

CASE REPORT



Squamous cell carcinoma of the ascending colon: two cases

Abdelhai Abdelqader^a, Ramez Jabaji^a, Mohammed Albugeaey^b and Caren Palese^b

^aDepartments of Internal Medicine, MedStar Franklin Square Hospital Center, Baltimore, MD, USA; ^bDepartment of Gastroenterology and Hepatology, MedStar Georgetown University Hospital, Washington, DC, USA

ABSTRACT

Squamous cell carcinoma (SCC) of the colon without known primary source is a rare finding that needs aggressive management. We report two cases of SCC of the colon without any clear extra-colonic source despite extensive workup. In our experience, the clinical course and prognosis are largely dependent on the presence of metastatic disease at diagnosis. The main treatment is surgery, with chemotherapy having less defined role.

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Colon; primary; squamous cell carcinoma; treatment

1. Introduction

Colorectal cancer is the fourth most common malignancy, with an estimated incidence of 132,700 new cases and an estimated 49,700 deaths a year as of 2015 [1]. A minority of these are squamous cell carcinoma (SCC) of the colon, with less than 100 cases reported in the literature. The most frequent location has been reported in the rectosigmoid colon [2]. The pathogenesis of this histologic variant is unclear. In cases with little to no risk factors, a commonly reported theory suggests that multipotent cells or uncommitted basal cells differentiate into squamous cells from mucosal injury [2–5]. Applying the modified Dukes criteria for colorectal cancer staging, based largely on adenocarcinomas, the 5-year survival for stage B is 56%, stage C 15%, and stage D 5% [6]. Due to the rarity of primary SCC of the colon, clinical manifestations, treatment, and prognosis remain poorly defined.

A 27-year-old female was evaluated for epigastric pain, hematochezia and amenorrhea for 3 months with 20 pounds of unintentional weight loss. She had a history of human papilloma virus (HPV) and cervical dysplasia treated with loop electrosurgical excision procedure and subsequent normal papanicolaou (pap) smears. A transvaginal ultrasound and esophagogastroduodenoscopy (EGD) were normal. Colonoscopy showed a 15 cm mass in the ascending colon not amenable to endoscopic resection. Staging computed tomography (CT) showed 11 × 10 × 8 cm eccentric mass in the right colon with possible necrosis. Positron emission tomography (PET) CT revealed a hypermetabolic right colon and lymph nodes (LN).

Histology unveiled moderately differentiated, keratinizing SCC.

Two months later, ureteral stents were placed for obstructive uropathy. The patient underwent an exploratory laparotomy with an extended right colectomy with primary anastomosis. The mass encompassed the ascending to the middle of the transverse colon without perforation and total 0/36 LN positive. Histologically, there was benign squamous mucosa with patterns suggestive of esophageal tissue and staged IIa invasive SCC (Figure 1). The tumor stained positive for keratin-7 and p63, similar to esophageal mucosa. Chemotherapy was advised, however, the patient did not return for further management. Eight months later, repeat pap smear was normal. CT did not show any recurrent or metastatic disease. A year after surgery, repeat endoscopy was normal. Two-and-a-half years after surgery, the patient remains alive and well without any chemoradiation.

A 44-year-old man presented with abdominal pain and melena. CT showed a 4 cm mass in the right colon with multiple hepatic hypodensities consistent with metastatic disease. EGD was unremarkable, but colonoscopy identified mass in the hepatic flexure (Figure 2). Biopsies showed tubulovillous adenoma with focal intramucosal carcinoma. The extended right hemicolectomy revealed a 6.5 cm mass without signs of perforation. Histologic examination was consistent with an invasive, moderately differentiated, keratinizing SCC with overlying tubulovillous adenoma and 3/18 positive LN, pathologically staged as T3, N1b. Microsatellite instability was not detected, but mutated Kirsten ras oncogene homolog (KRAS)

CONTACT Abdelhai Abdelqader  abdelhai.abdelqader@medstar.net  Departments of Internal Medicine, MedStar Franklin Square Hospital Center, 9000 Franklin Square Drive, Baltimore, MD 21237, USA

All authors contributed equally to the creation of this manuscript. A. Abdelqader is the article guarantor.

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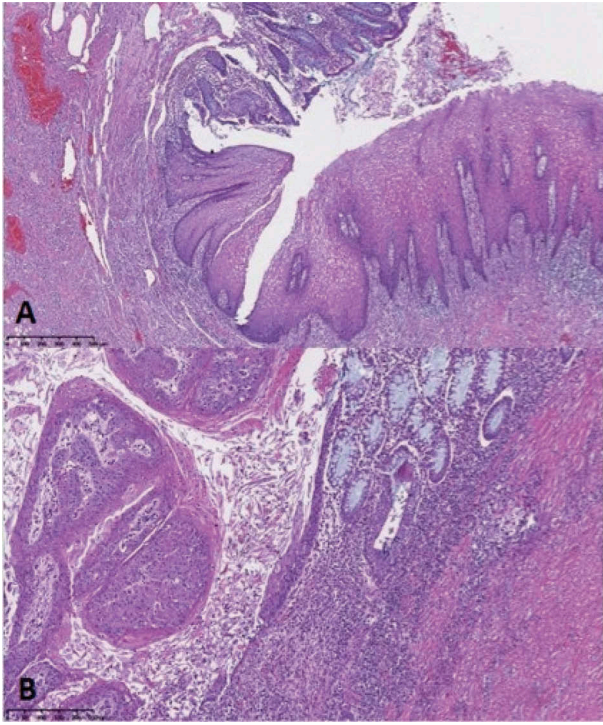


Figure 1. Ascending colon mass with hematoxylin and eosin (H&E) staining. (a) Low power view showing abrupt transition from colon mucosa to benign squamous mucosa, suggesting ectopic esophageal tissue in the right colon (5x). (b) Well-differentiated keratinizing SCC next to colonic glandular mucosa in the right colon (10x).

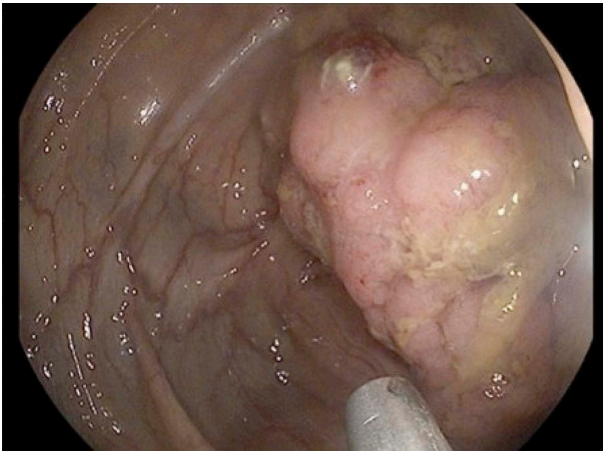


Figure 2. Colonoscopy showing a non-obstructing 6 cm hepatic flexure friable and ulcerating mass without any visible synchronous lesions.

gene was found, and patient tested positive for keratin-5/6 and p63. Two months after surgery, he was started on capecitabine. Repeat CT showed new 1 × 1 cm lung nodule, multiple new hepatic metastases, and a centrally enlarging necrotic mass in the hepatic flexure.

The patient had several complications requiring repeated hospitalizations. He developed a small bowel obstruction from mass compression treated with radiation and paclitaxel. Carboplatin was

later added. He was switched to palliative chemotherapy, receiving three cycles of 5-fluorouracil (5-FU), oxaliplatin, and leucovorin. He developed hypercalcemia, likely from paraneoplastic SCC, as parathyroid hormone-related protein was 23 pmol/L (normal <2 pmol/L), and there were multiple pulmonary emboli before and after inferior vena cava filter placement, and hepatic metastases progression despite radioembolization. Given the patient's worsening condition, the family chose hospice care only. Six months after diagnosis and 3.5 months after chemoradiation, the patient died.

2. Discussion

SCC of the colon is rare, with an incidence of 0.1–0.25 per 1,000 colorectal cancers [7] compared to incidence of colon adenocarcinoma of about 132,000 in 2015. Most SCC of the colon are in reported cases of adenosquamous cancer of the colon [8]. This can present with similar signs and symptoms as colorectal adenocarcinoma. Most pure SCC of the colon has been reported in the rectosigmoid colon, while our two cases were located in the ascending colon [2].

The pathogenesis of SCC has not been well established, but we will focus on hypotheses applicable to our cases. The pluripotent theory proposes that stem cells with multidirectional differentiation develop into SCC after mucosal injury [2–5]. Another theory highlights that uncommitted basal cells have potential for squamous differentiation after epithelial damage; however, our patients did not have any known chronic inflammatory diseases, nor does histology suggest squamous differentiation from adenocarcinoma [5,9]. HPV has been associated with esophageal cancer (CA), and suggested to be related to the pathogenesis of SCC of the colon. However, this remains an elusive association, not a cause [8,10]. Cytokeratin 7 has been used as a marker for low-grade squamous cervical lesions with high risk of progression [11]. Case 1 had benign squamous colonic tissue that resembled esophageal tissue. Furthermore, case 1 had cervical dysplasia that was excised, but in young females this is known to often revert back to normal. In both of our cases, the above hypotheses are plausible and we suspect that each may have played a multifactorial etiological role.

The optimal treatment combination and chemoradiation schedule in local and metastatic disease remains unknown. Although several cases suggest that, in addition to surgery, chemotherapy may have a role in most cases, the data is lacking due to the rarity of this disease. Copur et al. showed a favorable response from a combination of palliative chemotherapy with 5-FU, cisplatin, and etoposide in advanced

disease, which can be measured by the SCC antigen [12]. Juturi et al. reported 5-FU, cisplatin, and leucovorin as a combination therapy in metastatic SCC of the colon [7]. In the reports by Corpur et al. and Juturi et al., their patients each received six cycles of combination chemotherapy. Our young female had local disease and only received surgery, with no disease recurrence 3.5 years later. Case two was initially clinically diagnosed as stage 4 SCC and received capecitabine, then radiation with carboplatin and paclitaxel, and lastly three cycles of 5-FU, oxaliplatin, and leucovorins, each with disease progression. Another unique comparison is that both of our patients were much younger than the average reported mean age of 53–60 [2,13].

We conclude that our cases were primary SCC of the colon based on history, extensive objective findings, and lack of another primary source. The pathogenesis remains unclear, but is possibly related to HPV infection in case one and multidirectional differentiation in case two. These challenging cases highlight the need for a multidisciplinary approach for optimizing management. Early surgery remains the first step in reducing the high mortality rate. The role for chemoradiation regimen and duration remains unclear. The aggressive history of this disease suggests the need for more frequent disease recurrence surveillance than for conventional colorectal cancers.

Informed Consent

Informed consent was obtained from the patients and their families for educational use of the mentioned data, and no personal patient information has been disclosed.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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None of the authors have any financial or personal bias to declare.

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