

Case Report

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A rare case of three synchronous colorectal cancers and a closed loop large bowel obstruction

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ABSTRACT

Colorectal malignancies are a common general surgical presentation. However, synchronous colorectal cancers are less frequent and typically account for only 3.5% of all colorectal cancers. Of these 3.5% of synchronous colorectal cancers, only approximately 4% are incidental appendiceal malignancies. An 80-year-old gentleman presented with abdominal pain and distension to the emergency department. On examination, the patient had a peritonitic abdomen and a CT scan revealed a large bowel obstruction secondary to sigmoid and rectal neoplasms, concerning for a closed loop obstruction. He underwent an emergency laparotomy and Hartman's Procedure. Intraoperatively the tip of the appendix appeared dilated and was removed. Histology revealed T3N0M0 synchronous sigmoid and rectal cancers, as well as a low-grade appendiceal mucinous tumour. Whilst synchronous colorectal malignancies are a relatively common presentation they typically present in adjacent segments of bowel. They are less frequently seen in association with incidental appendiceal malignancies and no cases have been published in combination with a closed loop large bowel obstruction. This is the first published case of three synchronous colorectal cancers causing a closed loop large bowel obstruction.

Keywords: Closed-loop large bowel obstruction, Synchronous colorectal cancers, Appendiceal mucinous tumour

INTRODUCTION

Colorectal malignancies are a common general surgical presentation. However, synchronous colorectal cancers are less frequent and typically account for only 3.5% of all colorectal cancers.¹ Most patients with synchronous colorectal cancers only have two large bowel carcinomas and are more common in the proximal colon.² In general, synchronous colorectal cancers also tend to present on the same or adjacent segments of the large bowel.³

This report describes the management of an elderly man who was found to have three synchronous colorectal malignancies and the impacts of this diagnosis. The combination of three synchronous colorectal cancers and the fact the two of these were forming a closed loop large bowel obstruction were of interest to our team. Individually both conditions are uncommon, but together they are even more so. The rarity of their combination

raised concerns of possible genetic syndromes and the potential impact on the patient's prognosis. Furthermore, the patient's medical comorbidities along with complex social situations added to the overall complexity of the case and required a patient-centred management and multidisciplinary teamwork approach.

CASE REPORT

An 80-year-old gentleman presented to the emergency department via an ambulance with acute on-chronic abdominal pain and distension. He described a 2-month history of constant waxing and waning suprapubic pain, which had intensified over the last two days. 24hrs prior to his presentation, the patient noted that he could not open his bowels or pass flatus. The patient has a past medical history of prostate cancer, schizophrenia, early dementia and iron deficiency anaemia. A colonoscopy was initially arranged in 2014 to investigate the patient's

iron deficiency anaemia and positive faecal occult blood test; however, he declined on two separate occasions.

On examination, the patient was tachycardic to 105, however, all other observations were within normal limits. An abdominal examination elicited abdominal distension, generalised peritonism and tinkling bowel sounds on auscultation. The remainder of his system examination was unremarkable.

Prior to the general surgical review, the emergency department had arranged bloods and a CT abdomen/pelvis, due to concerns for an intestinal obstruction. Blood tests revealed a raised white cell count ($16.4 \times 10^9/L$; reference range 3.5-11.0), raised C-reactive protein (111 mg/L; reference range <5.0), raised lactate (2.6 mmol/L; reference range 0.5-2.2) and a normal carcinoembryonic antigen (2.5 μ g/L; reference range <5.0). A portal venous contrast-enhanced abdominal and pelvis CT revealed a large bowel obstruction secondary to a stenosis sigmoid neoplasm, which was concerning for a closed loop obstruction due to a competent ileocecal valve (Figure 1).

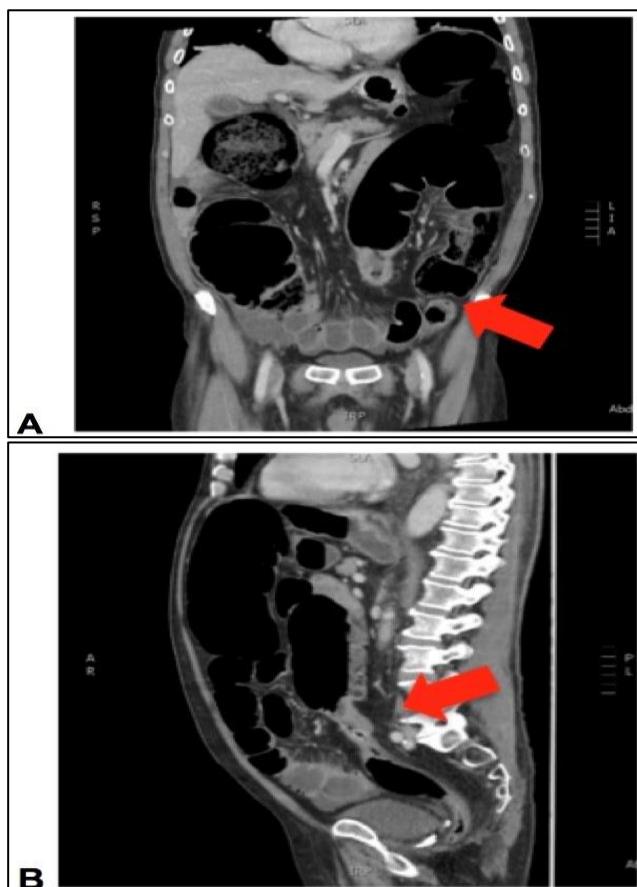


Figure 1 (A and B): Portal venous contrast enhanced CT abdomen and pelvis in the coronal plane and sagittal planes: Large bowel obstruction with a transition point in the mid sigmoid secondary to stenosing lesion and sigmoid colon thickening measuring 4.4 cm.

By virtue of these clinical and radiological findings, the patient was taken urgently for an urgent emergency laparotomy. Intra-operatively he was found to have synchronous sigmoid and rectal cancers forming a closed loop large bowel obstruction. The patient underwent a Hartman's Procedure, which took a total of 4 hours. The operation was compounded by several challenges, these included a difficult dissection of the duodenal-jejunal flexure from the sigmoid cancer, which resulted in a small serosal tear as well as difficulty identifying the left ureter during the dissection of the rectal cancer from the pelvis. Urology was consulted intra-operatively and advised to conduct a cystoscopy and retrograde pyelogram at the end of the case.

Further difficulty was encountered when attempting to mobilise the descending colon to form an end colostomy due to significant adhesions in the left upper quadrant. At this point in the operation, a cystic structure was noted at the tip of the appendix. Due to the atypical appearance of the appendix and concerns for an underlying mucinous tumour, the decision was made to remove the appendix. The remainder of the operation was uneventful and an end-colostomy was formalised in the left upper quadrant.

The on-call senior urology registrar attended at the end of the case and completed a retrograde pyelogram, which did not demonstrate any extravasation of contrast to suggest a ureteric injury (Figure 2).

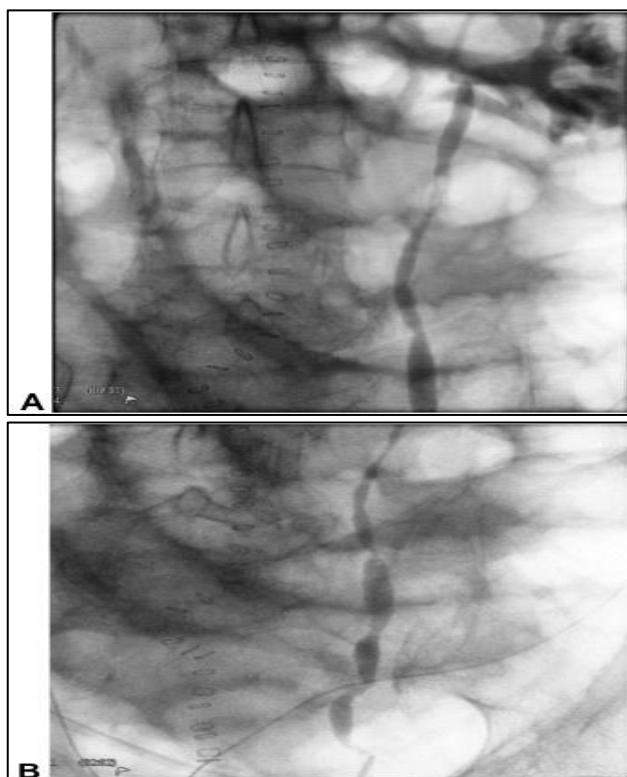


Figure 2 (A and B): Intra-operative retrograde pyelogram: flow of contrast from the left ureter into the kidney and flow of contrast from the catheter inserted into the left ureteric opening into the ureter.

Postoperatively, the patient was admitted to the intensive care unit (ICU) for ongoing respiratory support due to the prolonged exposure to anaesthesia, as recommended by the attending anaesthetist. Day 1 postoperative, the patient was extubated and was commenced on total parenteral nutrition. While in ICU, the patient received early engagement of stomal therapy education for both the patient and nursing staff. Day 2 postoperatively, the patient developed new atrial fibrillation, which resolved following electrolyte replacement and he was stepped down to the surgical ward later that afternoon. The remainder of the patient's hospital stay involved a slow upgrade of their diet once his stoma became functional in addition to stoma education and allied health support for functional deconditioning. Over the patient's stay, concerns were raised regarding their ability to cope at home with a new stoma with their compounding cognitive impairment. An interdepartmental meeting involving the occupational therapists, social workers and the geriatrics team was held and made a recommendation for a home care package for assistance with activities of daily living, with the option to upgrade to residential care if needed. By day 15 postoperatively, the patient was independent for the majority of their activities of daily living. However, the patient still required assistance with caring for their stoma. As a result, it was decided to step down the patients care to a smaller hospital closer to their home for ongoing discharge planning.

DISCUSSION

Synchronous colorectal cancers account for approximately 3.5% of all colorectal cancers. Of the 3.5% of synchronous colorectal cancers, only approximately 4% are incidental appendiceal malignancies.³ Primary adenocarcinoma of the appendix is quite rare, and is often only detected incidentally following appendectomy for acute appendicitis. There are four main types of neoplasms in the appendix: adenocarcinoma, mucinous neoplasm, goblet cell carcinoma, and neuroendocrine neoplasms.⁴ Appendiceal mucinous tumours, as seen in the case presented, accounts for approximately only 8% of all appendiceal malignancies. Clinically appendiceal mucinous tumours typically present as a mucocele, resulting from the accumulation of mucin within the appendiceal lumen.⁵

The appendix is susceptible to developing any neoplastic change seen in the colon and/or rectum since it is also developed embryologically from the large bowel via the endoderm germ layer. As with most cancers, both genetic and environmental factors play a critical role in the development of colorectal and appendiceal tumours.¹ Recent advances in molecular biology have also discovered that chromosomal instability, microsatellite instability (MSI), and gene methylation plays a role as predisposing factors in synchronous colorectal cancers. In fact, chromosomal instability typically accounts for 60% of all synchronous colorectal cancers. Chromosomal instability develops through gross structural alterations

such as deletions, insertions, and loss of heterozygosity, resulting in an altered karyotype.⁵ The most commonly associated genes in these mutations are APC (5q deletion), TP53 (17p deletion), and DCC/MADH2/MADH4 (18q deletion).¹ The 30% of synchronous colorectal cancers are due to gene methylation; most commonly, this is seen in association with CpG islands (cytosine-glycine dinucleotides). The subsequent methylation of the CpG islands results in the silencing of the tumour suppressor genes through the reduction in the transcriptional activity of the gene.^{1,6}

Microsatellite instability is a predisposing factor in approximately 10% of all synchronous colorectal cancers. MSI results in the dysfunction of the mismatch repair pathway through mutations in its associated genes (most commonly MLH1, MSH2, MSH6, and PMS2). The resulting accumulation of damaged DNA cannot be repaired and promotes the deletion or insertion of genes. Therefore, the subsequent frameshift in the production of condensed/altered proteins results in an increase in neoantigens.^{1,5} Microsatellite positive colorectal carcinomas can be hereditary, as seen in hereditary nonpolyposis colorectal cancer (HNPCC), or sporadic through methylation of MSI genes. Sporadic microsatellite cancers typically show methylation of MLH1 promoters, and the resulting condition is strongly correlated to the V600E mutation of the BRAF gene.¹ BRAF is an important mutation as it can be associated with microsatellite instability, hypermethylation, and chromosomal instability. Clinically these mutations are associated with a poorer prognosis due to its potent activation of MEK and resulting dysregulation of the cell cycle.⁵

Since 1947 to date, only 14 cases synchronous colorectal and appendiceal neoplasms have been published.⁷⁻¹⁸ Of these cases, none present with the combination of three synchronous colorectal cancers of the rectum, sigmoid and appendix; or the addition of a closed loop large bowel obstruction. In regards to our case, there was a high clinical suspicion of two synchronous cancers at the sigmoid and rectum based on the pre-operative CT. Unfortunately, the appendiceal tumour was not noted on the CT scan and was only identified at the time of the operation. It is important to note that, the significant overlying large bowel distension could have obscured this.

The potential for additional missed synchronous colorectal cancers, presents the question of whether further investigations should be undertaken to exclude the presence of further malignancies. The current colorectal guidelines by the national health and medical research council (NHMRC) and the American society of colon and rectal surgeons recommend staging colorectal cancer with only a CT chest/abdomen/pelvis.^{19,20} However, previous research has demonstrated incidental synchronous appendiceal neoplasm in 169 patients, with 4.1% of patients exhibiting synchronous appendiceal neoplasm

following a coincidental appendicectomy at the time of their surgical resection for their known colorectal malignancy.²¹ This is a marked number of potentially missed malignancies and may ultimately influence the patient's overall prognosis. The consequence of missing an appendiceal malignancy is more significant, as the entirety of the lumen cannot be adequately surveilled, unlike that of the remainder of the colon.²¹ Despite this, there are no specific guidelines pertaining to synchronous cancers in the workup of colorectal cancers or whether further investigations are required. They do however, recommend pre-operative colonoscopy to exclude any other colonic luminal lesions as well as a thorough inspection at the time of the surgical resection.¹⁹

CONCLUSION

This is the first published case of three synchronous colorectal cancers causing a closed loop large bowel obstruction. Despite a reasonable number of published cases there still is no guidelines pertaining to the work up of synchronous colorectal cancers. This gap in the recommendations could lead to several missed malignancies and influence the patient's overall prognosis.

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