood that cancer is present elsewhere in the large bowel.

Colorectal polyps measuring less than five mm in diameter may be treated by an endoscopic method that simultaneously destroys the polyp by electrocaugulation and provides a biopsy, sometimes referred to as the “hot biopsy” technique. Pedunculated polyps may be excised by endoscopic snare cautery.

Operative excision is limited to polyps too large to be removed endoscopically, to polyps in the distal rectum, and to malignant colorectal adenomas when endoscopic excision has been deemed inadequate.

Larger sessile adenomas can sometimes be removed endoscopically, although this procedure requires greater endoscopic skill and experience than does removal of small or pedunculated polyps and carries a greater risk of perforation. When such a lesion is removed in several pieces, it may be difficult for the pathologist to reconstruct and assess accurately, especially if some pieces were not recovered. It also may be difficult to be certain that the adenoma has been removed completely. In the latter circumstance, a series of follow-up examinations of the polypectomy site may be necessary, provided no invasive cancer was found in the lesion. If invasive cancer is found in the pieces of a sessile polyp removed at colonoscopy, surgery is indicated.

Even when a pedunculated adenoma contains focal invasive cancer, endoscopic removal is generally considered adequate treatment if the endoscopist is satisfied that excision has been complete, the margin is composed solely of normal tissue, and the polyp contains no poorly differentiated (Grade III) histology or evidence of lymphatic and/or vascular invasion by cancer. When invasion is limited to the head or stalk of a pedunculated polyp and these criteria are met, excision is generally regarded as curative. However, the prognostic significance of invasive cancer within a polyp is debated, and some authors regard invasion into the submucosa of the bowel wall as sufficiently threatening to merit resection.11

Careful histopathologic assessment of all excised adenomas is mandatory for proper management of patients. It is there-
Fig. 1. Adenomas may be purely tabular, composed entirely of tabular glands extending downward from the surface as shown.

fore necessary to resect and retrieve all polyps and to submit these specimens promptly in the fresh state to the pathologist. Larger specimens should be oriented for proper prosection.

The importance of an interdisciplinary approach to the detection and management of colorectal adenomas is highlighted in the following clinical histories.

Problems of Detection and Management

Case 1
A single polyp seven mm in diameter was detected in the rectum of a 60-year-old person during flexible sigmoidoscopy. Histologic examination showed a tubular adenoma. Is total colonoscopy indicated?

Thorough scrutiny of the remaining colon is warranted, and colonoscopy is probably the technique of choice. The likelihood of finding adenomas in the remaining colon approximates 30.0 percent, and that of finding cancer approximates 0.5 to 1.0 percent.12,13 Although a meticulous, dou-
ble-contrast, barium enema examination can reveal all mucosal lesions larger than five mm in diameter, colonoscopy is preferable because it also permits histologic diagnosis and treatment.

The above patient had a cholecystectomy in the distant past, and the colonoscope could not be inserted beyond the hepatic flexure. Is an air-contrast, barium enema x-ray examination now indicated?

Yes, because it is necessary to scrutinize the entire colon mucosa.

If the seven-mm rectal polyp in the above patient had been hyperplastic rather than adenomatous, would surveillance of the colonic mucosa still be necessary?

Yes. Although the subject of hyperplastic polyps is controversial, the likelihood of finding benign or malignant neoplasia elsewhere in the colon may be the same.14,15

Case 2

A 50-year-old asymptomatic person had a 10-mm, pedunculated polyp in the descending colon completely removed by endoscopic snare cautery. The remaining colorectal mucosa was normal. Histologic examination of the polyp showed a tubular adenoma without dysplasia. The patient had no risk factors other than the adenoma itself. What is the proper follow-up of this patient?

Although the correct intervals for follow-up cannot be precisely defined with currently available data, most gastroenterologists would prefer total colonoscopy for this patient one year later and, if the results were negative and the patient remained asymptomatic, subsequent colonoscopy examinations would be recommended at intervals of two to three years. Alternative follow-up procedures would be sigmoidoscopy, preferably flexible, plus an air-contrast barium enema examination. In addition, the patient should undergo a fecal occult blood test annually.

Would the presence of additional risk factors in the above patient—namely, a family history of colorectal cancer in a first-degree relative, a prior colorectal adenoma or cancer, multiple adenomas, prior endometrial breast or ovarian cancer, or dysplasia or villous morphologic characteristics in the adenoma—make a difference in the timing of future surveillance?

The recommended intervals for surveillance colonoscopy are rough guidelines based on average clinical situations. Certain elements in a patient's past history or family history imply increasing levels of risk for the development of adenomas and/or cancer. Therefore, the surveillance intervals should be modified according to the circumstances of the individual patient. A villous histology seems to make no difference with respect to risk elsewhere in the colon. A strong family history of colorectal cancer is associated with a greater likelihood of finding polyps, as well as a greater tendency for neoplasia to be located in the right side of the colon. Removal of multiple adenomas is associated with a risk of subsequent adenoma development that is greater than that for removal of a single adenoma. Dysplasia in a removed adenoma is associated with a greater risk of subsequent development of adenomas. Increased age and male rather than female gender are also risk factors.16,17

Case 3

A 75-year-old woman with disabling cardiopulmonary disease was found to have a three-cm-wide, sessile, non-ulcerated, mobile polyp in the transverse colon. Four biopsies showed villous adenoma, and one showed in situ carcinoma. Should this patient be treated by fractionated, or piecemeal, endoscopic removal of the polyp?

Based on the pathologic type and gross morphology of this lesion, there is a significant chance that it contains invasive cancer.
The presence of in situ carcinoma in one biopsy specimen offers no reassurance that the cancer is superficial throughout the polyp. Rather, this finding is actually a cause for greater concern with respect to the presence of invasive cancer. Unless cardiopulmonary status or other concurrent disorders represent an overriding risk for surgery, patients with large sessile adenomas should have operative resection to exclude the presence of invasive cancer. The decision for surgical versus endoscopic treatment therefore depends in this case on the overall assessment of the patient’s ability to undergo surgery. If the risk of surgery is judged to be prohibitive, colonoscopic treatment may be considered, with the recognition that a serious complication of colonoscopic treatment can be life-threatening in such a patient. In addition, when fractionated colonoscopic excision is performed, precise histopathologic scrutiny for the presence of, and depth of invasion by, cancer is unreliable.

If surgery for an adenoma in the transverse colon is warranted, what should be the extent of resection?

The extent of lymphadenectomy should be that of a cancer operation, because surgery for colonic adenomas is now restricted to patients with greater risk of lymph node metastasis. Sessile or pedunculated configuration of the adenoma should make no difference. Because the adenoma has already been identified, colostomy is unnecessary and undesirable. Since the colonic mucosa has already been scrutinized, intraoperative colonoscopy is also unnecessary. A partial colon resection for an adenoma of any type does not eliminate the need for subsequent endoscopic surveillance for the occurrence of new adenomas in the remaining colon.

Case 4

A 63-year-old person had a two-cm-wide pedunculated polyp in the midsigmoid removed by snare cautery. The endoscopist was satisfied that the excision was complete. Histopathologic examination showed a well-differentiated, invasive carcinoma in the submucosa of the head of the polyp. There was an ample margin of normal stalk to the base. Lymphatic or venous invasion could not be identified. Is resection of the sigmoid colon indicated?

A considerable body of evidence indicates that under these conditions the operative risk entailed in resection is greater than the likelihood of finding lymph node metastasis in a resected specimen. Accordingly, this patient should have a repeat endoscopy performed in approximately three months to inspect the site of the malignant colorectal polyp. If the tumor was sessile or poorly differentiated, contained venous or lymphatic invasion, involved the margin, or extended into the submucosa of the bowel wall, resection would be indicated.

Case 5

During colonoscopy, a 50-year-old person was found to have a three-cm-wide colorectal polyp 12 cm above the anal verge. The rest of the colon mucosa was normal. Histopathologic examination of the excised adenoma showed cancer with invasion of the base, and an operation was recommended. Are any additional endoscopic procedures indicated before surgery?

It is important that the tumor be accurately located by rigid sigmoidoscopy. Distances measured by flexible endoscopy can be unreliable. A precise determination of the relationship of the cancer to the dentate line is critical for selection of operative treatment.
Case 6

A 68-year-old woman had a three-cm-wide, freely mobile tumor on the distal left lateral rectal mucosa. The non-ulcerated tumor was visualized two cm above the dentate line. Air-contrast barium enema examination showed no other mucosal pathology. Several biopsies were obtained from the tumor, and histologic examination showed a superficially infiltrating, well-differentiated adenocarcinoma in a villous adenoma. What is the appropriate treatment for this patient?

This patient may be a candidate for transanal, full-thickness, local excision of the cancer, including a margin of normal tissue. The excision constitutes a total biopsy and, if the specimen meets specific histopathologic criteria similar to those for malignant colorectal polyps, the local excision may be sufficient treatment. Other alternatives to abdominal perineal resection include diathermy, or electrocoagulation, and primary radiation therapy.

Case 7

A 25-year-old man had 15 rectal polyps found during proctosigmoidoscopy. Colonoscopy shows more than 100 polyps scattered across his colonic mucosa. A presumptive clinical diagnosis of familial adenomatous polyposis is made. Should the patient now be scheduled for surgery?

It is important that an accurate histologic diagnosis of adenoma be established before treatment is provided. Other histologic types of polyposis—namely, the hamartoma in the Peutz-Jeger syndrome and the retention polyp in juvenile polyposis—have far less risk for cancer and may merit different treatment. In addition, preoperative systemic surveillance, including upper gastrointestinal endoscopy, is advised. The polyposis patient is at risk for upper gastrointestinal neoplasia, particularly perianpillary cancer. Familial adenomatous polyposis may occur in patients who have no family history of the disease.

Summary

The last 20 years have witnessed dramatic technological advances in the diagnosis and treatment of colorectal polyps. These developments, in addition to an increased understanding of large bowel carcinogenesis, have shifted the risk/benefit balance toward a more aggressive approach to colorectal polyps. Mounting evidence for the adenoma-carcinoma sequence supports the position that all colorectal polyps should be removed, recovered, and evaluated. Moreover, in most cases polypectomy can be achieved endoscopically. To justify surgery today, adenomas must be too large to be removed endoscopically, located in the distal rectum, or malignant with submucosal invasion or questionable margins.

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