Primary Submucosal Squamous Cell Carcinoma of the Rectum Diagnosed by Endoscopic Ultrasound: Case Report and Literature Review

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Abstract
Primary colorectal squamous cell carcinoma (SCC) is one of the very rare malignancies of the gastrointestinal tract. The diagnosis cannot be made before ruling out other common primary sites. Using the endoscopic ultrasound (EUS) technique to get a tissue biopsy for submucosal tumors has not been demonstrated as the best diagnostic approach in the literature. Surgery is the gold standard treatment with arising evidence of good efficacy following conventional chemoradiation therapy. A 49-year-old male presented with rectal discomfort. Sigmoidoscopy revealed multiple submucosal masses in the rectosigmoid colon. Mucosal biopsies showed nonspecific inflammation. Subsequently, an EUS with fine needle biopsy was done and established the diagnosis of rectal SCC. There were no other primary sites noticed in the extensive evaluation. The patient chose to be treated only with chemoradiation without surgery. At the time of writing this report he had no evidence of recurrence achieving 2.5 years of survival. EUS is an emerging excellent approach to diagnose submucosal colorectal SCC. This case will add supportive evidence of having a complete response following combining treatment with squamous cell directed chemotherapy and external beam radiotherapy without preceded surgery.
**Introduction**

Colorectal carcinoma is a common malignancy and more than 90% of cases are of adenocarcinoma type [1]. However, colorectal squamous cell carcinoma (SCC) is a rare entity. Up to the present, less than 100 cases have been reported in the literature [2–7]. The etiology of colorectal SCC is still unclear. Different proposals regarding its origin and its relation to other entities have been reported in the literature [2, 8–15]. We report a case of primary submucosal colorectal SCC which was diagnosed based on endoscopic ultrasound (EUS) fine needle biopsy and treated successfully with chemoradiation without preceded surgery upon the patient’s request. The patient in this case is now 2.5 years post therapy with no evidence of disease recurrence. In this interim, a focused review of the literature was provided with a summary of the treatment options of this rare malignancy.

**Case Report**

49-year-old male presented with a one-month history of rectal discomfort, small stool caliber and occasional rectal bleeding. He had no weight loss or new changes in his skin moles. The patient had neither prior cancer history nor family history of colon or skin cancers; however his mother had breast cancer. He is a nonsmoker but drinks 3–4 beers weekly. He had no prior exposure to radiation in a therapeutic dose. Physical exam was unremarkable with no suspicious skin moles but some subcutaneous lipomas in the forearm and rib cage and a scalp lesion which turned out to be benign on biopsy; no lymphadenopathy was appreciated. Rectal exam revealed a soft mobile mass in the rectum with no internal or external hemorrhoids. Colonoscopy showed three submucosal rectosigmoidal tumors (fig. 1), two of them in the distal part 2–10 cm proximal to the anal verge; the proximal tumor extended from 10–20 cm proximal to the anal verge. Biopsies taken during colonoscopy revealed acute on chronic nonspecific inflammation with fibrosis and superficial ulceration, but no malignant cells were found. A repeated colonoscopy using ultrasound (fig. 2) showed the tumors to be originating from or infiltrating the muscular layer with intact mucosa, multilobulated, heterogeneous with hypoechoic foci suggesting necrosis. The prostate did not seem to be involved. Fine needle biopsies were obtained under ultrasound guidance. The pathology report revealed moderately differentiated SCC with no glandular component identified. A computed tomography (CT) scan of the chest, abdomen and pelvis was negative for distal metastases or cutaneocolonic fistulas, but showed two lymph nodes in the pelvis along the poster superior left margin of the rectosigmoid colon measuring 8 and 9 mm. A positron emission tomography (PET) scan suggested the rectal tumor to be primary with the adjacent lymph nodes mentioned formally. The patient declined surgery, so he received only a combined treatment with 5-fluorouracil (5-FU) and mitomycin-C along with external beam radiation therapy. He achieved complete remission confirmed by colonoscopy and ultrasonic fine needle biopsies six months and one year post treatment. At the time of writing the patient is 2.5 years post treatment with no clinical or histological evidence of recurrence.

**Discussion**

The first case of primary colorectal SCC was reported by Schmidtmann in 1919 [16]. Its incidence rate ranges from 0.25 to 0.1 per 1,000 colorectal neoplasms [9, 17, 18]. The etiology of colorectal SCC is still unclear. Some authors proposed the role of stem cell differentiation [10]. Others pointed on possible squamous metaplasia [8] or squamous differentiation in areas of preexisting adenomas [9]. Schneider et al. suggested an etiology of proliferation of uncommitted mucosal basal cells into squamous cells which subsequently undergo a malignant change [2]. Lam and Ho proposed the pathogenesis to be related to the oncogenic effect of chronic renal failure and long-term use of immunosuppressive therapy in the way the carcinogenic viruses or the direct carcinogenic effect of the immunosuppressive therapy may account for the activation of uncommitted stem cells in the pathogenesis of SCC [19]. There has been some possible
association between colorectal SCC and previous radiation exposure [11, 12],
colocutaneous fistula [13], ulcerative colitis [14], Entamoeba histolytica colitis [9],
duplication of the colon [20], homosexual men [21], immunossupression [19],
schistosomiasis [15] and a controversial association with HPV [22, 23].

Colorectal SCC predominantly occurs in the sixth decade [3, 5]. Some authors leaned
towards male predominance [3, 24], others described women to be most commonly
affected by this tumor [5]. The clinical presentation for colorectal SCC ranges from some
rectal discomfort with mild constipation to rectal bleeding and/or acute surgical abdomen
in rare cases [25, 26].

Williams et al. [9] have established reasonable guidelines before labeling the diagnosis
as colorectal SCC, which include ruling out the following entities: other primary sites, a
squamous-lined fistula tract to the affected bowel and an extension of the tumor from the
anal squamous epithelium. Usually, the visual diagnosis of the tumor followed by tissue
diagnosis (incisional or excisional biopsy) is enough to establish the diagnosis of
colorectal SCC. However, extensive evaluation is crucial to prove the colonic origin as a
primary site and to rule out metastatic disease. This will include careful skin surveillance
and biopsy for any suspicious lesion, whole body CT scan and/or PET scan. Schneider et
al. used CT-guided biopsy to establish a tissue diagnosis in one of their reported cases of
colorectal SCC with intact colon mucosa [2]. A tissue diagnosis of the colorectal SCC with
intact colon mucosa using the EUS technique has not been reported in the literature as a
standard method.

Most authors have agreed that surgery is the gold standard treatment for colorectal
SCC if not contraindicated by diffuse metastatic disease or patient preference [2, 4, 27].
The treatment options in the literature varied between surgical excision alone [2],
chemotherapy alone [27], radiation therapy alone [9], external beam radiation with
chemotherapy alone [2, 27] versus surgical excision followed by external beam radiation
and combination chemotherapy [2, 27]. Nigro et al. suggested the protocol of combining
squamous cell directed chemotherapy (5-FU and mitomycin-C) with external beam
radiation therapy if the lesion is less than 5 cm, followed by appropriate surgical excision
if needed [28]. Schneider et al. suggested the treatment of choice for rectal SCC to be
sphincter-saving excision followed by combined chemotherapy (5-FU and mitomycin-C)
and high-dose external beam radiation therapy (4,500 cGy) [2]. They as well as Lafreniere
and Ketcham [25] suggested that combination radiotherapy and chemotherapy (5-FU
with mitomycin-C) might be useful.

Detecting local disease or distant recurrence is the follow-up goal. Recurrence of the
symptoms including rectal bleeding should be investigated with at least sigmoidoscopy if
not colonoscopy. A documented remission for local disease following treatment with
colonoscopy and biopsy should be done 3–6 months after finishing the treatment.
Follow-up colonoscopies every 6 months can be done for 2 years after the treatment, then
eyear every unless symptoms recur. Copur et al. were the first to use the level of SCC
antigen as a tumor marker to detect recurrent metastatic disease of colorectal SCC [29].

5-year survival is 34% in colorectal SCC, which is worse than the survival ratio for
colorectal adenocarcinoma [7], maybe due to the delay in diagnosis [1]. Comer et al.
reported a similar prognosis for rectal adenocarcinoma in the early stages
(node-negative), but worse with nodal involvement [17]. The features associated with
poorer prognosis in the Frizelle et al. retrospective study were right-sided lesions,
ulcerated or annular carcinomas, node-positive, grade 3 or 4, or stage IV disease [7].
Conclusion

Rectal SCC is an extremely rare tumor. Its etiology is not exactly known. The presentation of this disease is the same as that of adenocarcinoma. The diagnosis is challenging, especially for submucosal lesions. Combining the technologies of endoscopy and ultrasound, EUS with fine needle biopsy greatly improves the ability to diagnose and stage gastrointestinal cancers. Surgical resection is the treatment of choice. The Nigro protocol [28] using 5-FU with mitomycin-C along with external beam radiation has been used widely as an adjunctive therapy. Our patient showed complete response with chemoradiation-based therapy without surgery, with no evidence of recurrence in 2.5 years. This will add supportive evidence of the efficacy of this therapy.

Fig. 1. Colonoscopy view showing the submucosal rectosigmoidal tumors. The mucosa is intact. The distal tumor is 2 cm to the anal verge.
**Fig. 2.** EUS view showing tumors in the rectosigmoidal area. Note the infiltration into the muscular layer. Also note the multilobulated nature, heterogeneous with hypoechoic foci which suggest necrosis. The measurement unit is centimeters.
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