Alimentary tract and pancreas

Histopathology and prognosis of malignant colorectal polyps treated by endoscopic polypectomy

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SUMMARY The histopathological features and results of treatment of malignant polyps removed by endoscopic polypectomy from 60 patients are presented. The patients were followed for a minimum of five years. Forty six patients were treated by polypectomy alone as local excision was judged complete and the invasive carcinoma was well or moderately well differentiated. Thirty seven of these patients are alive and well after five years and the remaining nine have died of other causes up to four years later: there was no evidence of recurrence in any of these cases. Fourteen patients underwent a subsequent major surgical resection and residual tumour was found at the site of polypectomy in two cases but regional lymph nodes were not involved. Only one patient from this group with a high grade tumour developed metastases although the operative specimen was free of tumour. Malignant polyps can be successfully treated by polypectomy alone provided both the laboratory techniques of examination and the histopathological criteria are strictly applied.

A previous study from this hospital established the histopathological criteria for the selection and treatment of early cancers of the distal colon and rectum by local excision alone.¹ Many of these tumours were malignant polyps treated by endoscopic polypectomy using the rigid proctosigmoidoscope, others were small rectal cancers, and a few were lesions treated by colotomy. During the past 10 years there has been rapid development of the techniques of fibre-optic colonoscopy and polypectomy which have eliminated the operation of colotomy and increased the yield of malignant polyps removed by endoscopic methods.

Recent reports²⁻⁴ have challenged the policy of polypectomy alone for malignant polyps of the colorectum which has been established at this hospital during the past 10 years. The object of this paper is to report the pathology and results of treatment of 60 patients followed up for a minimum of five years, of whom 46 were treated by polypectomy alone and 14 by polypectomy and subsequent major surgery. It must be emphasised that these are the results of a prospective study in the sense that it was a deliberate policy to advise

polypectomy only in all those patients who fulfilled the required histopathological criteria. This advice was not accepted in all cases for various reasons and these, together with others thought at the time to be unsuitable for polypectomy only, constitute the group of patients who had further major surgery.

Methods

The preparation of individual polyps for histological examination has particular importance. The technical procedures are designed to produce histological sections in which the normal micro-anatomical relationship of the head of the polyp to its stalk is preserved. For sessile lesions the specimen must be embedded and sections cut to show the correct micro-anatomical orientation of the tumour and underlying submucosa. Failure to adhere strictly to such methods makes accurate interpretation by the pathologist difficult or impossible both for diagnosis and advice about treatment.

The polyp is fixed in buffered formalin: if it is larger than 2 cm in diameter, it will take up to 48 hours for the formalin to penetrate to the core of the polyp. If the polyp is embedded and sectioned before the core is properly fixed, it may not be possible to give a sufficiently accurate report.

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Pedunculated polyps may have either long or short stalks. Before embedding, the base or stalk of the polyp should first be identified. If the stalk retracts it can usually be identified by the whitish appearance of the diathermy mark where the polyp was snared. The polyp is embedded *whole* on its side but if necessary with slight trimming of two sides of its head so that it lies flat in the deep type of Tissue-tek mould. If the polyp is very large, even the large mould may be too small so in this situation the polyp is embedded on a plate. After embedding, the block is trimmed to a level where sections can be cut through the head of the polyp and its stalk in continuity: the level is recognised as the microtome cuts through the block by the paler colour of the connective tissue of the core and stalk compared with the head of the polyp: this colour is easily seen through the translucent wax. In this way, the head of the polyp, its core and stalk are sectioned in their

correct micro-anatomical relationship to one another. Moreover, the diathermy mark at the cut edge of the stalk can be clearly identified (Figs. 1, 2(a), (b), and 3).

If the polyp is sessile, parts of the surface may curl round and cover the base: in such cases, the cut edges are gently lifted aside so that the base can be seen. Again, this may be identified from the whitish appearance of the submucosa and diathermy burn. A small sessile polyp, less than 1.0 cm across, is embedded on its side in the mould without trimming. Sections can be cut across the block so that the edge of the polyp where it merges with the normal mucosa is examined, and the tumour is in the correct micro-anatomical relationship to the submucosa.

The larger sessile tumours should be cut with a scalpel into parts which are embedded separately. Intact specimens removed by endoscopists are

Fig. 1 Tubular adenoma showing invasion into the stalk of polyp by well differentiated adenocarcinoma of low grade of malignancy (dotted line). Diathermy burn (A) is clearly seen. Multiple levels showed that local excision was histologically complete and further major surgery was not advised. Patient remains alive and well more than five years after polypectomy. Haematoxylin and eosin, $\times 12$ (original magnification).

Fig. 2(a) Villous adenoma on a stalk. Focus of undifferentiated carcinoma (arrowed) is invading the core of the polyp. Diathermy burn (A) can be clearly seen. Multiple levels showed that local excision was histologically complete but further major surgical procedure was performed because of high grade carcinoma. No residual tumour in the bowel wall or regional lymph nodes was found in the operation specimen. Haematoxylin and eosin, $\times 8.6$ (original magnification). (b) High power view of undifferentiated carcinoma of high grade of malignancy seen in Fig. 2(a). Haematoxylin and eosin, $\times 800$ (original magnification).

seldom larger than 5.0 cm across, even those removed from the rectum, but it is impossible to process large tumours in one block. It is important, however, that the entire specimen should be cut up into parts and all pieces embedded in such a way that histological sections show normal micro-anatomical orientation of tumour and any surrounding mucosa with the submucosal layer. Only in this way can diagnosis be accurate and completeness of excision be assessed with confidence.

REPORTING MALIGNANT POLYPS (Figs. 1, 2(a), (b), and 3)

The most important objectives are: (1) To identify the histological variety of adenoma: whether tubular, tubulo-villous or villous types.³ When the whole of the head of the polyp is composed of carcinoma the lesion is reported as a polypoid adenocarcinoma. (2) To detect the presence of invasion by adenocarcinoma across the line of the muscularis mucosae into the core or stalk of the polyp or into the submucosa beneath a sessile adenoma.⁶ It is important to recognise the distinc-

tion between genuine carcinoma and pseudocarcinomatous invasion.⁷ (3) To assess the grade of malignancy of the carcinoma, whether well, moderately well or poorly differentiated.⁵ (4) To judge the adequacy of excision by examination of multiple levels (serial sections are unnecessary) through the head and stalk of the polyp or the tumour and underlying submucosa. In the case of stalked lesions up to 10 levels may be required. Most polyps are removed by diathermy snare and this leaves a diathermy mark at the margin of excision which can be recognised by a zone of eosinophilic coagulative necrosis (Figs. 1 and 2). (5) To offer advice about treatment.

Nomenclature is important because of the quality of the message that words can convey. It is our practice to avoid the use of the expression 'carcinoma-in-situ' because it may be misinterpreted by the endoscopist or surgeon and possibly lead to unnecessary major surgery. For this reason, we review each case together and a joint report is always issued. Only those polyps are included in this study which show unequivocal evidence of invasion

Fig. 3 Tubular adenoma with invasion of its stalk by well differentiated mucinous adenocarcinoma of low grade of malignancy. This illustration is one of multiple levels which suggested that local excision was histologically 'doubtfully complete' because carcinoma was present in diathermy burn at the limit of excision (arrows). No further major surgery was performed and patient remains alive and well more than five years after polypectomy. Haematoxylin and eosin, $\times 15$ (original magnification).

by carcinoma across the line of the muscularis mucosae.^{6,8}

The adequacy of local excision is reported as 'complete', 'doubtfully complete', or 'incomplete'. The first requires no detailed explanation. 'Doubtfully complete' was used when carcinoma was present within the tissues of the diathermy burn at the margin of excision. In such cases, the tissue received by the pathologist is not representative of all that has been removed. Some diathermied tissue is invariably left behind at the site of the polypectomy. 'Incomplete' was used when there was endoscopic and/or histological evidence which suggested that carcinoma was left behind at the site of polypectomy.

If local excision was judged to be 'complete' and the invading carcinoma was histologically well or moderately well differentiated, then the advice was offered that no further major surgical treatment was required. 'Doubtfully complete' local excision for well or moderately well differentiated carcinomas was often the subject of discussion between pathologist and surgeon and the procedure followed varied considerably according to the age, general health of the patient and other clinical considerations. 'Incomplete' local excision was not a judge-

ment based on histological evidence alone but was a decision made jointly with the endoscopist. If the polypectomy specimen contained poorly differentiated adenocarcinoma a bowel resection was advised, whether or not local excision appeared to be complete.

Results

Twenty four of 60 patients had malignant polyps removed from the rectum and lower sigmoid colon via the rigid proctosigmoidoscope; 36 had polyps removed from the proximal colon by colonoscopic polypectomy.^{9,10} One patient had two malignant polyps removed from the sigmoid colon during the one procedure.

AGE AND SEX

The series included 27 men of average age 66 years (range 32 to 89 years) and 33 women of average age 63 years (range 46 to 89 years). The age distribution is shown in Table 1.

SITE

The sites from which malignant polyps were removed are shown in Table 2. These figures correlate closely with others previously published from this institution.¹¹

SIZE

The sizes of the malignant polyps are shown in Table 3. The majority (52%) varied from 1.0–1.9 cm across, showing clearly that invasive malignancy is not limited to larger polyps.

HISTOLOGICAL TYPE (Table 4)

Fifty two polyps showed histological evidence of a pre-existing adenoma: 25 were in tubular adenomas, 17 were in tubulovillous adenomas and 10 were in villous adenomas. Nine were classified as polypoid adenocarcinomas.

Table 1 Age distribution

	Men		Women	
	27	(45%)	33	(55%)
30+	1	3.7%	—	—
40+	3	11.1%	1	3%
50+	3	11.1%	9	27%
60+	9	33.3%	10	30%
70+	10	37.0%	8	24%
80+	1	3.7%	3	9%
NK*	—	—	2	6%

* NK = not known.

Table 2 Site distribution

Site	Number	%
Transverse colon	1	1.6
Descending colon	5	8.2
Sigmoid colon	33	54.2
Rectosigmoid	10	16.4
Rectum	12	19.6

HISTOLOGICAL GRADE (Table 5)

In twenty five patients the polyps contained well differentiated carcinoma (40%), 33 had moderately well differentiated carcinoma (56%) and three patients only had poorly differentiated carcinoma (4%). Well and moderately well differentiated carcinomas effectively form one group in planning further management.

HISTOLOGICAL COMPLETENESS OF EXCISION (Table 6)

Excision was judged to be complete in 40 patients: this group includes the patient who had two malignant polyps and both of these were assessed histologically as being completely excised. In a further nine patients excision was doubtfully complete. Eight of these were all advised to have no further treatment on the grounds that the diathermy coagulation would have destroyed any malignant cells within the burnt area. In the ninth patient of this group the tumour contained poorly differentiated carcinoma and so surgical excision would have been advised regardless of the completeness of excision. In the remaining 11 patients excision appeared to be incomplete as judged by both histological and endoscopic criteria; however, this group includes one patient part of whose polyp was lost on withdrawal of the colonoscope thus making accurate assessment of completeness of excision impossible. The endoscopist was confident that excision was complete and so this patient alone of these 11 patients did not undergo a subsequent resection.

TREATMENT AND PROGNOSIS

In the 'excision complete' group of 40 patients (one

Table 4 Histological type

Type	Number	%
Polypoid adenocarcinoma	9	14.75
Cancers in villous adenoma	10	16.40
Cancers in tubulovillous adenoma	17	27.85
Cancers in tubular adenoma	25	41.00

with two malignant polyps) the cancers were all well or moderately well differentiated. One patient had a cancer thought to be completely excised histologically but the endoscopist was not confident that the tumour had been completely removed: this patient therefore underwent operative treatment but no residual tumour was found in the operative specimen. Two other patients in this group underwent subsequent surgery: both of them were patients referred to this hospital from elsewhere and both underwent surgery at their hospital of origin. After a lapse of years, it is not possible to be sure what the indications were for further surgical treatment in these patients but no residual tumour was found in the operation specimen.

In nine patients tumour extended into the diathermy mark and excision was reported as 'doubtfully complete': in eight of these it was considered that the diathermy coagulation would have destroyed any malignant cells and no further treatment was performed. Only one of these patients, whose cancer was poorly differentiated, underwent a major resection but no residual tumour was found in the operative specimen.

Ten of the 11 patients whose tumours were judged to be incompletely excised were referred for operative treatment: only two from this group had residual tumour at the site of the original polypectomy but there was no extension of tumour through the bowel wall and regional lymph nodes were not involved—that is, both had Dukes A cancers. The one patient who had no further surgery was the one described above part of whose polyp was lost: as the endoscopist was convinced that this polyp had been entirely removed and histological assessment could only be regarded as incomplete,

Table 3 Size distribution

Size	Number	%
Less than 1 cm in diameter	3	4.9
1 cm+	32	52.5
2 cm+	16	26.2
3 cm+	8	13.1
4 cm+	2	3.3

Table 5 Histological grade

Grade	Number	%
Poorly differentiated	3	4
Moderately well differentiated	33	56
Well differentiated	25	40

Table 6 *Completeness of excision*

Excision	Number	%
Excision definitely complete	40*	67.5
Excision doubtfully complete	9	14.5
Excision incomplete	11	18.0

* Includes the patient who had two malignant polyps, both completely excised.

the patient did not undergo an operation but was closely followed up with repeat endoscopies at frequent intervals. This decision has been justified as the patient remains well and free of recurrence five years later.

Forty six patients were treated by polypectomy only and 37 of these remain alive and well with no evidence of recurrence five years or more after polypectomy. Nine patients have died: three from unrelated causes after five years and five from unrelated causes from six months to four years later. The cause of death in the one remaining patient is obscure. A malignant polyp was removed from the sigmoid colon which contained well differentiated carcinoma and excision was complete. This patient was adamant in refusing further follow up. She was not seen again at St Mark's Hospital and when she died 18 months later at age 82 necropsy was not carried out.

Fourteen patients (23%) underwent subsequent bowel resection: only two had residual tumour in the operative specimen (see above). Both are alive and well more than five years later. Twelve patients had no residual tumour in the operative specimen: 10 of them remain alive and well five years later and one further patient died after a myocardial infarction four years after surgery. Only one patient died of carcinoma of the colon: his resection specimen

showed no residual tumour (see Table 7). The original histology in this case showed very poorly differentiated carcinoma. It is doubtful whether major surgery influenced the prognosis in this patient. Altogether three patients in our series had poorly differentiated carcinoma and all three underwent prompt major resection: two of them remain alive and well after five years and only the one patient mentioned above with very poorly differentiated carcinoma died of his cancer.

Discussion

We consider any malignant polyp completely removed endoscopically as a 'total excisional biopsy' until the histological grade and completeness of excision are established. The final decision about further treatment is made at this time. The term 'total excisional biopsy' should not be confused with forceps biopsy: partial biopsy of polyps should be avoided because of the difficulties in the histological interpretation of malignancy and the possibility of sampling error.

The main reasons why patients with malignant polyps, selected in the way described, do so well after local excision only is based on studies of the risk of lymph node metastasis having already taken place when the invading carcinoma has spread no further than the submucosal layer.¹² The risk is about one in ten, but the small minority of cases which do metastasise to lymph nodes are almost invariably poorly differentiated carcinomas of a high grade of malignancy. In our experience, malignant colorectal polyps uncommonly contain poorly differentiated carcinoma (three out of 60 in this series) compared with an incidence of 15% in the general series of colorectal cancers. Although the polyps containing high grade tumour in this series did not metastasise to regional nodes the policy of

Table 7 *Flow chart of histopathology and prognosis*

* For poorly differentiated carcinoma.

† Two for poorly differentiated carcinoma: no residual tumour in operation specimen.

further major surgery in such cases seems to us to be justified on the basis of experience with other patients not included in this study as well as the statistical risk of nodal spread (*vide supra*).

The results in the most important group, those 46 patients treated by polypectomy alone, are excellent. This illustrates the precision with which treatment can be planned and prognosis predicted on the basis of the endoscopic method¹⁰ and the histological criteria described above. Forty five of these 46 patients remained free of any recurrence during a follow up period varying from five to 10 years or until death (the cause of death was obscure in the 46th patient described above).

The 14 patients undergoing a subsequent resection form a useful control group: the results here should be considered as those of the major surgical procedure. Eleven patients had resections because of doubtful completeness of excision of tumour (either histological or endoscopic or both) and three had resections because the tumour was poorly differentiated. Yet there was residual tumour at the primary site in only two patients and none had any metastases in the regional lymph nodes. In retrospect, the residual tumour at the primary site could have been as successfully treated by polypectomy alone.

Careful selection of patients to be treated only by endoscopic polypectomy is based on several considerations. There must be cooperation between endoscopist, surgeon, and pathologist and each must be aware of the limitations of pathological and endoscopic methods. For this reason, we have dealt with the technical aspects of the preparation of polyps for histological examination and method of reporting at some length. If the polyp is sectioned by the method which is described above there is no loss of tissue and an accurate assessment of histological grade and completeness of excision can be made. Polyps are, however, often cut in half by some to fit the embedding mould and, with the inevitable loss of tissue that occurs as the first sections are cut, the important central part of the core may be missed. This could explain the difficulties that some pathologists have experienced in predicting which patients will have residual tumour at the primary site or in the regional lymph nodes and, therefore, the over-emphasis on the need for excisional surgery.

In all our patients there was opportunity for close cooperation between pathologist, endoscopist, and surgeon and this is reflected in the results of treatment of both the polypectomy only group and those patients undergoing resection. No patient treated by polypectomy alone has developed recurrence of tumour either locally at the site of polypectomy or at a distant site over the follow up

period of five years. Only one patient in the resection group developed recurrence and this was also the only patient to die of carcinoma of the colon in this series: this patient had a very poorly differentiated carcinoma and underwent resection although excision of the polyp was complete.

Controversy has arisen in the literature about the adequacy of polypectomy alone: Colacchio *et al*¹³ have reported a 35% false positive and 50% false negative rate in indications for further surgery. In their series patients were submitted for surgery often without removal of the original polyp and six out of 24 of these patients had metastases in the regional lymph nodes. The conclusion is drawn that resection is needed in all such cases. This would suggest inappropriate selection of patients for polypectomy according to our criteria. For this reason, we have emphasised the processing of malignant polyps as 'total excisional biopsies' in enabling us to reach a decision about further management.

Other reports have suggested that local excision is adequate for long stalked polyps but not for short stalked polyps or sessile tumours.⁴ This is not our experience although complete polypectomy is technically simpler for long stalked lesions. Histological completeness of excision is insufficient in the management of malignant polyps in the absence of histological grading and endoscopic completeness of excision.¹⁴

The good results of endoscopic polypectomy for completely excised tumours are also seen in those patients with doubtful completeness of excision. The assumption was made that diathermy coagulation would destroy any residual malignant tissue at the site of polypectomy and this has proved to be the case: of the eight patients treated by polypectomy only, none has developed local or distant recurrence. Eight out of 10 patients in whom the excision was judged to be incomplete had no residual tumour in the operative specimen: presumably the diathermy current was also effective in destroying any residual malignant tissue in these cases and they can therefore be said with hindsight to have had unnecessary surgery.

Finally, appropriate selection of patients with malignant polyps by endoscopic polypectomy means that they can be treated on an outpatient basis so that treatment is cost effective for both patient and hospital resources without compromising the individual patient's chance of cure.

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Since submitting this paper there has been a report of a similar study on the surgical pathology of endoscopically removed malignant polyps of the colon and rectum. Cooper HS. *Am J Surg Pathol* 1983; **7**: 613–23.

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