Case Report of Synchronous Squamous Cell Carcinoma and Adenocarcinoma of the Colon

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Introduction

Squamous cell carcinoma (SCC) of the gastrointestinal tract is a rare malignancy usually found in the esophagus or anal canal. Squamous cell carcinoma of the rectum is very unusual, representing a small fraction of colorectal malignancies, at which more than 90% are adenocarcinomas. There is little information on etiology and optimal management of this tumor. In this article we describe a patient with synchronous SCC and adenocarcinoma of the colon who underwent a lower anterior resection (LAR).

Case Presentation

A 48 year old female with past medical history including mental retardation, bipolar disorder, hyperlipidemia, hypothyroidism, and migraines presented to the gastroenterologist as an outpatient with complaints of diarrhea and abdominal pain. Initial questioning revealed that she had multiple family members, including her father, who were diagnosed with colon cancer. Based on patient’s history, it was recommended that the patient undergo a colonoscopy. When she arrived for her elective colonoscopy, the patient was hypertensive. Physical exam showed increased abdominal distention since her last exam. Because of her increased distress and discomfort, she was transferred to the emergency room for further evaluation.

Examination of the patient in the emergency room showed that she was in slight distress with blood pressure 166/110, but all other vital signs were stable. On physical examination, the abdomen was soft, distended, tender to palpation of the right lower and left lower quadrants without rebound or guarding, tympanic to percussion with hypoactive bowel sounds. Blood work including a CBC and CMP were within normal limits. However a CT scan of the abdomen and pelvis with contrast revealed a 6x7 cm mass at the rectosigmoid junction with mild distention of the proximal colon with air fluid levels indicating a partial obstruction. There was no evidence of a mass within the liver, metastatic disease, or regional lymphadenopathy (Figure 4 and 5).

The patient underwent flexible sigmoidoscopy the same day where a rectal mass was seen approximately 10 cm from the anal verge. Multiple biopsies were taken. The sigmoidoscope was not able to traverse through the mass. She was taken to surgery two days later where a low anterior colon resection was performed with primary anastomosis. Surgical pathology report identified separate squamous cell carcinoma of the rectum, moderately to poorly differentiated with involved margins (Figure 1 and 3), and adenocarcinoma of the sigmoid colon, moderately to well differentiated (Figure 1 and 2). Metastatic adenocarcinoma was found in 4 of 45 lymph nodes. The malignancy was classified as Stage IIIB (mpT3pN2aM0).

Discussion
Schmidtmann in 1919 described the first case of squamous cell carcinoma of the large intestine localized to the cecum, and Raiford described the first case involving the rectum in 1933 (4). Approximately 120 cases have been reported since that time (10). The incidence is 0.10 to 0.25 per 1000 cases of colorectal cancer. The rectum is most frequent location of the disease followed by the right colon. Individuals between the ages of 39 to 93 years are affected with a median age of 57 years. This disease occurs more commonly in women in a 2:1 ratio.

Four hypotheses have developed in regards to pathophysiology of the disease. The first hypothesis suggest that inflammation or irritation for inflammatory bowel disease, infections such as Schistosomiasis, Entamoeba histolytica and human papilloma virus (HPV) or radiation leads to squamous metaplasia resulting in carcinoma (1,4). Cheng et al described a case where a 51 year old female with a 17 year history of ulcerative colitis had an initial colonoscopy showing inflamed and granular rectal mucosa with biopsy showing squamous metaplasia with parakeratosis. The histological findings were similar to that seen of HPV-related squamous atypia. Another surveillance colonoscopy seven years later showed a 2 cm ulcer in the rectum at the junction of the squamous metaplastic and columnar mucosa with biopsy showing SCC arising in an area of active colitis. It was thought that the patient first developed squamous metaplasia in the setting of chronic UC; the squamous metaplasia was then infected by HPV which than lead to dysplastic changes and malignant transformation.

Besides inflammation or irritation leading to SCC, the possibility of pluripotent stem cells capable of squamous differentiation exists. Thirdly, epithelial damage causing proliferation of uncommitted basal cells into squamous cells which then undergo malignant transformation. The final hypothesis is the possibility that squamous carcinomas may differentiate from preexisting adenomas or adenocarcinomas (4). Kulaylat et al reviewed 16 reported cases of SCC complicating IBD which found that only twenty percent of the cases were adeno-SCC while eight percent were purely SCC (7).

The symptoms of patients with squamous cell carcinoma of the rectum is similar to those with adenocarcinoma of the rectum which are rectal bleeding, abdominal pain, change in bowel habits and weight loss. Symptoms are usually experienced for several weeks to months. The primary tools of diagnosis include proctoscopy or colonoscopy with forceps biopsies. Endoscopic appearance can range from a polyp to an ulcerated obstructing mass. However, techniques such as narrow band imaging (NBI) can allow for identification of more subtle lesions. CAM 5.2, AE1/AE3, and 34B12 are immunohistochemical stains that will help characterize these lesions. For example, CAM 5.2 helps differentiate rectal from anal lesions and AE1/AE2 stain positively for cells of squamous origin (4).

Williams et. al (13) formed diagnostic criteria for squamous cell cancer of the rectum in 1979 which included absence of evidence of squamous cell carcinoma of any other part of the body indicating metastasis, careful proctoscopy to exclude proximal extension of anal squamous cell carcinoma, and lack of a fistulous tract lined by squamous cells. The above findings along with histology consistent with a squamous carcinoma without glandular differentiation are required for diagnosis.

Squamous cell carcinoma antigen (SCC Ag) is a tumor marker that has been associated with squamous carcinoma of the anus. In 2001, Comer et al found elevated SCC Ag along with metastatic
disease in a patient previously treated for rectal squamous cell cancer. Retreatment with chemotherapy and radiation lead to improvement in SCC Ag levels which leads to the possibility that SCC Ag levels may not suitable for initial diagnosis but may be used to monitor disease progression and response to treatment (3).

Staging of tumor is required after diagnosis which can be aided by trans-rectal endoscopic ultrasound (R-EUS). R-EUS helps determine the depth of tumor invasion along with assessing local nodal involvement. R-EUS should be performed along side with computed tomography (CT) for complete staging. R-EUS provides better tumor and local lymph node evaluation while CT allows for detection of distant metastasis. The TNM classification system used for squamous cell cancer of the anus is also used for evaluation of tumor spread of SCC of the rectum. There is a worse prognosis stage for stage when nodal involvement occurred (4).

The best treatment option for squamous cell carcinoma of the rectum is surgery. Local excision can be performed for stage T1 (invasion to the mucosa or submucosa) cancers or possibly stage T2 (invasion to the muscularis propria) lesions. More advanced disease require low anterior resection (LAR) or abdominoperineal resection (APR) depending on location of the tumor. Tumors located in the proximal two-thirds of the rectum, LAR can be performed to allow for anastomosis of the descending colon with the distal rectum or anus and thus maintaining rectal continuity. APR is performed for distal rectal tumors and for locally advanced disease. APR allows for excision of the anus and rectum along with abdominal exploration for metastatic disease before creating an ostomy. APR is associated with higher postoperative complications (4).

Case reports have described chemoradiation therapy (CRT) as the primary treatment modality in high risk surgical candidates. The treatment regimens used mainly were 5-fluorouracil based treatment along with either mitomycin-C or cisplatin. Rasheed and Clark et al treated 13 patients with CRT and only three needed further treatment with surgical resections (9). Iannacone et al described a case of a 78 year old female with squamous cell rectal cancer who was considered a high risk surgical candidate due to age and other comorbidities and thus underwent chemoradiation for curative treatment. Pt was first given combination of 5-FU with mitomycin followed by radiation therapy. Patient was revaluated at 7 weeks, 10 weeks, 3 months and 7 months post treatment with combination of modalities including digital rectal exam, endoscopic rectal ultrasound, total body CT scan and proctoscopy which showed a progression of healing where there was eventually no lesion seen (6).

There has been evidence of combination of chemoradiation and surgery as treatment options for rectal SCC. Nigro et al suggested the protocol of combining 5-FU and mitomycin-C with external beam radiation if the lesion is less than 5 cm followed by appropriate surgical excision if needed (8). On the other hand, Schneider et al suggested that rectal SCC be treated by sphincter-saving excision followed by combined chemotherapy (5-FU and mitomycin-C) and high-dose external beam radiation therapy (11).

Follow up surveillance is important. Detecting local disease or distant recurrence should be the goal. Recurrence of symptoms including rectal bleeding should be evaluated with at least a
sigmoidoscopy if not a complete colonoscopy. After finishing treatment, there should be documentation of remission for local disease consisting of colonoscopy and biopsy within 3-6 months. Afterwards, follow-up colonoscopies can be done every 6 months for 2 years after treatment, then every year unless symptoms recur (5).

Overall prognosis of SCC of the rectum is poor due to the fact that it presents at a later stage and due to the tendency of local lymph node involvement. Overall five year survival rates are 32%. Features that predict a worse outcome include nodal involvement, small cell or undifferentiated histological characteristics, ulcerated or annular carcinomas, grade 3 or 4 and stage IV disease (12).

**Conclusion**

Squamous cell carcinoma of the rectum is a rare entity. There are multiple hypotheses regarding etiology. This case report describes the possibility of the squamous cell carcinoma of the rectum arising from a previous adenocarcinoma since pathology report showed the findings of both types of malignancies simultaneously. Primary treatment is lower anterior resection which can be followed by chemoradiation, but chemoradiation can be solely used in high risk surgical candidates. Prognosis is poor due to the fact the malignancy is usually diagnosed at a later stage and due to lymph node involvement.
Figures

Figure 1: Hard, large mass seen in rectum and smaller mass seen in distal sigmoid colon

Figure 2: Adenocarcinoma of Sigmoid Colon
Figure 3: Squamous Cell Carcinoma of the Rectum with involved margins
Figure 4: CT A/P with contrast showing rectal mass on axial image

Figure 5: CT A/P with contrast showing rectal mass on coronal view

Figures