Colorectal cancer: features and investigation

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Abstract

Colorectal cancer is a common malignancy affecting 35,000 people a year in the UK. Most cancers are sporadic but a few, occurring at young age, have a clear genetic basis. The majority are in the rectum or rectosigmoid and give rise to symptoms of rectal bleeding, often with a looser or more frequent stool. Right-sided cancers typically give rise to anaemia, because the blood in the stool is occult and unnoticed by the patient. Almost all the symptoms of malignancy can also be caused by benign disease. Diagnosis relies on luminal imaging, with colonoscopy being the gold standard. Pre-operative staging should include imaging of the liver and chest with computed tomography. For rectal cancers, magnetic resonance scanning of the pelvis provides accurate information about the local tumour and nodal status, and is used to inform decisions regarding pre-operative chemoradiotherapy. All colorectal cancers should be discussed at multidisciplinary meetings to enable optimum treatment to be determined.

Keywords colonoscopy; colorectal neoplasms; colorectal surgery; neoplasm staging; virtual colonoscopy

What's new?

- Screening programmes are increasing the numbers of 'polyp cancers'
- Genetic analysis of individual tumours is feasible and will impact on future therapy

Colorectal cancer, often known simply as bowel cancer, is a common solid organ malignancy affecting 35,000 patients a year in the UK,[1] about half of whom will die from it. At all ages it is more common in males (especially rectal cancer) but because of the greater longevity of women the overall sex distribution is equal. It is generally a disease of advancing years, with a peak age at diagnosis of 70 years; the lifetime risk by the age of 80 years is about 5–10%.

Epidemiology

Colorectal cancer is common in 'Westernized' populations, probably due largely to dietary factors. Europe, the USA and Japan have high rates compared to Africa and Asia. Bowel cancers are thought to arise through a combination of hereditary predisposition, exposure to environmental agents (e.g. diet), lifestyle, and chance. Dominantly inherited strongly penetrant syndromes, such as familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (Lynch syndrome), are responsible for a small percentage of colorectal cancers, often developing before the age of 40 years.[2] A much greater proportion may be the result of weakly penetrant but more common susceptibility genes, which are yet to be identified.[3] Other known risk factors include diets high in red meat and low in fibre, lack of exercise, obesity, alcohol and (probably) smoking, personal history of adenomatous polyps or previous colorectal cancer, and long-standing colonic inflammatory bowel disease.[4,5] Aspirin and non-steroidal anti-inflammatory drugs are thought to be protective against polyps and cancer but their use as chemo-preventative agents is not currently recommended.[6]

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Pathology and pathogenesis

Adenoma–carcinoma sequence

Analysis of the histological and molecular changes of colorectal polyps and malignancies has led to the adenoma–carcinoma hypothesis that now underpins our understanding of carcinogenesis in many other malignancies.[7] There are two common molecular pathways – the 'classical' or chromosomal instability pathway and the microsatellite instability pathway. The majority of sporadic cancers follow the classical pathway in which large segments or whole chromosomes may be lost or duplicated; but about 15% follow the other pathway in which small changes in DNA, often at repeated nucleotide sequences (microsatellites), result in cancer-causing genetic mutations. These pathways have their counterparts in hereditary syndromes – FAP cancer follows the classical pathway whereas Lynch syndrome follows the microsatellite instability pathway.[8,9] Detailed genetic analysis of individual tumours is becoming a reality with ever-decreasing costs and improved technology. This will help to predict behaviour and response to therapy.

The large majority of colorectal cancers are adenocarcinomas arising from the mucosa. Rare tumours include carcinoids, lymphoma and melanoma.

Distribution

About two-thirds of sporadic cancers arise distal to the splenic flexure, with about 40% arising in the rectum. In patients with Lynch syndrome, this proportion is reversed with caecal cancer being the most common site.[10]

Spread

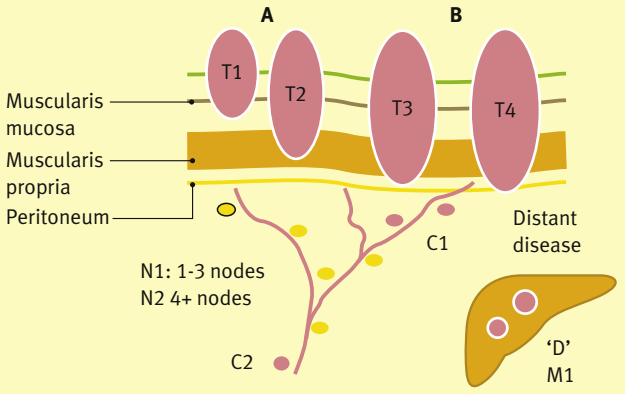
Like many cancers, colorectal carcinoma spreads locally, via lymphatics and through the bloodstream. The liver is the most common metastatic site, via the portal venous system, followed next by pulmonary seedlings. Rarer sites include the skin, brain and bone. Trans-coelomic spread leads to the development of multiple peritoneal nodules, though ascites is usually minimal.

Pathological staging

Histological staging of colorectal cancers is performed post-operatively. Dukes' and TNM staging (Figure 1) are widely used to inform decisions about adjuvant therapy.

Dukes' staging: node-negative tumours are staged A if they have not penetrated the muscularis propria, B if they have. If there is lymph node spread, the tumour is automatically a Dukes' C.[11] A C2 tumour is one in which there is lymphatic invasion at the

Histological staging of colorectal cancers



This illustrates the two common staging methods – Dukes' (stage A to D) and TNM (T1-4, N0-2, M0-1). T1 and T2 are Dukes' A cancers and do not invade past the muscularis propria. T3 and T4 are Dukes' B tumours: they penetrate the muscularis and T4 disease extends either beyond the peritoneum or into adjacent organs. N status depends on the number of involved lymph nodes as shown.

Figure 1

node furthest away from the tumour — at the 'high tie'. Although not described by Dukes, it is now conventional to label any metastatic spread as stage D.

TNM staging is more precise than Dukes' staging but clinically less useful because there are so many subgroups.

Malignant polyps: with the advent of screening programmes, earlier detection of cancers has led to an increased detection of 'polyp cancers', which are T1 lesions. Many of these are cured by polypectomy alone. Use of other staging methods that take into account the depth of penetration, such as the Haggitt[12] and Kikuchi[13] classifications, is helpful in judging the risk of lymph node metastasis and thus in deciding whether a formal resection is indicated.

Circumferential margin: for surgery to be potentially curative, especially for rectal cancers, it is important to remove a margin of normal tissue around a cancer. Measurement of whether the circumferential resection margin (CRM) is involved with cancer can be a very useful predictor of local and even distant recurrence.[14,15]

Diagnosis

Symptoms

Gastrointestinal symptoms are common, even in the absence of pathology, and there is a wide overlap of symptomatology for malignant and benign causes. Based on a large clinical database in Portsmouth, referral criteria have been developed that identify patients with colorectal cancer most reliably (Table 1),[16] but only about 10–14% of patients meeting such criteria harbour a malignancy.

Obstructive symptoms: as tumours enlarge they tend to narrow the bowel lumen. This commonly leads to a looser more frequent stool rather than constipation, though any persistent change in bowel habit should be investigated. Distal tumours are more likely than proximal tumours to lead to an alteration in bowel habit, as the stool consistency is more solid. Proximal tumours may produce no symptoms at all until they obstruct completely. In the rectum, the mass effect of a cancer leads to tenesmus (a feeling of incomplete evacuation).

Criteria for referral to fast-track colorectal clinic

- A change in bowel habit (looser and/or more frequent stools) persisting >6 weeks without rectal bleeding in a person aged 60 years or older
- Rectal bleeding persisting >6 weeks without a change in bowel habit and without anal symptoms, in a person aged 60 years or older
- Rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more, in a person aged 40 years or older
- A palpable right lower abdominal mass or a palpable rectal mass (intraluminal and not pelvic)
- Iron-deficiency anaemia with a haemoglobin of 11 g/dL or less in a man, or of 10 g/dL or less in a non-menstruating woman

Table 1

Bleeding: rectal bleeding, especially if associated with a change in bowel habit, is a worrying symptom. Low rectal tumours can bleed bright blood just like haemorrhoids; bleeding from left-sided tumours may be darker red and mixed in with the stool. Although right-sided tumours bleed, this is not visible in the stools and so these cancers classically present with iron-deficiency anaemia because there is no warning sign to the patient.

Symptoms not usually associated with colorectal malignancy: bowel cancers are biologically inert and do not display paraneoplastic features. Weight loss and anorexia are very uncommon unless there is widespread metastatic disease. Pain is also unusual unless a tumour is so advanced that it is nearly obstructing the bowel lumen or invading bone or nerves.

Acute presentation: about 20% of patients with colorectal cancer present as emergencies — usually with obstruction but occasionally with perforation or abscess formation. Most of these will require emergency surgery.

Signs

Patients with symptoms suggestive of colorectal pathology should undergo abdominal examination, rectal examination and a rigid sigmoidoscopy in the clinic.

Palpable mass: many colorectal cancers are palpable — typically, a right colon cancer gives rise to a firm mass in the right iliac fossa. Rectal cancers can often be felt on digital examination, and a rolled edge or circumferential nature can easily be appreciated. If a tumour is found, the surgeon will be greatly helped by information about the height of tumour from the anal verge, whether it is mobile, tethered or fixed, and which quadrants are involved.

Sigmoidoscopic findings: a rigid sigmoidoscope will be able to examine most of the rectum and sometimes the distal sigmoid, so