5. Management of malignant polyps

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Synopsis

Malignant polyp is a term that is used when a polyp is removed by colonoscopy that appears grossly benign but has adenocarcinoma identified histologically (Fig. 1). The clinical issues in this setting are more difficult than in a patient who has had a surgical resection because of a large sessile polyp or suspected malignancy where a surgical specimen and adjacent lymph nodes are available for staging. The management of patients with malignant polyps has assumed increased importance in recent years as a result of more widespread screening in the general population, and especially with introduction of colonoscopy as a screening option [1,2]. A decision must be made in each of these patients whether to consider the colonoscopic polypectomy curative or refer the patient for surgery. This decision is compounded when an asymptomatic person has been induced to have a screening test that uncovers the unsuspected pathology. Management decisions require an assessment of the pathology, risk of adverse outcome, risk of surgery and colonoscopic follow-up, and the available surgical options. There are additional considerations in high-risk patients, e.g. those with a family history suggesting hereditary non-polyposis colorectal cancer (HNPCC), long-standing inflammatory bowel disease, and familial polyposis. This chapter deals primarily with the average risk patient.

Pathology

Definition of malignancy and polyps

Malignant polyps are adenomas with adenocarcinoma that has invaded beyond the muscularis mucosa (Fig. 2). The cancer cells have thus gained access to the submucosa, which contains lymphatics and blood vessels, which can permit spread to adjacent lymph nodes and less commonly to distant organs. Spread to the deeper layers of the colonic wall can also occur by direct extension. In pedunculated adenomas, the submucosa is in continuity with the core of the stalk and head of the polyp. In sessile adenomas, invasive carcinoma is directly into the submucosa of the bowel wall. Intramucosal carcinoma is a term used to describe invasion of cells through the basement membrane of the crypts into the lamina propria of the surrounding mucosa but with no penetration into or through the muscularis mucosa into the submucosa. There is therefore no opportunity for regional or distant spread and there is no clinical significance regarding the initial management of the patient. The older term carcinoma-in-situ has now been replaced by the term high-grade dysplasia, which also includes severe dysplasia. The pathology diagnosis of high-grade dysplasia also has no clinical significance in terms of the initial management of the patient. All adenomatous polyps have at least low-grade dysplasia, which incorporates mild and moderate dysplasia [1,2].

Assessment of polyps

Accurate assessment of the resected polyp is required for rational clinical decision-making. Every effort must be made to retrieve the entire specimen for examination and classification. This is easier for pedunculated polyps than for large sessile polyps that are removed in piecemeal fashion. Saline injection to provide a cushion of normal mucosa under a sessile polyp can greatly aid in the completeness of removal. An attempt should be made to identify the base of the polyp. Contraction of the muscularis mucosa after resection may cause a specimen to curl into a ball making subsequent
identification of the resected site difficult. To avoid this, sessile polyps can be placed flat on a piece of cardboard, thick paper, on absorbable gelatin sponge (Gelfoam) or on a frosted glass slide before insertion into fixative. Histological sections are made from stepwise sagittal blocks of the entire polyp, taking care to represent the stalk and polyp resection margin. When invasive adenocarcinoma is identified the report should include the grade of differentiation of the carcinoma, lymphatic or vascular space invasion, volume of polyp replaced by carcinoma, depth of invasion and proximity to resection margin. Pseudoinvasion with adenoma misplaced into the stalk or submucosa should be distinguished from true invasion (Fig. 3). Reporting should include whether there is adenomatous tissue at the resection margin as well as whether there is cancer at the margin to indicate the completeness of the removal histologically.

Risk factors for malignant polyps

The frequency of finding malignancy polyps was 1.5% in the National Polyp Study, which was a multicentre study with a database of approximately 5000 polyps removed in 2000 patients [3] (Fig. 4). These patients were mostly average risk men and women. In recently reported screening colonoscopy studies, approximately 10% of asymptomatic average risk people had advanced neoplasia including 1% with malignant adenomas [4]. The vast majority of adenomas removed in these studies were benign. It has been estimated that only 0.25% of adenomas will demonstrate conversion to malignancy each year [5].

Polyp size and villous component

Analysis of the National Polyp Study database has confirmed that polyp size is a major determinant of the likelihood that high-grade dysplasia will be found in a colorectal adenoma. The amount of villous growth in the adenoma is also an independent determinant of this risk, with an effect of comparable magnitude to that of size. Furthermore, the effects of size and villous component have been found to be multiplicative, that is, their combined effect is greater than the sum of their individual effects. Frequency of high-grade dysplasia in adenomas is unrelated to gender of the patient, according to the National Polyp Study data analysis, but logically appears to increase significantly with advancing age. When a patient has multiple adenomas, which will be the case in almost 50% of the adenoma-bearing population, the patient's risk of harbouring an adenoma with high-grade dysplasia is proportionately increased, but this increased risk from multiplicity appears to be dependent on the associated factors of size and villous component [3].

Increased polyp size, villous histology, and severe dysplasia are all associated with an increased risk of cancer and adenoma (Fig. 5). A study from St. Mark's Hospital in London analyzsed factors associated with malignancy.

Polyp size

- 1.3% of adenomas less than 1 cm in size
- 9.5% between 1 and 2 cm
- 45% over 2 cm were malignant

Pathology

- 4.8% of tubular
- 22.5% of tubulovillous
40.7% of villous adenomas were malignant

**Dysplasia**
- 5.7% of mild
- 18% of moderate
- 34.5% of adenomas with severe dysplasia [6–8]

Molecular changes parallel the histopathologic progression of the adenoma-carcinoma sequence.

**Flat lesions**

The adenoma-carcinoma sequence may not always evolve within a polypoid lesion. Small flat invasive cancers have been described which are thought likely to have developed within a preceding flat adenoma [9,10]. Flat adenomas, originally, described by Muto et al. have been reported to have greater propensity to develop into cancer, and invade the submucosa more readily than polypoid adenomas [11]. An association between small, flat adenomas and cancer has been reported in HNPCC. While these associations are controversial, it is accepted that cancer may develop in flat non-polypoid adenomas and present particular problems for diagnosis and resection. These tumors may be difficult to identify endoscopically. Dye spraying with either topical spray of 0.2% indigo carmine on the colonic surface or by oral ingestion of dye during the preparation phase prior to colonoscopy may aid in their endoscopic visualization.

Small, flat adenomas, some of which contain invasive carcinoma, have been resected and cured by the submucosal injection of saline followed by removal with an endoscopic snare.

**Are flat lesions missed in the West?**

There are only a few reports of flat adenomas in the English literature, leading to speculation that they are not recognized and therefore ‘missed’ during colonoscopy. The relative paucity of English-language reports may reflect either a difference in prevalence or the fact that they are seen and removed but not separately categorized by western endoscopists. Either of these two possibilities is more plausible than the theory that these small lesions are being repeatedly and systematically overlooked, since rigorous follow-up of patients by the National Polyp Study (NPS) has demonstrated an extremely low incidence of subsequent cancer in colons from which all adenomas were removed by the NPS endoscopists [12]. The latter of these two explanations would appear to be the ‘best fit’ to available data, since, when specifically sought, flat adenomas are found in North Americans. O'Brien et al. reclassified as flat or polypoid all non-pedunculated adenomas detected at the initial colonoscopy in the National Polyp Study. Flat adenomas did not have an increased presence of high-grade dysplasia. In addition, patients with flat adenomas did not have an increased risk of subsequent advanced adenomas [13].

**Initial endoscopic evaluation and treatment of polyps**

**Visual assessment**

The endoscopic appearance of a polyp may suggest a malignant component although most malignant polyps have a benign appearance at endoscopy (Fig. 1). Gross features of malignancy include an irregular surface contour, ulceration, firm (or hard) consistency when the head is pushed with a snare or forceps, and broadening of the stalk [1,2,14–18](Fig. 6).
Although polyps with these features are not invariably malignant, the endoscopist should pay special attention to any lesion with malignant characteristics, since it may be desirable to resect these somewhat differently than the routine adenoma. If cancer is suspected by any of the above criteria, the snare should be placed more toward the wall when resecting a pedunculated polyp than toward the head, as is the usual practice. Special care must be directed toward recovering all of the fragments for histopathological evaluation and to localize the polyp’s position in the colon precisely should subsequent surgery be a consideration by the endoscopist at the time of the polypectomy.

The initial evaluation by the endoscopist may be of great significance, since the morphology of the lesion may be difficult to assess accurately once the resection is done.

**Difficulties after resection**

Following resection, it may not be possible to ascertain whether a polyp was sessile or pedunculated, because a short pedicle may retract completely into the polyp head. Polyps tend to curl up in formalin and the site of attachment of sessile polyps may not be recognizable in the pathology laboratory [19,20]. The endoscopist can usually tell, with some confidence, whether a complete polypectomy has been done when the polyp is pedunculated, since the stalk is readily identified and the absence of residual adenoma is easily discerned. The determination is more difficult when a sessile polyp is resected, although a clean base without adjacent, evaluated, reddened tissue usually indicates completeness of resection. This assurance may be difficult to achieve when a polyp has been removed in piecemeal fashion, because fragments at the base could equally prove to be non-viable coagulum or residual adenomatous tissue.

**Localization of polyps, tattooing**

Precise localization of the polypectomy site may be desirable even if surgery is not to be performed and the patient is to be followed endoscopically. Reliance on the centimeter distance of colonoscopy insertion is unreliable as are intraluminal landmarks. The best method for localizing the polypectomy site is by injection of a surgical marker such as India Ink or a suspension of pure carbon particles, whereby a dilute suspension of sterile black carbon particles is injected at the site (Fig. 7). The area is stained forever and can be readily detected by the surgeon or by the endoscopist on repeat examination. The injection, or tattoo, should be made circumferentially around the polypectomy site using 10 mL of solution in 2–3 mL fractions. Precise localization of the polypectomy site is critical since a resection may be done by laparoscopic technique.

**Surgery or endoscopic follow-up?**

**Pedunculated adenomas**

The pedunculated malignant polyp has by long convention been placed in a different category than the sessile malignant polyp by many clinicians. When polyps are pedunculated, the submucosa of the polyp is separated from the submucosa of the colon wall by a thin tubular segment of submucosa, whereas in sessile polyps the submucosa of the polyp is directly contiguous with the submucosa of the colon wall. The literature on malignant polyps is inconsistent, with several authors utilizing their own classification system for depth of invasion, rendering it difficult to compare extent of tumor invasion and its significance from one paper to another. Some reports mix the results from surgically resected specimens with those removed colonoscopically, which tends to unfavorably skew the outcomes by including cases that would not have been considered for endoscopic resection.
However, guidelines for endoscopic polypectomy are fairly well accepted when discussing pedunculated polyps.

Factors suggesting no need for surgery

When certain favorable clinical and histologic criteria are met following removal of pedunculated malignant polyps, it is the general consensus of the literature on this subject that surgery should not be performed since the risk of having residual cancer at the site or nodal metastasis is extremely low and less than the mortality from surgical resection. These favorable criteria are that the tumor be well or moderately differentiated, the resection margin be clear of malignant cells, and the cancer not invade lymphatic channels or vascular spaces within the polyp (Fig. 8).

Factors favoring surgery after polypectomy

Poorly differentiated carcinoma is rare in malignant polyps, but is seen in 15% of surgical resection specimens for colorectal carcinoma [21]. Poor differentiation appears to be a feature that can be correlated with tumor mass and with vascular space invasion. Its presence in malignant polyps is an ominous prognostic sign and mandates surgical resection if the patient's clinical condition does not preclude it (Fig. 9).

Invasion of lymphatics or veins within the submucosa of the polyp head or stalk is also a relatively rare phenomenon and is thought to be a poor prognostic sign, although there have not been enough cases reported to constitute a series that would bear a statistical analysis of its impact, independent of other negative factors. A recent report indicates that this type of vessel invasion is found more frequently if a combination of H&E and elastin stains is used [22].

What is a safe margin?

The acceptable distance from invasive carcinoma to the endoscopic diathermy burn is variable among many reports in the literature. Some authors insist that the margin must be ‘healthy’, while others permit upon a minimum of a 1-mm margin, a 2-mm margin, or a 3-mm margin [23–26]. Lipper [24] states that the presence of malignant cells at the resection margin is the only criterion that reliably predicts a poor outcome. Morson [28] has found good long-standing results in cases with a tumor at the resection margin that was deemed to be safe because the endoscopist considered that all abnormal tissue had been removed during colonoscopy. Morson felt that in such cases the diathermy burn caused sufficient cell necrosis to eradicate all residual malignant cells at the margin of the tumor.

Sessile adenomas

Sessile malignant polyps are often considered separately by both clinicians and pathologists. The concern is that malignant cells that cross the muscularis mucosa of a sessile polyp are actually invading into the portion of the submucosa that is directly contiguous with the rest of the bowel wall submucosa and are not protected by a ‘buffer zone’ of submucosa as in pedunculated polyps. Many authors feel, however, that there is no sound basis for this assertion and that malignant polyps, which are sessile, should not be considered any differently from those that are pedunculated [24,27–29]. A review of the literature in 1988 [25] drew the conclusion that sessile and pedunculated malignant polyps did not differ in their risk for residual or metastatic disease if favorable criteria were applicable (Figs 10 and 11).

However, a paper on decision analysis and the therapeutic options in malignant polyps concluded that
all sessile malignant polyps should have an operative resection if the patient is a good-risk candidate. Other authors have also expressed the view that sessile malignant polyps should be treated by further surgical resection \[30–34\]. In one report \[35\], sessile malignant polyps had a high frequency of residual or nodal cancer, but all eight of the cases in this series found to have residual disease also had positive resection margins. It has been suggested that only sessile malignant polyps resected in a piecemeal fashion should be subjected to surgery because of the possibility of error in orienting tissue received by the pathologist \[29\].

**Role of the clinician**

There is a consensus that if no unfavorable criteria are present in pedunculated malignant polyps, there is a low or nonexistent risk of residual tumor or lymph node metastases and therefore surgery is not indicated \[23,36–38\]. Many also contend that this equally applies even if the polyp is sessile, but it is reasonable to consider a resection in these patients if their surgical risk is low \[28,29,39\]. Some authors have attempted to add other risk factors to the above-mentioned criteria such as deep stalk invasion \[39\] or extensive tumor invasion of over one-third of the polyp's submucosa \[23\].

**Follow-up protocols**

After colonoscopic removal of a malignant polyp with favorable risk criteria a follow-up colonoscopy is generally performed in about three to six month to assess the polypectomy site for completeness of removal, particularly if the polyp was sessile \[1,2\]. If residual cancer is found the individual is referred for surgical resection, providing that the patient is a good surgical candidate. If there is no residual cancer, a one-year follow-up colonoscopy may be performed, and if this examination is negative it may be repeated again in three years. Additional clinical follow-up with CT scanning and other tests such as CEA may be appropriate in select patients. Endoscopic ultrasound is usually not helpful postpolypectomy because of the inflammatory reaction at the polypectomy site and possible reactive changes in regional lymph nodes \[40,41\].

**Balancing the risk of surgery**

In order to achieve the best outcome, the decision to operate on a patient who has had an endoscopically resected malignant polyp involves balancing the risk of residual cancer at the excision site and regional lymph node metastases against that of mortality from abdominal surgery. In general, the risk of death from elective colonic surgery varies from 0.2 to 2%, with the patient below age 50 being at lowest risk \[42,43\]. A summary analysis of the recent literature yields an estimate of the risk of residual tumor or nodal cancer in colonoscopically resected pedunculated malignant polyps with favorable criteria as 0.3% that for sessile malignant polyps as 1.5% \[2\] (Fig. 12).

Patients of any age with favorable resection criteria who have pedunculated malignant polyps resected endoscopically should not have a subsequent surgical resection, nor normally should patients over 50 years of age with sessile malignant polyps with favorable resection criteria \[44\]. Among healthy patients under age 50 with sessile malignant polyps with favorable criteria, the risk of residual tumor or nodal disease is similar to or slightly higher than the risk of death from surgery, and the argument can be made that this group of patients should have surgical resection of that segment of bowel. Subsequent cancer surgery with bowel resection and node dissection will result in a cure of residual cancer in only about 50% of the patients with nodal metastases.
Rectal lesions

Malignant polyps in the distal rectum require special consideration because permanent colostomy is an issue. Malignant polyps in this location are also unique in that they are amenable to proctologic surgical techniques that permit deep excisions, which are not applicable in the colon. In patients who have a positive margin at colonoscopic polypectomy, a trans-anal surgical excision may reverse the situation to a favorable margin free tumor. A low anterior or abdominal perianal resection can thus be avoided. If the decision is made to refer the patient for surgery, the endoscopist should re-scope the patient as soon as possible and tattoo the polypectomy site if this had not been previously done. This is critical because often there is delay in the final decision until multiple consultations have been sought by the patient and the precise polypectomy site may not be identifiable.

Patients with family history

Patients who have a family history of HNPCC should be considered separately from the above considerations. The presence of a malignant polyp regardless of ‘safe’ margins or other adverse pathology mandates a surgical resection. They may have an accelerated adenoma-carcinoma progression and have a high synchronous and metachronous rate of additional adenomas. For these reasons, surgery in these patients should be a subtotal colectomy.

Conclusion

The clinician's role is to take into account the many factors relevant to each patient with a malignant polyp. The first step is to examine the histological slides along with the pathologist in order to have an accurate understanding of the pathological characteristics of the cancer. Other factors that need to be considered by the clinician include: the completeness of the polypectomy, ease or difficulties of the colonoscopy, anatomic location of the polyp, its configuration, and the patient's comorbidity. If a decision is made to refer the patient for surgery, there should be a discussion with the surgeon regarding the above factors as well as the surgical options including trans-anal excision, and standard resection vs. subtotal colectomy. The surgery needs to be a cancer operation that will include an adequate number of regional lymph nodes as well as adequate lateral and deep margins, and the clinician needs to assist the surgeon by placing a tattoo at the polypectomy site. Effective management of patients with malignant polyps therefore requires a team approach that involves the pathologist, the clinician, and possibly the surgeon. Following this, the final decision must be made jointly with the patient, who because of comorbidity, age, personal philosophy, and other reasons will influence the final decision and ultimate outcome.

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