Treating malignant colorectal polyps

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Colorectal cancer (CRC) is preventable, yet it remains the second leading cause of cancer-related death in the western world with the vast majority of cancers arising from adenomatous polyps. Mortality is related to the stage of disease at initial diagnosis with a 5-year survival for patients who present with metastatic disease of only 10% or less. Early presentation however carries a 5-year survival of greater than 90% [1]. Patients who present to hospital as a colorectal cancer emergency carry a far higher mortality risk than those that present electively [2].

Thirty to fifty percent of the general population will develop adenomatous large bowel polyps at some point in their lives. One to three percent of these will undergo malignant transformation. Only a small minority of patients overall can be identified as high risk for the development of colorectal cancer [3] with the vast majority (86%) arising sporadically. With an inherent 3% complication rate, opportunistic asymptomatic colonoscopic screening for CRC is of little value. There is currently a large Medical Research Council trial aimed at evaluating once-only flexible sigmoidoscopy [4–9] in asymptomatic patients aged 50–60 years. The results of this trial will not however be known for several years.

Sporadic CRC appears to arise as part of a multistep process although no single genetic event has been uniformly identified. Adenomatous Polyposis Coli (*APC*) gene mutation is thought to be an early event in the development of sporadic cancers as it is found in sixty percent of adenomas and carcinomas [10]. Mutation of the *K-ras* and *p53* gene and deletion of the Deleted in Colorectal Cancer (*DCC*) gene also appear to be important events in the adenoma-carcinoma sequence. In the National Polyp Study, colonoscopic polypectomy followed by surveillance colonoscopy reduced the incidence of colorectal cancer by up to 90% compared with reference populations with elimination of mortality in CRC [11].

Genetic predisposition

Familial adenomatous polyposis (FAP) accounts for only about 1% of cases of colorectal cancer, with the defective tumour suppressor *APC* gene identified on chromosome 5q that is inherited in an autosomal dominant fashion. FAP is characterised by hundreds of colorectal adenomatous polyps presenting in the second or third decade of life. The lifetime risk for colorectal cancer in FAP approaches 100%.

The second common genetic predisposition to CRC is hereditary non-polyposis colon cancer (HNPCC). This condition should be suspected in patients describing three or more cases of colorectal cancer (or adenocarcinoma of the uterus) within their family [12]. HNPCC is not aptly named in terms of its presentation, as these tumours present predominantly as polyps distributed on the right-side of the colon. Patients suspected of having HNPCC according to the Amsterdam criteria [12] should be referred for colonoscopic screening from the age of twenty-five, as colonoscopic surveillance significantly reduces the risk for CRC development in this condition [13,14].

HNPCC exhibits microsatellite instability at multiple loci, including chromosomes 2p and 2q. The mutated genes that would ordinarily form protein products to repair newly formed DNA paired bases are incapable of performing this function, thereby increasing DNA instability.

Carcinoma *in Situ*

Carcinoma *in situ* refers to any polyp with malignant cells above the muscularis mucosae T1NxMx [15]. Because of the absence of lymphatics extending above the crypts of Lieberkühn, carcinoma *in situ* does not generally metastasise. By definition, invasive carcinoma refers to any lesion that has penetrated beyond the muscularis mucosae thus giving rise to the potential for metastasis.

Peduculated Polyps

Prognostically, Haggitt recognised a transition boundary between the stalk (Level 3) and the submucosa of the bowel wall (Level 4). Haggitt [16] reported twenty-six patients with invasion limited to the head of the polyp (Level 1) and the neck (Level 2) without adverse outcome. One patient out of eight with Level 3 invasion, who also had vascular invasion, had an adverse outcome. The risk of lymph node metastasis in levels 1–3 is generally low (16–19). The risk of lymph node metastasis in a pedunculated polyp with Level 4 invasion is 10% which is approximately the same as in sessile lesions [20].

Sessile polyps

In 1993 Kudo and colleagues [21] divided submucosal invasion of sessile lesions into three levels (Sm1–3) based on the depth of invasion. Sessile lesions have a relatively high incidence of lymph node metastasis [17,20,22]. Nascimbeni and colleagues [23] studied the risk of lymph node involvement in 353 sessile lesions using multivariate analysis and noted that the significant risk factors were depth of invasion ($P < 0.001$), lymphovascular invasion ($P < 0.009$) and site in the lower third of the rectum ($P < 0.001$). Kikuchi and colleagues [24] also concluded that the only independent risk factor for lymph node metastasis was invasion into Sm3.

Indications for Resectional Surgery

Indications for bowel resection in patients with polyp(s) are:

- Involved resection margins following ' curative' polypectomy
- Highly undifferentiated cells
- Presence of lymphatic or vascular invasion
- Familial Adenomatous Polyposis (FAP)
- DALM
- Caecal polyp
- Haggitt Level 4
- Sessile Polyp Sm3
- Patient preference

Polyps with epithelial dysplasia in ulcerative colitis (UC) represent either dysplasia-associated lesions or masses (DALMs) [25,26].

Endoscopic Management of Malignant Colonic Polyps

Lesions found at the time of colonoscopy should be removed by polypectomy or Endoscopic Mucosal Resection (EMR). The presence of invasive cancer within a polyp may preclude complete excision with EMR. Multiple samples from the lesion should be taken using biopsy forceps to determine likely pathological stage. Endoscopic ultrasound (EUS) can also serve as a useful tool in the evaluation of colonic lesions by determining depth of invasion and by identifying enlarged lymph nodes that may suggest metastasis. The accuracy of EUS for T staging ranges from 80 to 95% [27,28].

Preoperative endoscopic marking can be helpful in localising discrete colonic lesions for subsequent identification during surgery. Currently available marking techniques include endoscopic tattooing and metallic clipping which may also be useful in non-resected colonoscopic surveillence to aid identification and rebiopsy of bowel mucosa immediately adjacent to previously excised polyps.

Staging and treatment of Rectal Polyps

For rectal lesions, polypectomy may be performed during examination under anaesthesia (EUA) or during transanal endoscopic microsurgery (TEM) (Fig. 1) [29]. TEM is a minimally invasive technique that was developed in Germany in the early 1980s for the treatment of rectal sessile polyps (>3 cms) (Fig. 2) [29–31]. Transanal access to the rectum up to 20 cms from the anal verge is gained under gas insufflation with the opportunity to perform similar techniques to those used in more conventional surgery.

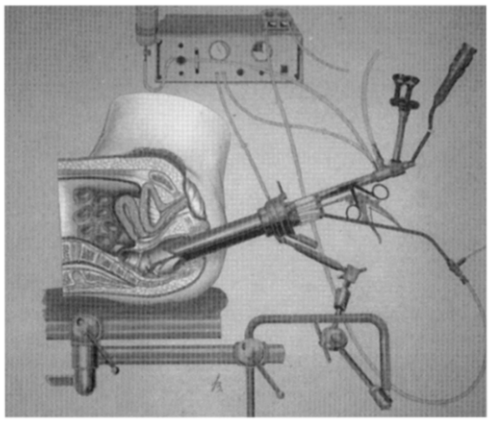

Fig. 1. Transanal access to the rectum up to 20 cms from the anal verge is gained under gas insufflation

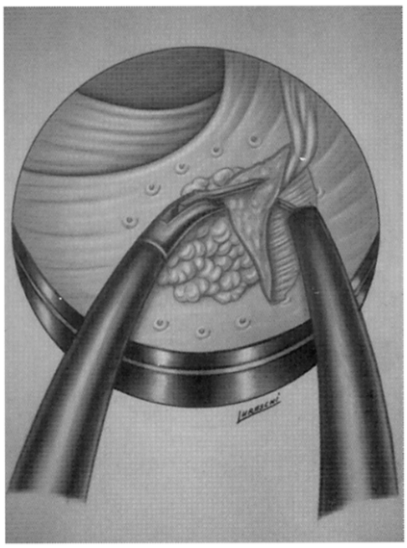

Fig. 2. TEM for a sessile rectal polyp.

Early T1 or well or moderately differentiated (G1–G2) polyps are ideally suited to excision using this technique.

EUS is superior to computed tomography (CT) in determining the T stage of rectal cancer. Abdominal CT, in combination with EUS, appears to be the most cost-effective strategy in the pre-operative evaluation of rectal cancer.

References

1 Holliday HH, JD. Delay in diagnosis and treatment of symptomatic colorectal cancer. *Lancet* 1979, **1**, 309–11.

2 Umpleby H, Williamson RCN. Survival in acute obstructing colorectal carcinoma. *Dis Colon Rectum* 1984, **27**, 299–304.

3 St John DJ, McDermott FT, Hopper JL, Debney EA, Johnson WR, Hughes ES. Cancer risk in relatives of patients with common colorectal cancer. *Ann Intern Med* 1993, **118**(10), 785–90.

4 Atkin WS, Cuzick J, Northover JM, Whynes DK. Prevention of colorectal cancer by once-only sigmoidoscopy. *Lancet* 1993, **341**(8847), 736–40.

5 UK Flexible Sigmoidoscopy Screening Trial Investigators. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial. *Lancet* 2002, **359**(9314), 1291–300.

6 Choi HK, Law WL, Chu KW. The value of flexible sigmoidoscopy for patients with bright red rectal bleeding. *Hong Kong Med J* 2003, **9**(3), 171–4.

7 Macadam RC, Lovegrove JE, Lyndon PJ, Byrne P, Baldo O. Effect of a rapid access flexible sigmoidoscopy clinic on the yield of early stage rectal cancer. *Gut* 2003, **52**(8), 1229.

8 Wheeler WE, Scott-Conner CE, Stone RA. Flexible sigmoidoscopy as a screening procedure for asymptomatic colorectal carcinoma in patients with inguinal hernia. *South Med J* 1985, **78**(12), 1417–20.

9 Wheelera WE, Wilson SL, Kurucz J, Flanigan J, Ratliff D, Scott-Conner C. Flexible sigmoidoscopy screening for asymptomatic colorectal disease in patients with and without inguinal hernia. *South Med J* 1991, **84**(7), 876–8.

10 Powell SM, Zilz N, Beazer-Barclay Y, *et al*. APC mutations occur early during colorectal tumorigenesis. *Nature* 1992, **359**(6392), 235–7.

11 Winawer SJ, Zauber AG, Ho MN, *et al*. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 1993, **329**(27), 1977–81.

12 Vasen HF, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterol* 1999, **116**(6), 1453–6.

13 Thorson AG, Knezetic JA, Lynch HT. A century of progress in hereditary nonpolyposis colorectal cancer (Lynch syndrome). *Dis Colon Rectum* 1999, **42**(1), 1–9.

14 Jarvinen HJ, Mecklin JP, Sistonen P. Screening reduces colorectal cancer rate in families with hereditary nonpolyposis colorectal cancer. *Gastroenterol* 1995, **108**(5), 1405–11.

15 Cancer AJCo. AJCC Cancer Staging Manual: Springer-Verlag; 2002.

16 Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. *Gastroenterol* 1985, **89**(2), 328–36.

17 Coverlizza S, Risio M, Ferrari A, Fenoglio-Preiser CM, Rossini FP. Colorectal adenomas containing invasive carcinoma. Pathologic assessment of lymph node metastatic potential. *Cancer* 1989, **64**(9), 1937–47.

18 Ehrinpreis MN, Kinzie JL, Jaszewski R, Peleman RL. Management of the malignant polyp. *Gastroenterol Clin North Am* 1988, **17**(4), 837–50.

19 Eckardt VF, Fuchs M, Kanzler G, Remmele W, Stienen U. Follow-up of patients with colonic polyps containing severe atypia and invasive carcinoma. Compliance, recurrence, and survival. *Cancer* 1988, **61**(12), 2552–7.

20 Nivatvongs S, Rojanasakul A, Reiman HM, Dozois RR, Wolff BG, Pemberton JH, et al. The risk of lymph node metastasis in colorectal polyps with invasive adenocarcinoma. *Dis Colon Rectum* 1991, **34**(4), 323–8.

21 Kudo S. Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. *Endoscopy* 1993, 25(7), 455–61.

22 Cooper HS, Deppisch LM, Gourley WK, *et al*. Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. *Gastroenterol* 1995, 108(6), 1657–65.

23 Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Dis Colon Rectum* 2002, **45**(2), 200–6.

24 Kikuchi R, Takano M, Takagi K, *et al*. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. *Dis Colon Rectum* 1995, **38**(12), 1286–95.

25 Fogt F, Urbanski SJ, Sanders ME, *et al*. Distinction between dysplasia-associated lesion or mass (DALM) and adenoma in patients with ulcerative colitis. *Hum Pathol* 2000, **31**(3), 288–91.

26 Sjoqvist U. Dysplasia in ulcerative colitis–clinical consequences? *Langenbecks Arch Surg* 2004, **389**(5), 354–60.

27 Norton–SA, Thomas–MG. Staging of rectosigmoid neoplasia with colonoscopic endoluminal ultrasonography. *Br J Surg* 1999, **86**(7), 942–6.

28 Akasu T, Kondo H, Moriya Y, *et al*. Endorectal ultrasonography and treatment of early stage rectal cancer. *World J Surg* 2000, **24**(9), 1061–8.

29 Chiavellati L, D' Elia G, Zerilli M, Tremiterra S, Stipa S. Management of large malignant rectal polyps with transanal endoscopic microsurgery. Is there anything better for the patient? *Eur J Surg Oncol* 1994, **20**(6), 658–66.

30 Buess G, Theiss R, Hutterer F, *et al*. Transanal endoscopic surgery of the rectum – testing a new method in animal experiments. *Leber Magen Darm* 1983, **13**(2), 73–7.

31 Buess G, Mentges B, Manncke K, Starlinger M, Becker HD. Technique and results of transanal endoscopic microsurgery in early rectal cancer. *Am J Surg* 1992, **163**(1), 63–9; discussion 69–70.