INTRODUCTION

Signet ring cell cancer (SRCC) is characterized by cells with abundant intracellular mucin (so-called signet ring cells). SRCCs usually originate in the stomach, with the rest originating in other organs, including the breast, gallbladder, pancreas, urinary bladder, and large intestine. The reported incidence of SRCC of the colon and rectum ranges from 0.1-0.9%. The prognosis of SRCC of the colon has been reported to be worse than classic adenocarcinoma of the colon; however, there is no difference in the post-operative surveillance for SRCC. We report a case of SRCC of the colon with negative resection margins that recurred at the anastomosis site 26 months after curative resection. A 55-year-old male presented to the hospital with abdominal pain. The initial colonoscopy and abdominal computed tomography revealed SRCC of the proximal ascending colon. He underwent extensive curative surgical resection and adjuvant chemotherapy for 8 months. However, 26 months post-operatively, the cancer recurred at the anastomosis site without peritoneal dissemination. Physicians should be aware that SRCC may have different recurrence patterns compared with classic adenocarcinoma, and may need more vigorous surveillance, even after curative surgery. (Intest Res 2010;8:58-62)

CASE REPORT

A 55-year-old male presented to the hospital with abdominal pain of 7 days duration. His diet, medication, and past medical history were unremarkable. He appeared well, and the physical examination showed no abnormalities, except tenderness in the right lower quadrant with increased bowel sounds. The laboratory findings present a case of primary SRCC of the colon that recurred at the anastomosis site after extensive curative resection.
revealed a white cell count of 8,200/mm$^3$, a hemoglobin of 14.9 g/dL, and a hematocrit of 43.4%. The routine blood chemistries, serum CEA, and serum CA 19-9 were within normal limits.

The initial colonoscopy revealed complete luminal narrowing at the proximal ascending colon due to an ulceroinfiltrating lesion (Fig. 1). An endoscopic biopsy demonstrated adenocarcinoma with signet ring cells. An abdominal CT revealed contraction of the cecum and intestinal wall thickening of the ileocecal valve, terminal ileum, appendix, and ascending colon (Fig. 2). This finding, resembling inflammation, is unusual for classic colon cancer, but may be characteristic of SRCC of the colon. The patient underwent a right hemicolecotony and anastomosis of the jejunum and transverse colon. The ileum was also resected due to adhesions involving the ileum.

The resected ulceroinfiltrative mass was 7×4×1.2 cm in size. The proximal and distal free margins were 28 cm and 38 cm from the mass, respectively (Fig. 3A). Microscopically, the mass was characterized by malignant cells with abundant intracellular mucin, which was compatible with the diagnosis of signet ring cell cancer (Fig. 3B).
Fig. 4. PET scan image showing increased uptake at the anastomosis site at the 2-year follow-up.

Fig. 5. Colonoscopy finding at 26-month follow-up confirmed recurrence at the anastomosis site.

3B). The tumor penetrated the visceral peritoneum, and the regional lymph node examination revealed metastasis to 1 of 40 regional lymph nodes without peritoneal seeding. Therefore, the final post-operative stage was pT4N1M0 (stage IIIB). Post-operatively, the patient received 8 cycles of single-agent adjuvant chemotherapy with 4,300 mg of oral capecitabine for 8 months because he declined combination chemotherapy. A follow-up colonoscopy, abdomino-pelvic CT, and positron emission tomography (PET) scan 1 year post-operatively demonstrated no evidence of tumor recurrence.

However, a PET scan 26 months post-operatively revealed a suspicious, mild uptake (max SUV, 2.9) at the anastomosis site of the colon (Fig. 4). A colonoscopy was immediately performed to reveal an ulceroinfiltrative mass at the anastomosis site (Fig. 5). A biopsy showed adenocarcinoma with numerous signet ring cells. At the time of diagnosis of the recurrence, the patient had no symptoms, and the CEA and CA 19-9 levels were normal. The second surgical procedure revealed an encircling tumor mass at the previous anastomosis site measuring 5×1 cm. Post-operatively, the patient received 12 cycles of 5-FU (1,200 mg/m²) + leucovorin (400 mg/m²) + oxaliplatin (85 mg/m²). Currently, 8 months post-operatively, he is in good condition without any evidence of recurrence.

DISCUSSION

Due to the rarity of primary SRCC of the colon, SRCC has only been partially characterized, primarily based on a few case reports.9-12 The reported mean age of patients diagnosed with SRCC is younger than the mean age reported for classic adenocarcinoma (23-53 years vs. 68.9 years).13 A gender predominance is not apparent. Some studies have reported no difference in gender,6 however, other studies have reported a higher incidence in males, and others in females.7,13 In a study analyzing 154 SRCC patients, the most common location was the rectum, followed by the left colon, and right colon.6 The common gross types of SRCC of the colon, in order of decreasing frequency, are the schirrous (linitis plastic; 45.8%), ulcerated (34.5%), superficial (16.9%), and polypoid types (2%).6 Our case was not typical, in that it presented with an ulceroinfiltrating mass of the right colon. The common gross types of SRCC of the colon, in order of decreasing frequency, are the schirrous (linitis plastic; 45.8%), ulcerated (34.5%), superficial (16.9%), and polypoid types (2%).6
The prognosis of SRCC of the colon and rectum is very poor, with an overall 5-year survival rate of 9.1-50%, which is less than classic adenocarcinoma of the colon. The grave prognosis for SRCC is largely due to a delay in diagnosis in most cases. Bonello et al. cited the following three factors for the delayed diagnosis in SRCC of the colon: rarity of the tumor, minimal symptoms and heme-negative stools, and radiographic resemblance to an inflammatory process. These factors were in agreement with the findings pertaining to the case described herein. The patient did not report any symptoms, and the abdominal CT findings were atypical, in that there was a thickening and mass of the adjacent distal ileum, ileocecal valve, and appendix. SRCC of the colon and rectum are known to have a worse prognosis than classic colorectal cancer. Therefore, it may be necessary to survey recurrence of SRCC more vigorously after curative resection. Although common risk factors for local recurrence in patients with colorectal cancer after curative resection include the pathologic TNM stage and lymphovascular invasion, the recurrence pattern of SRCC of the colon and rectum after curative resection is not well known because the disease is usually inoperable at the time of diagnosis. In a Japanese review of 154 patients with SRCC of the colon and rectum, 18 patients (12.4%) had recurrence after curative resection. Hematogenous metastasis (33.3%) was the most frequent pattern of recurrence, followed by local recurrence (27.8%), peritoneal recurrence (27.8%), and lymph node metastasis (11.1%). Our case was unusual in that SRCC recurred at the anastomosis site without peritoneal or liver metastasis. It was also unusual because the negative resection margins (28 cm and 18 cm) were extensive. The possible explanations for the recurrence could be microscopic seeding of the anastomosis site during surgery, or cancer cell recurrence from cells that penetrated the serosa; however, these are very unlikely because there was no evidence of peritoneal dissemination and there was a long, unremarkable follow-up. Recurrence after curative resection, especially at the anastomosis site, is very rare for classic adenocarcinoma. In one study, anastomotic recurrences were reported in 5-10% of patients, 80% were detected within 2.5 years of primary resection, and the majority (>70%) were rectal rather than colon cancers due to difficulty in mobilization of the extensive resection margins. Although surgical resection of SRCC of the colon may be curative in most cases, the possibility of local recurrence should be stressed because SRCC may recur, as in our case, without symptoms or laboratory abnormalities, even after 26 months. This case suggests the need for more vigorous surveillance in patients with SRCC of the colon.

In summary, we have reported a case of primary SRCC of the colon that recurred at the anastomosis site 26 months after curative resection. Careful post-operative surveillance is necessary in patients with primary SRCC of the colon, even after curative resection.

REFERENCES