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Review

Malignant tumours of the small intestine

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ABSTRACT

Adenocarcinoma, neuroendocrine tumours, sarcomas and lymphomas are the four most common malignant tumours arising in the small intestine, although over forty different histological subtypes are described. Collectively these account for only 2% of cancers of the digestive system. The incidence of small bowel cancer has increased in recent decades with a four-fold increase in carcinoid tumours. Risk factors for small bowel tumours include coeliac disease, inflammatory bowel disease and a number of genetic abnormalities. The non-specific nature of their symptoms and the difficulty in visualising these tumours with normal endoscopic techniques often results in late diagnosis. Furthermore the paucity of literature on this topic has made it difficult to standardise management. There has however been marked improvement in imaging methods resulting in earlier diagnosis in many cases. As expected, early detection of localised, well differentiated tumours followed by surgical resection with negative margins offers the best chance of long term survival. Better adjuvant treatment, notably for gastrointestinal stromal tumours, has improved 5-year survival rates significantly. Development of surveillance guidelines for at risk populations may be a valuable way of improving early diagnosis of this challenging group of conditions.

Introduction

Small bowel tumours include a heterogenous group of benign and malignant lesions. The most common malignant lesions are adenocarcinoma, neuroendocrine tumours, sarcomas and lymphomas but more than forty different histological subtypes are described. Adenocarcinoma of the small bowel, while infrequently encountered, accounts for 40% of all malignant small intestinal tumours. Most originate in the duodenum followed by jejunum then ileum with about 10% having an unknown origin.[1] Tumours of the ampulla of Vater and the periampullary region are generally considered separately. Other tumour types arising from small intestine include, in order of frequency, carcinoid tumours, lymphoma and sarcoma. The incidence of all malignant tumours of the small intestine ranges from 0.5 to 1.5/100,000 in males and 0.2–1.0/100,000 in females.[2] The incidence appears to be

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higher in North America and Western Europe than in Asia,[3] with higher incidence rates in US black populations for both males and females.

The incidence of small bowel cancer is increasing, particularly the incidence of carcinoid tumours.[4] The mean age at diagnosis of any small bowel cancer is 65 but sarcoma and lymphoma tend to present earlier than adenocarcinoma and carcinoid tumours. The incidence rises after the age of 40 years for all histological subtypes.[5] It is not uncommon for the small bowel to be the site of metastasis from another primary particularly in advanced peritoneal carcinomatosis, however, haematogenous spread is rare, most common attributable to melanoma and breast or lung cancers.[6]

Predisposing factors

Crohn's disease

Crohns disease is a risk factor for future small bowel adenocarcinoma. A relative risk of 33 (95% CI: 15.9–60.9) was reported in a 2006 meta-analysis.[7] Male gender, fistulating disease, early age at diagnosis, distal jejunal or ileal disease and extended duration of disease are associated with increased risk.[8]

Coeliac disease

Patients with coeliac disease have an increased risk of both T-cell non-Hodgkin's lymphoma and adenocarcinoma of the small intestine[9] with the relative risk of the latter reported to be between 60 and 80 compared to normal populations.[10]

Small intestine adenomas

The prevalence of adenomas in the small intestine is lower than in the colon, but similarly appears to be a precursor of adenocarcinoma.[11] Most occur in the duodenum. The risk of malignant transformation is greatest with villous morphology, increasing size and higher grade dysplasia.[12]

Peutz Jeghers syndrome

This autosomal dominant condition is characterised by the presence of small intestinal polyps with melanin spots on the lips and buccal mucosa. Polyps are found most commonly in the jejunum and less frequently in the ileum and duodenum. The condition is due to a mutation on the serine/threonine kinase 11 (STK11) gene and carries an increased risk of cancers including breast, ovarian, testicular, pancreas, stomach, oesophagus and several others. Meta analysis confirms Peutz Jeghers syndrome carries a relative risk of small bowel cancer of 520 compared with the general population.[13]

Familial adenomatous polyposis (FAP)

This autosomal dominant condition is associated with an increased risk of small bowel cancer, caused by mutations of the adenomatous polyposis coli (APC) gene on chromosome 5.[14] Most patients with FAP (50–90% depending on series) have duodenal adenomatosis with 3–5% developing duodenal cancer.[15]

Hereditary non-polyposis colorectal cancer

HNPCC, another autosomal dominant condition, is caused by a germline mutation in the Mut S homologue 2 (hMSH2) or Mut L homologue 1 (hMLH1) mismatch repair gene.[16] Patients with HNPCC have a relative risk of small bowel cancer of more than 100 compared to the general population, with the risk reported to be higher in MLH1 mutation carriers than in those with MSH2 mutations.[17]

Other familial syndromes

Multiple endocrine neoplasia type 1 (MEN-1), von Hippel Lindau disease and neurofibromatosis type 1 each carry increased risk of carcinoid tumours.

Sporadic colorectal cancer

Patients with sporadic colorectal cancer (CRC) have a higher than average risk of developing small bowel cancer, while those diagnosed with primary small bowel cancer should be considered at risk of CRC. This relationship suggests shared risk factors.[18]

Diet and alcohol consumption

Evidence regarding dietary factors and alcohol consumption is inconclusive. While some authors report an increased risk of small bowel adenocarcinoma with greater red meat consumption,[19] a larger series did not confirm this association.[20] Similar variability is noted in studies linking alcohol use to small bowel cancer risk.[21]

Body mass index (BMI)/obesity

Several studies have shown an increased risk of small bowel cancer in overweight and obese people although most of these studies involve very few cancers.[22] One case control study showed no association with small bowel cancer and BMI and another study showed an inverse relationship between BMI and small bowel cancer.[23]

Cigarette smoking

Some studies suggest smoking increases small bowel cancer risk.[24,25]

Gallstones

A Danish series reports an elevated risk for cancer of the small intestine, mainly carcinoid tumours, in patients with gallstones.[26]