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Brief Report

An overview of colorectral cancer

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ABSTRACT

In this article, the pathogenesis, stages, and management of colorectal cancer (CRC) are reviewed. A concise overview of the known risk factors related with CRC is provided. CRC is the second most common cause of cancer death in UK. There are several factors considered to be causally associated with the development of CRC. For example, the risk of CRC is clearly increased by a Western diet. High quality surgery is of paramount importance in gaining good outcomes, but adjuvant chemotherapy and radiotherapy also have significant roles to play.

1. Introduction

Colorectal cancer (CRC) is the development of cancer in the colon or the rectum (parts of large intestine). CRC is also known as Colon cancer, Rectal cancer, or Bowel cancer. Patients with Inflammatory Bowel Disease (IBD) are at an increased risk of developing CRC.[1–3] The etiological factors mainly include abnormal growth of cells that have the ability to invade or spread to other parts of the body. The common signs and symptoms include blood in the stool, a change in bowel movements, weight loss, and feeling tired all the time. The cancer starts in the cells that line the inside of the colon and rectum. It results from an accumulation of genetic and epigenetic changes in colon epithelial cells, which transforms them into adenocarcinomas. Over 95% of colon and rectal cancers are adenocarcinomas. The majority of cases are sporadic, with hereditary colon cancer contributing up to 15% of all colon cancer diagnoses.[3,4] In the United States, CRC is the third most common type of cancer diagnosed and the third most common cause of cancer-related death in men and women. In 2010, an estimated 102,900 new cases of colon cancer were diagnosed (49,470 male and 53,430 female) and 51,370 patients (26,580 male and 24,790 female) died from CRC.

Risk factors for CRC include older age, male sex, cholecystectomy, ureterocolic anastomosis, hormonal factors (nulliparity, early menopause), obesity, and diabetes mellitus. Dietary factors, such as a diet rich in red processed meat while low in fibers, are also responsible for CRC. Besides all the above -mentioned factors certain environmental and genetic factors

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also cause CRC. Screening has the potential to prevent CRC because it can detect precancerous growths, called polyps, in the colon and rectum. Regular screening helps in the detection of cancer at an early stage, and when they are more likely to be cured, treatment is less extensive, and recovery is faster.

2. Pathogenesis

It originates from the epithelial cells lining the colon or rectum of gastrointestinal tract and mostly occurs due to mutations in Wnt Signaling Pathway.[5,6] The APC gene is the most commonly mutated gene in all CRCs. APC protein (produced by APC gene) prevents the accumulation of β-catenin-protein. These genes are normally important for stem cell renewal and differentiation, but when inappropriately expressed at high levels, they can cause cancer.

Though APC is mutated in most colon cancers, some cancers have increased β-catenin because of mutations in β-catenin (CTNNB1) that block its own breakdown, or have mutations in other genes, such as AXIN1, AXIN2, TCF7L2, or NKD1,[7] which functions similar as APC.

Beyond the above-mentioned defects, other mutations must occur for the cells to become cancerous. The p53 protein (produced by the TP53 gene) normally monitors cell division and kills cells if they have Wnt pathway defects. Eventually, a cell line acquires a mutation in the TP53 gene and transforms the tissue from benign epithelial tumor into an invasive epithelial cell cancer. Sometimes, the gene encoding p53 is not mutated, but another protective protein named BAX is mutated instead.[7] Some oncogenes are over expressed in CRC, such as genes encoding the proteins KRAS, RAF, and PI3K.

3. Stages of CRC

Staging is a way of describing where the cancer is located, or where it has spread, or whether it is affecting other body parts. Diagnostic tests are used to find out the cancer's stage. Knowing the stage helps the physician to decide what kind of treatment is best and a patient's prognosis can be predicted, which is the chance of recovery. There are different stage descriptions for different types of cancer.[8,9]

TNM system is one of the tools that is used by the physicians to describe the stage of cancer. TNM stands for Tumor (T) Node (N) Metastasis (M). The stages are assigned by combining the T, N, and M classifications.

Stage 0: This is called cancer in situ. The cancer cells are only in the mucosa, or the inner lining, of the colon or rectum.

Stage I: The cancer has grown through the mucosa and has invaded the muscular layer of the colon or rectum. It has not spread into nearby tissue or lymph nodes (T1 or T2, N0, M0).

Stage IIA: The cancer has grown through the wall of the colon or rectum and has not spread to nearby tissue or to the nearby lymph nodes (T3, N0, M0).

Stage IIB: The cancer has grown through the layers of the muscle to the lining of the abdomen, called the visceral peritoneum. It has not spread to the nearby lymph nodes or elsewhere (T4a, N0, M0).

Stage IIC: The tumor has spread through the wall of the colon or rectum and has grown into nearby structures. It has not spread to the nearby lymph nodes or elsewhere (T4b, N0, M0).

Stage IIIA: The cancer has grown through the inner lining or into the muscle layers of the intestine and spread to one to three lymph nodes, or to a nodule of tumor in tissues around the colon or rectum that do not appear to be lymph nodes, but has not spread to other parts of the body (T1 or T2; N1 or N1c, M0 or T1, N2a, M0).

Stage IIIB: The cancer has grown through the bowel wall or to surrounding organs and into one to three lymph nodes or to a nodule of tumor in tissues around the colon or rectum that do not appear to be lymph nodes, but it has not spread to other parts of the body (T3 or T4a, N1 or N1c, M0; T2 or T3, N2a, M0; or T1 or T2, N2b, M0).

Stage IIIC: The cancer of the colon, regardless of how deep it has grown, has spread to four or more lymph nodes but not to other distant parts of the body (T4a, N2a, M0; T3 or T4a, N2b, M0; or T4b, N1 or N2, M0).

Stage IVA: The cancer has spread to a single distant part of the body, such as the liver or lungs (any T, any N, M1a).

Stage IVB: The cancer has spread to more than one part of the body (any T, any N, M1b).

4. Management of CRC

The treatment of CRC is multidisciplinary, and is guided by precise staging and histopathology. So all patients should be discussed and treated appropriately by a team consisting of pathologists, radiologists, surgeons, oncologists, and colorectal nurse specialists.

Before starting with the management of CRC, it is important to diagnose the disease at an appropriate time. The symptoms, which suggest a diagnosis of CRC, mainly consists of change of bowel habit, rectal bleeding of short duration, and blood in the stool.[10] Any of these symptoms should prompt a digital rectal examination, as up to 80% of rectal cancers are palpable,[11] followed by urgent investigation. Iron deficiency anemia is an important mode of presentation and this finding always raise the risk of CRC particularly in an individual over the age of 50 years.[12] The gold standard investigation for suspected CRC is colonoscopy. This has been shown to be more sensitive and specific than barium enema,[13] but it must be acknowledged that small lesions can be missed on colonoscopy,[14] and even in expert hands a 100% cecal intubation rate is not achievable.[15] A colonoscopy service is highly dependent on sufficient expertise, and in the UK, double contrast barium enema **(DCBE)** is still widely used. However, this investigation can miss cancers, particularly in a patient with severe diverticular disease of the sigmoid colon, and on the right side of the colon, spasm can be misinterpreted as a malignant structure.[16] Thus, DCBE should be supplemented by flexible sigmoidoscopy and radiological evidence of lesions in the caecum should be treated by colonoscopy unless appearances are unequivocal.