An Extremely Rare Case of Rectal Signet Ring Cell Carcinoma

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Abstract

Signet ring cell carcinoma of the rectum is a rare variant of colorectal cancer. When found, it is often diagnosed in late stages and has poor prognosis. This case depicts a patient with a history of Crohn's disease who presented to the hospital for perirectal abscesses. During the evaluation of both the abscesses and Crohn's disease, he was found to have stage IV adenocarcinoma with signet ring cell features. The patient was started on chemotherapy before surgical resection was considered, however, showed little response. The patient's family eventually pursued hospice care with comfort measures only. Colorectal signet ring cell carcinoma is rare but has poor prognosis as it is diagnosed generally at late and advanced stages. There is a need for more research in earlier detection of these rare cancers.

Keywords: Signet ring cell carcinoma; Rectum; Colorectal cancer; Chemotherapy

Introduction

Colorectal cancer (CRC) is the third most common cancer and second leading cause of death from cancer for both men and women. CRC affects approximately 135,439 new patients in the United States of America every year. The incidence of CRC has been declining almost 3% each year due to better screening guidelines and removal of precancerous lesions [1]. Mortality has been declining as well due to better screening and therapy modalities.

A majority of CRCs are adenocarcinomas which can be further differentiated in mucinous, signet ring cell, and other less common subtypes [1]. Signet ring cell carcinoma (SRCC) is defined by the presence of greater than 50% extracellular mucin by volume with the stomach being the most common site [2, 3].

Signet ring cell morphology is a rare pathological finding for CRC, making up less than 1% of CRCs and about 1.39% of rectal cancers [4, 5]. It is associated with advanced tumor stage at presentation in young patients, hence diagnosis is made usually after it has progressed, making prognosis to be poor.

Case Report

A 57-year-old male with a past medical history of cerebral palsy, autism, mental disability, and 25-year history of Crohn's disease with perirectal abscesses presented to the emergency department (ED) complaining of rectal pain. The patient was known to have chronic rectal pain secondary to numerous perirectal abscesses and had these abscesses drained 3 months prior. A computed tomography (CT) scan was done showing increased wall thickening and pericolonic inflammation involving the rectosigmoid colon which was new compared to the CT scan performed a month ago, with several new perianal fluid collections and tracts. In the ED, an incision and drainage of the large perirectal abscess was performed at bedside. The patient was started on antibiotic treatment and was admitted for the same.

During the admission, he had episodes of hematochezia. So, gastroenterology was consulted. A flexible sigmoidoscopy was done for better evaluation of the patient's Crohn's disease showing necrotic, friable tissue in the entire rectosigmoid area. A colonoscopy was later done confirming a large colonic mass and necrotic friable ischemic circumferential mucosa (Fig. 1). Pathology report showed fragments of infiltrating poorly differentiated adenocarcinoma with mucinous and signet ring cell features (Fig. 2). Pathology report of the rectosigmoid mass immunohistology was cytokeratin (CK) 7 positive, CK20 positive and SATB2 positive. The tumor was positive for hMLH1, hMSH2, hMSH6, and PMS2. The tumor was shown to have normal nuclear expression of all proteins seen in tumor cell nuclei and no evidence of mismatch repair deficiency by immunohistochemical evaluation. Rectal endoscopic ultrasound (EUS) showed circumferential hypodensity at the anal verge, extending to and breaching the muscularis propria (Fig. 3) along with two lymph nodes (Fig. 4) with malignant features in the deep layers surrounding the malignancy, classifying as T3N2 disease. Of note, patient had no history of CRCs or any other malignancies in the family.

CT scan of abdomen had shown increased perirectal soft tissue thickening and rectosigmoid wall thickening with pericolonic inflammation extending to the level of the distal de-
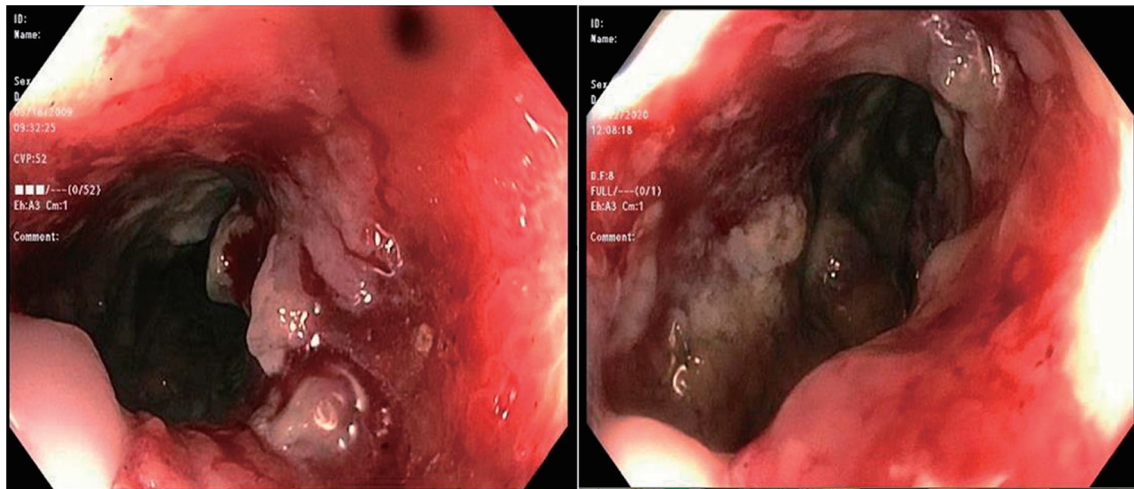
Figure 1. A colonoscopic image showing large circumferential ischemic, necrotic and friable areas in rectum.

scending colon with some evidence of pelvic lymph node enlargement but an absence of any lesions in the stomach. Upon conversation with surgery, mass was likely a rectal based cancer, extending up to the rectosigmoid area. CT of chest showed no evidence of metastatic disease to the lungs or evidence of lesions in esophagus. Magnetic resonance imaging (MRI) of the abdomen was done and showed thickening and abnormal signaling of the posterior urinary bladder wall along with partially visualized distal bilateral hydroureter, suspicious for bladder invasion. There was suspected metastasis in the peritoneum as the tumor was seen to abut the peritoneal reflection with suspected invasion. MRI also showed deposits along the right pelvic sidewall and irregular contour of the levator ani and puborectalis muscle. Decreased signal intensity along the anterior sacrum was also noted. Distance from inferior border of tumor to anal verge was 1 cm. MRI showed at least stage T4a, suspected T4b disease. Rectal examination under anesthesia showed the lesion extending to the prostate and coccyx.

During a multidisciplinary discussion during tumor board, the plan was decided to give chemotherapy with folinic acid (leucovorin)-fluorouracil-oxaliplatin (mFOLFOX6) and then repeat imaging in 3 months to assess for response. Then based on the response, go for surgical resection. Patient soon started chemotherapy with mFOLFOX6 and was to receive chemotherapy every 2 weeks for 3 - 6 months. He was to be reevaluated with imaging and colonoscopy, and based on the response, the patient was to undergo surgical resection. One month later, the patient later developed acute kidney injury secondary to obstructive hydronephrosis. On cystoscopy, it was seen that cancer had spread to the bladder, with the apical portion of bladder encased with cancer and no visualization of the trigone. Biopsy showed fragments of urothelial mucosa showing extensive replacement by mucinous adenocarcinoma, consistent with the involvement by CRC.

One month later, when the patient was on cycle 6 of chemotherapy, a repeat CT scan of the abdomen and pelvis was done, showing evidence of progression with little response. CT of chest remained unremarkable. After discussion with the family, the decision was made to place the patient on hospice with comfort measures only.
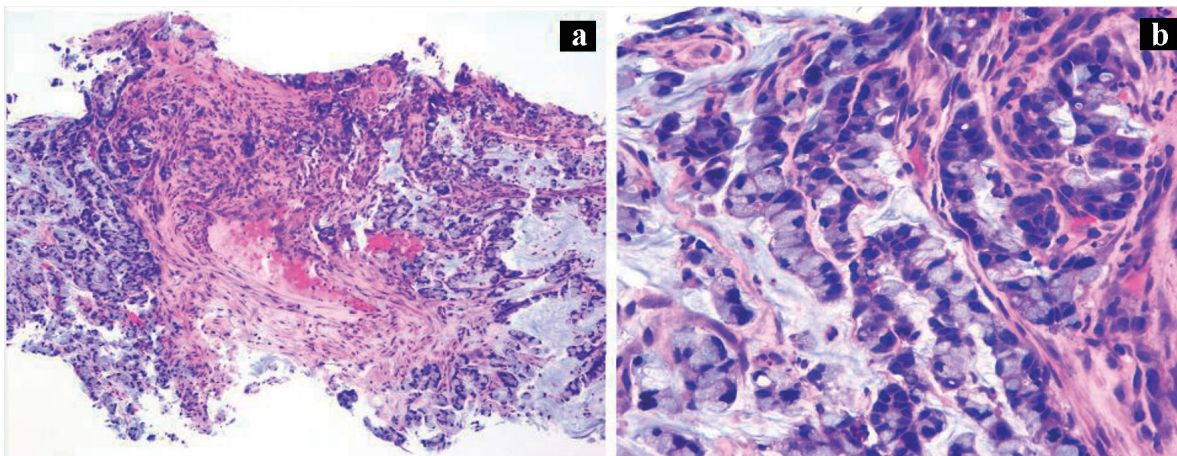

Figure 2. (a) Rectosigmoid biopsy (H&E, × 100) showing infiltrating malignant glands, poorly differentiated in the background of necrotic debris. (b) High power (H&E, × 400) image showing mucinous and signet ring features.
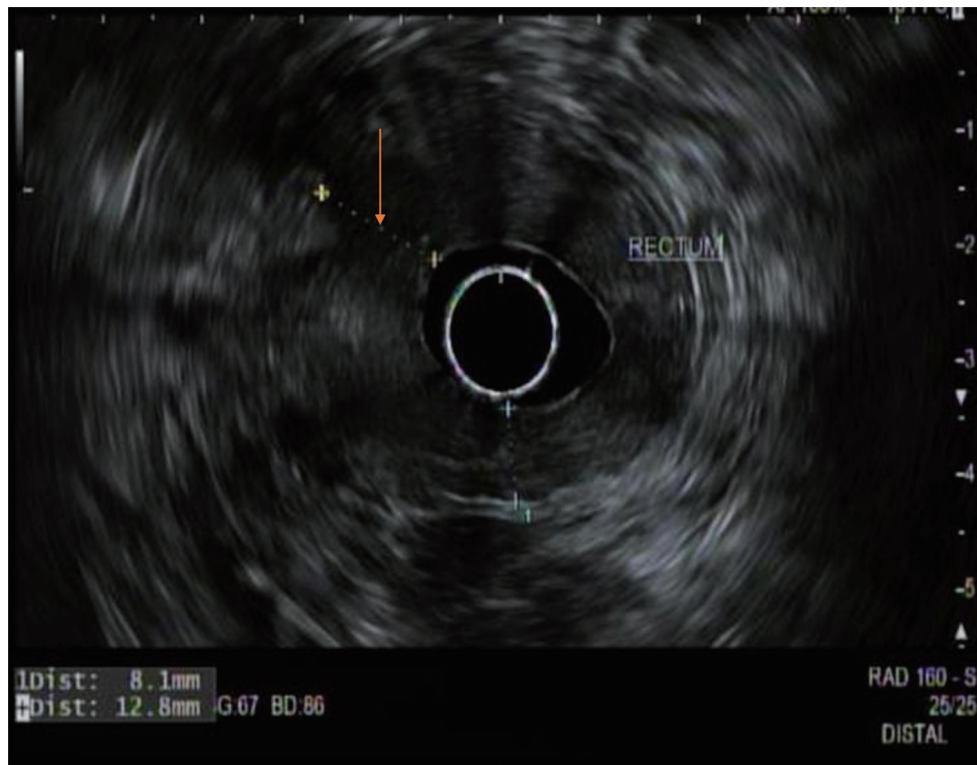
Figure 3. A radial rectal endoscopic ultrasound image showing an irregular hypodense rectal mass (arrow) invading the muscularis propria.
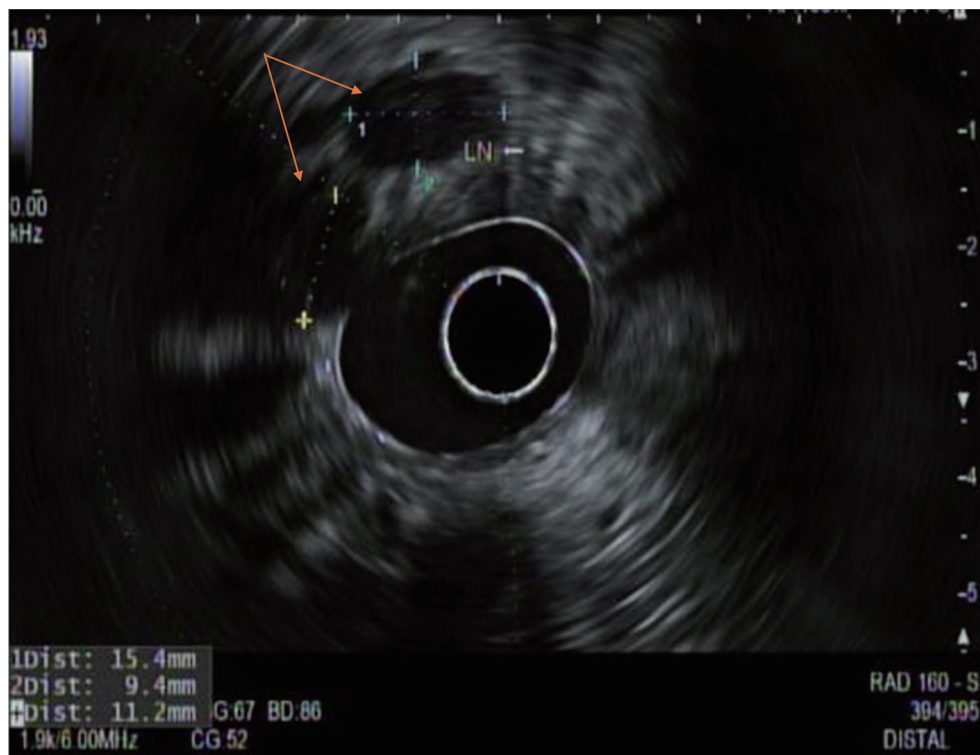

Figure 4. A radial rectal endoscopic ultrasound image showing two enlarged perirectal lymph nodes (arrows) with sizes approximately 15 and 11 mm.

Discussion

Colorectal SRCC is a rare form of CRC. In a 2012 study (N = 244,794), SRCC made up 1% of colorectal carcinomas [4]. The incidence of SRCC makes up 1.39% of rectal cancers [5]. The clinical symptoms of colorectal SRCC are often similar to those of most CRCs such as abdominal pain, hematochezia, changes in bowel habits, change in appetite and unintentional weight loss [6]. On colonoscopy, the gross appearance of colorectal SRCC often presents with more diffuse circumferential thickening of the bowel wall than the gland forming adenocarcinoma [7]. The location of the mass from SRCC can vary. In a 2020 population-based study (N = 3,278), primary colorectal SRCC was most seen in the cecum-transverse colon (60.49%), following the rectum (19.52%), then descending colon-sigmoid (15.71%) [8]. Primary rectal SRCC often presents in young males [5]. In a retrospective study comparing the clinical data of rectal SRCC with non-signet ring cell mucinous rectal adenocarcinomas (NSMR) and non-mucinous rectal adenocarcinomas (NMR), primary rectal SRCC had a male predominancy of 67.2% and the average age of patients of 48.1 years compared to 57.4 years for NSMR and 62.6 years for NMR [5]. Some general risk factors for CRC such as inflammatory bowel disease, hereditary risk factors such as Lynch syndrome and familial adenomatous polyposis, cigarette smoking, low fiber consumption, low physical activity, and high BMI could be possible risk factors for SRCC [9, 10]. However, due to the limited number of cases and instances of SRCC in patients with no history of familial cancers, there may be other yet unknown risk factors or unidentified correlations to certain environmental risks.

The most common immunostainings for colorectal carcinoma are CK20, CK7 and CDX2. Positive CK20 and negative CK7 are usually the findings for colorectal origin [11]. Positive SATB also favors lower gastrointestinal tract primary [12]. However, these immunostainings may not be specific enough to identify colorectal SRCC. SRCC has a unique immunohistology involving CK20, CDX2, MUC2, and MUC5AC; variable MUC1 and HepPar1 [13]. In colonic SRCC, negative Hep Par 1, homogenous CDX2 nuclear positivity and diffuse cytoplasmic MUC2 and MUC5AC positivity is seen. This staining profile can also be used to differentiate SRCC of gastric origin which will have positive Hep Par 1 and heterogeneous CDX2 staining [13]. Primary urinary bladder SRCC and primary colorectal SRCC overlap for CK7, CK20, and CDX2. However, it was shown that the absence of nuclear positivity for β-catenin is more specific for urinary SRCC [14]. SRCC should also be differentiated from benign processes with signet ring cell change, such as pseudomembranous colitis. In this case, benign signet ring cell change will be positive for E-cadherin and negative for p53 and Ki-67, while SRCC will be positive for p53 and absent/weak positivity of E-cadherin [15]. When comparing genomic alterations for colorectal SRCC versus non-signet ring cell colorectal adenocarcinoma, colorectal SRCC was shown to have low rates of KRAS, PIK3CA and APC mutations while amplified Bcl-2 [16, 17].

Primary colorectal SRCC also has a poor prognosis as it frequently presents at late stages with rapid progression [18].

In a 2016 retrospective study (N = 170), it was seen that 91.2% of patients diagnosed with SRCC presented in stage III and IV of disease [19]. Patients with primary SRCC usually present late, hence had a worse 5-year prognosis in comparison to mucinous or adenocarcinoma of the colon [20]. The overall SCCR survival rates at 1, 2 and 5 years are 73.9%, 36.3%, and 23.3%, respectively [5]. According to a multivariate adjusted survival analysis from the National Cancer Data Base (NCDB), signet ring cell histology for both colon and rectal cancers is associated with 57% higher risk of death relative to non-signet ring adenocarcinoma [4]. Much of the poor prognosis of primary colorectal SRCC is related to its highly malignant biological behavior. It has characteristic peritoneal seeding and low incidence of hepatic metastasis [19, 21]. In a 2016 retrospective study (N = 170), about 86% of patients with stage IV rectal SRCC had isolated peritoneal metastasis. Up to 83% of patients with rectal SRCC had peritoneal metastasis [19]. SRCC was shown to have reduced expression of E-cadherin which causes a loss in epithelial differentiation and acquisition of more invasive and motile properties. This allows the cancer cells to detach from their surroundings and become more metastasizing [22, 23]. The down regulation of E-cadherin reduces cell adhesion of high mucus content areas and promotes tumor scattering [24]. This characteristic contributes to advancing tumor stages and is an indication of its malignant potential. SRCC with peritoneal involvement was shown to have rapid progression and poor prognosis despite systemic and intraperitoneal chemotherapy [25].

Effectiveness of chemotherapy and surgical intervention for colorectal SRCC is limited. There has been evidence that patients with stage III and high microsatellite instability were more responsive to single agent 5-FU adjuvant therapy [26]. However, many of the advanced SRCCs are microsatellite stable and are classified as high grade, hence associated with poor outcome [24]. Surgical resection is offered to these patients but because the patients present very late in disease course, usually only palliative surgery is possible. Surgical intervention is often aggressive and overall survival ranges from 19 to 57 months [21, 27]. Low survival chances and reduced chances of curative resection are due to the delay in diagnosis and possibility of local or distal metastasis [28].

Our patient's SRCC occurred in the rectum and had metastasized to peritoneum, coccyx, prostate and bladder. Due to late disease of stage IVb and microsatellite stability in our patient, mFOLFOX6 was initiated to delay tumor progression. However, due to some of these late features discussed, the cancer was too aggressive, and chemotherapy was not effective.

Conclusion

SRCC of the rectum is a rare variant of CRC. Compared to other forms of CRC, SRCC has a younger onset and is diagnosed in later stages. It is a highly malignant cancer with poor prognosis even with optimal treatment. This indicates that more research in detection and treatment therapies should be promoted to allow early detection to improve prognosis in these patients.

Acknowledgments

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Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Informed patient consent was obtained to write and publish the case report.

Author Contributions

Woo Jin Seog has written the manuscript. Samyak Dhruv has written the manuscript and edited it. Abhishek Polavarapu has provided the images.

Data Availability

The authors declare that data supporting the findings of the study are available within the article.

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