COLORECTAL NEOPLASIA—II: LARGE BOWEL CANCER

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Deaths from cancers in England and Wales, 1989.

Aetiology

Pathological specimen showing colonic cancer.

Global variation in colorectal cancer.

Carcinoma of the large bowel is a common malignancy. It is predominantly a disease of older people, though it may occur at any age. Less than 5% of patients are under the age of 40 and more than half are over 60, with the peak incidence in people aged 70-80.

There are about 25 000 new cases each year in the United Kingdom, and it is second only to cancer of the bronchus as a cause of death from cancer, with an annual mortality of about 19 000. There is no noticeable sex difference; in women it is less common than carcinoma of the breast. There has been no significant change in mortality from large bowel cancer over the past 40 years and half the cases present beyond surgical cure.

Most, if not all, colorectal cancers arise from an adenoma. The risk of malignant transformation in any individual polyp is low. It increases with the size of the adenoma, and villous adenomas are much more prone to malignant transformation than tubular adenomas.

Colorectal tumorigenesis is considered to be a multistep process, including hyperproliferative mucosa, adenomas, and carcinomas. A combination of both environmental and genetic factors play an important part in pathogenesis.

Environmental factors

There is considerable variation world wide in the incidence of colorectal cancer. It seems to be particularly prevalent in highly developed countries, so that there is a high rate in the United Kingdom, the United States, Australasia, and western Europe, but a low incidence in central Africa and Asia. This geographical variation has been ascribed by many to different diets. Initially a low fibre diet was suggested as the causative factor, and subsequently an excess of animal fat or protein. Epidemiological evidence is contradictory. Part of the problem is that there are usually multiple differences in diet between different ethnic groups and it becomes difficult to know which component or components can be considered responsible. The paradox is illustrated by the Eskimos, who have a low fibre, high fat diet and a very low incidence of large bowel cancer. However, dietary factors do seem to play some part because when black Africans adopt a Western diet their incidence of colorectal tumours progressively increases.

It is thought that diet produces its effect through generating intraluminal carcinogens. Fibre has been propounded as a protective agent because it decreases bowel transit time, increases stool bulk, and binds intraluminal carcinogens, which reduces the contact time of any potential carcinogen with the mucosa.

A second hypothesis is that dietary alterations may alter the bacterial flora in the gut. Certain bacteria are known to degrade bile salts to form carcinogens. In epidemiological studies such bacteria and higher quantities of bile salts have been found in the faeces from a cancer prone population compared with those from a low risk population.

A third hypothesis is that fat or protein in the diet is broken down into a potential carcinogen. There is also an association between smoking and alcohol consumption and colorectal neoplasia, but coffee drinking does not seem to be implicated.

Pathological specimen showing familial adenomatous polyposis.

Diseases that predispose to large bowel cancer

- Ulcerative colitis
- Crohn's disease
- Familial adenomatous polyposis
- Hereditary non-polyposis colon cancer (Lynch types I and II)
- Colonic ureteric implants
- Cholecystectomy (?)

Genetic factors

Family history—There is no doubt that some families have a high incidence of colorectal cancer. This is easily explained in those with familial adenomatous polyposis, which is inherited as an autosomal dominant condition. Other families with a high incidence of large bowel cancer do not have familial adenomatous polyposis. Many of these have so called hereditary non-polyposis colon cancer (HNPCC), which is also inherited as an autosomal dominant condition and accounts for about 5% of patients with large bowel cancer. It is seen in two forms: as familial site specific colon cancer, and in association with other forms of cancer.

Molecular biology—The recent revolution in molecular biology is uncovering a rapidly growing list of genetic abnormalities in patients with colorectal neoplasms. The most important genetic events are: (a) mutations which inactivate tumour suppressor genes and (b) mutations which activate oncogenes. In colorectal neoplasia these usually arise by point mutation or deletion of the relevant genes or segment of chromosome. These genetic events combine to influence tumour behaviour.

Predisposing diseases—Certain chronic diseases of the colon predispose to cancer. In particular, longstanding ulcerative colitis and, to a lesser extent, Crohn's disease are associated with carcinomatous change. Other causes of chronic inflammation, such as schistosomiasis, amoebic dysentery, and tuberculosis, do not seem to predispose to cancer. Implantation of the ureters into the sigmoid colon predisposes to large bowel neoplasia, but this form of urinary diversion has been largely abandoned. Cholecystectomy has been thought to be associated with an increased risk of colorectal cancer, but the evidence is equivocal.

Pathology

Pathological specimen showing stenosing colonic cancer.

Ulcerating carcinoma.

Rectal carcinoma close to the anus.

Coincident polyp and polypoid carcinoma.

Large bowel cancers appear as polypoid, ulcerating, or stenosing lesions. They spread directly to invade local structures, this being especially important in rectal cancer owing to the proximity of the other pelvic structures. They metastasise through lymphatic vessels to mesenteric and para-aortic lymph nodes and through the portal venous system to the liver and onwards. Tumour cells may also be dispersed by transcoelomic spread across the abdominal cavity.

Colorectal cancers show a range of histological features, varying from well differentiated tumours with recognisable glandular structures to poorly differentiated lesions.

Patients may develop more than one large bowel carcinoma. The prevalence of multiplicity on presentation is variously quoted as between 3% and 12% of cases. These are so called synchronous tumours. There is also a higher incidence of further colorectal tumours after successful treatment of carcinoma of the colon. These are called metachronous tumours. Ten years after resection of a large bowel cancer there is a 3-4% incidence of a further malignancy in the remaining large bowel.

Clinical features

Most tumours (about 70%) lie in the sigmoid colon and rectum

The clinical features of colorectal cancer depend on the site of the tumour. About 20% of large bowel tumours lie in the right side of the colon. The transverse and descending colon are relatively rarely affected so most lie in the sigmoid colon and rectum.

About 40% of large bowel tumours are in the rectum. The clinical symptoms and signs differ depending on the area of bowel involved. From the point of view of symptoms it is best to consider three areas: the right colon, the left colon, and the rectum.

Barium enema radiograph showing carcinoma of the caecum.

Location of large bowel cancers.

Right colon

Presentation with obstruction—About a quarter of the patients present with signs of low small bowel obstruction—that is, colic, vomiting, constipation, and distension. Plain abdominal radiographs show dilated loops of small bowel.

Presentation without obstruction—Many patients who present without obstruction have no symptoms referable to the gastrointestinal tract. They give a history of anaemia and weight loss due to occult gastrointestinal bleeding. This complex of symptoms raises the possibility of carcinoma of the stomach, but carcinoma of the right colon, which is much more amenable to treatment, is often overlooked. The diagnosis is suggested by the finding of a palpable mass in the right iliac fossa. Whether this is present or not the whole colon must be examined by colonoscopy or barium enema examination.

Left colon

Presentation with obstruction—In all, 25-30% of patients with lesions of the left colon present as an emergency. They may have a perforation with pericolic abscess or even general peritonitis, but more usually large bowel obstruction. By far the commonest cause of large bowel obstruction is a carcinoma. It is important to exclude other causes of obstruction which may settle with conservative treatment. Emergency barium enema examination is indicated in all cases of large bowel obstruction to confirm the level of obstruction and to diagnose pseudo-obstruction, which does not require surgery. Emergency colonoscopy has been advocated as an alternative to barium enema examination.

Presentation without obstruction—Disturbance of the bowel habit is the rule in patients without obstruction. This may be either increasing constipation, diarrhoea, or alternation between the two. The patient commonly recognises blood with the stool and complains of low abdominal pain or discomfort. Weight loss is common and in general is a bad prognostic sign. A carcinoma can sometimes be felt by abdominal palpation.

Carcinoma of the rectum

Patients with carcinoma of the rectum almost never present as an emergency. The patient perceives obvious bleeding through the rectum. There may be alteration of the bowel habit and often tenesmus, a feeling of incomplete evacuation, with repeated calls to stool with the passage of only blood and slime. Tumours up to 10 cm from the anal verge can usually be felt. Tumours in the upper rectum can usually be seen on sigmoidoscopy.

Investigation

Barium enema radiograph of cancer of the sigmoid colon.

General abdominal, rectal, and sigmoidoscopic examination are part of the routine assessment of the patient in the clinic. If tumours are identified biopsy specimens are taken for histological confirmation. If no tumour is found on sigmoidoscopy either colonoscopy or barium enema examination should be performed. If a carcinoma is discovered synchronous tumours should be excluded. This may have to wait until the time of surgery or later if the tumour prevents adequate assessment of the more proximal colon. Ultrasonography and computed tomography may identify hepatic metastases, but their detection rarely preclude surgery as resection is largely the best form of palliation.

The photographs were produced by the department of medical illustration, Salford Health Authority.

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