SHORT REPORT

Concurrent diagnosis of Crohn's disease and colorectal carcinoma in a young man with abdominal pain

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Abstract

The lead time between diagnosis of Crohn's disease and presentation with a Crohn's related malignancy is generally twenty years from diagnosis. This case outlines that of a young man who presented to the emergency department with abdominal pain and was subsequently discovered to have a malignant stricture complicating underlying Crohn's disease that was previously quiescent and undiagnosed. It demonstrates that a new diagnosis of Crohn's disease does not rule out previously quiescent underlying disease and therefore risk of colorectal carcinoma.

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1. Introduction

The lead time between diagnosis of Crohn's disease and presentation with a Crohn's related malignancy is generally twenty years from diagnosis. This case outlines that of a young man who presented to the emergency department with abdominal pain and was subsequently discovered to have a malignant stricture complicating underlying Crohn's disease that was previously quiescent and undiagnosed. It demonstrates that a new diagnosis of Crohn's disease does not rule out previously quiescent underlying disease and therefore risk of carcinoma.

2. Case report

A 42-year-old male presented to accident and emergency with a one day history of central abdominal pain with no associated symptoms on a background of depression and alcohol abuse. He had no past surgical history and was not on any medications. He is a non smoker. He had a significant family history of colon cancer in his grandmother, aunt and uncle, all of whom were diagnosed after the age of 40 and all of whom are now deceased. His plain film of abdomen (PFA) demonstrated a grossly distended large bowel with normal small bowel calibre (Fig. 1).

He was admitted with a diagnosis of large bowel obstruction and a decision was made for computed tomography (CT) of the abdomen and pelvis to be carried out as the patient showed no signs of peritonism on examination. There was evidence on CT of gaseous distension and air fluid...
levels involving the large bowel and marginally extending into the proximal ileum. The large bowel was dilated to the level of the recto-sigmoid junction and there was a mass on the mesenteric border of the sigmoid. Tight narrowing of the sigmoid was seen distal to the mass. There was no evidence of lymphadenopathy. The impression was of a dilated large bowel to the distal sigmoid where a mass like appearance was demonstrated followed by a tight stenosis (Fig. 2).

Direct visualisation was advised to assess for the presence of sigmoid neoplasm. Clinical impression was of sigmoid neoplasm and this was discussed with the patient as well as the need for colonoscopy and histological diagnosis and the potential treatment options of a sigmoid malignancy including but not limited to: Hartmann’s Resection +/- subsequent reversal? Colonic Stenting as a bridge to definitive treatment? Total colectomy and ileocolic anastomosis?

Our patient was fully counselled regarding the risk of autonomic and sexual dysfunction and anastomotic seque-

lae. He was very keen to avoid a colostomy if at all possible therefore it was decided to perform colonoscopy and biopsy of the lesion and colonic stenting as a bridge to surgery with this measure decreasing the risk of stoma at primary surgery. The tumour was identified at 15–25 cm on flexible sigmoidoscopy. An erythematous rectum was noted at colonoscopy but no biopsy of the rectum was taken (Fig. 3).

Examination under anaesthesia and tattooing of lesion was performed and multiple biopsies were taken. In spite of a high suspicion endoscopically the histology result was very surprising: no viable neoplasia. Following full discussion with our patient the decision was made to proceed to surgical treatment of the endoscopically malignant tight stenosis. Our aim was for resection with primary anastomosis. At operation due to severe thickening of rectum, it was necessary to proceed with an anterior resection with temporary defunctioning loop ileostomy.
Histology demonstrated a complicated Crohn's stricture with multiple foci of dysplasia and infiltrating moderately differentiated adenocarcinoma. The TNM staging was T3 NO MO with the Dukes staging of B2 for the largest of the carcinoma. None of the twenty lymph nodes sampled were involved. Figs. 4 and 5 illustrate the gross abnormality of the resected bowel with a sharp delineation visible macroscopically between the normal bowel and the Crohn's stricture. The microscopic images demonstrate the transmural active chronic inflammation with mucosal ulcers lined by fibrinous exudates. Deep penetrating fissures to the level of muscularis propria with fibrotic submucosa are also seen. The surface epithelium shows cryptitis and regenerative hyperplastic changes and foci of severe dysplasia. Separate foci of infiltrating moderately differentiated adenocarcinoma are seen in the fibrotic submucosa.

He is currently undergoing oncological follow up with oral capecitabine cytotoxic chemotherapy and is of ECOG 1 status. He is due to finish chemotherapy in two months time. Repeat CT abdomen has not demonstrated any recurrent or metastatic disease. He is also undergoing gastroenterological management of his Crohn's Disease. He is very anxious for reversal of his ileostomy on completion of chemotherapy.

### 3. Discussion

Malignant transformation of a Crohn's stricture as the first presentation of Crohn's is very unusual and therefore it is regarded a trap for the unwary endoscopist. As our case shows even in the absence of clinical symptoms a transforming malignant stricture may be the first presentation of Crohn's disease (CD).

This was an interesting and thought provoking case. There were no symptoms in history to suggest Inflammatory Bowel Disease. On admission he denied any history of bowel symptoms. Post diagnosis we returned to this discussion and he stated he had periodic bouts of severe diarrhea that settled after approximately one week's duration and that he thought this was a variation of normal bowel habit.

This is a new diagnosis of Crohn's disease; he had no medical therapy prior to surgery. Surgical intervention in Crohn's disease is usually reserved for failure of maximal medical management or complications of the disease. However medical management would not have reversed stricture and surgical oncological intervention was necessary. It is now widely accepted that both Crohn's disease and ulcerative colitis are associated with an increased risk of developing cancer. A landmark review in GUT defined this as an 18 fold increased relative risk in Crohn's disease. The accepted risk factors for increased risk of CRC in inflammatory bowel disease (IBD) are young age at diagnosis of IBD, severe disease, increasing duration of disease, family history of CRC, backwash ileitis and primary sclerosing cholangitis.

The risk of developing carcinoma in Crohn's disease was first reported in 1948. The first epidemiological study reporting this risk was published by the Mayo clinic in 1973, it found a 20 times greater risk of developing colorectal cancer (CRC) in patients with CD compared with the general population. Recent studies have down scaled this estimated increased risk dramatically. A landmark metaanalysis published in Diseases Colon and Rectum looked at studies with 60,122 patients included in total. It found a relative risk (RR) of CRC in CD of 2.44. Interestingly the mean duration of diagnosis of CD of 18.1 years. Thus presenting with Crohn's and colorectal cancer in a Crohn's stricture without a known diagnosis of Crohn's is not in keeping with the linear nature of the association between CD and development of CRC.

Therefore our patients concurrent diagnosis of Crohn's disease and colorectal cancer is very unusual. We would have expected a longer interval between diagnosis of Crohn's disease and the development of CRC. The data in the literature on CRC in Crohn's disease is substantially less than that available for ulcerative colitis. A recent meta-analysis revealed a risk of CRC in Crohn's disease of 2.9% at 10 years, 5.6% at 20 years and 8.3% at 30 years.

Thus increased years of at risk mucosa and increased amounts of at risk mucosa logically increase the risk of development of CRC.

In patients with known IBD regular colonoscopic surveillance remains the principle measure to reduce mortality from CRC in Crohn's disease. The multifocal nature of our patients tumour is consistent with a Crohn's associated tumour as the disease related mucosal inflammation is widespread throughout the diseased area of the colon predisposing to multiple primary tumours.

Factors associated with a decreased risk of colorectal cancer in Crohn's disease include (1) surveillance colonoscopy (2) chemoprevention and (3) prophylactic panproctocolectomy. The survival benefit from surveillance colonoscopy in IBD patients is controversial, a recent Cochrane review concluded that there was no clear evidence that surveillance colonoscopy prolongs survival. It cautions that as cancers tend to be detected at an earlier stage and thus with improved prognosis, therefore lead time bias could be responsible for a portion of this apparent benefit. The authors concluded that there is only indirect evidence that it results in decreased death from Crohn's disease associated CRC. Despite this, the practice of colonoscopic surveillance remains our best option for follow-up of this group of patients who are at significantly increased risk of developing CRC.

There is much interest in the role of chemoprevention of CRC in patients with IBD. The best evidence for chemoprevention...
is for 5-aminosalicylate with Velayos et al. concluding from their meta-analysis that 5-aminosalicylate use resulted in a protective odds ratio of developing CRC of 0.51.

Our patient was commenced on oral capecitabine adjuvant chemotherapy. In the past the mainstay of chemotherapy for CRC consisted of 5-fluorouracil. Three new cytotoxic chemotherapeutic agents have been approved in the past ten years. They are irinotecan, a topoisomerase I inhibitor, oxaliplatin, a third generation platinum analogue and finally capecitabine, a fluoropyrimidine. The three new biological agents all approved in the last 5 years include cetuximab and panitumumab, both antibodies to epidermal growth factor receptors and finally bevacizumab an anti-vascular endothelial growth factor antibody. Ongoing trials are assessing the benefit of new combinations of the newer cytotoxic agents with the biological antibodies. Recent work is promising with three randomized studies demonstrating equivalency of the CAPOX (capecitabine+oxalaplatin) to the standard FOLFOX (5-fluorouracil/leucovorin/oxaliplatin) regimen.

4. Conclusion

Patients with known inflammatory bowel disease are at increased risk of CRC. While the literature supports a long history of a known diagnosis of Crohn’s disease our case demonstrates that patients with quiescent or subclinical Crohn’s are also at risk of Crohn’s associated colorectal carcinoma.

References