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Primary Signet-ring Cell Carcinoma of the Colon: A Case Report

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Abstract

Colorectal cancer (CRC) is one of the leading causes of death in Taiwan. Histopathologically, most CRC subtypes are classified as adenocarcinomas, and primary signet-ring cell carcinoma (PSRCC), which accounts for <1% of all cases of CRC is rare. Moreover, endoscopic detection of PSRCC is challenging. Colonic PSRCC, which is usually diagnosed at an advanced stage, is highly aggressive and shows poor prognosis. In this case report, we describe a 48-year-old man who presented with progressive left lower quadrant pain and was diagnosed with PSRCC at the rectosigmoid junction. (J Intern Med Taiwan 2022; 33: 308-311)

Key words: Signet-ring cell adenocarcinoma, Colorectal cancer, Signet-ring cell adenocarcinoma of the colon

Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide. Histopathologically, adenocarcinoma is the most common subtype of primary CRC; primary signet-ring cell carcinoma (PSRCC) is extremely rare and accounts for <1% of all cases of primary CRC. Reportedly, the incidence of PSRCC is 0.5%–2.6%. Although some studies have reported higher incidence rates in men, there is lack of consensus regarding male predominance of this cancer. Most patients are aged 48 to 70 years at the time of diagnosis. Colonic PSRCC is an aggressive malignancy with poor prognosis, which is attributable to its late presentation and delayed diagnosis with a predilection for peritoneal metastasis.

Case presentation

A 48-year-old previously healthy man visited our outpatient clinic with a 6-month history of progressively worsening left lower quadrant (LLQ) pain.

The patient had been in an apparently good state of health; however, he developed mild LLQ pain, tenesmus, decreased bowel movements, and passage of small-caliber stool, 6 months prior to presentation. He denied nausea, vomiting, anorexia, weight loss, or pain radiation. His recent travel or contact history was unremarkable. Notably, he did not seek medical help owing to fear of COVID-19 infection during the ongoing pandemic. However, he finally visited our gastroenterology clinic for

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evaluation of intractable pain. Physical examination revealed localized LLQ tenderness without rebound pain. Laboratory workup results, including tumor markers (carcinoembryonic antigen, cancer antigen-199, and alpha-fetoprotein levels) were within the reference range.

The change in bowel habits necessitated colonoscopy, which revealed whitish shiny nodules overlying the darkened surrounding mucosa 10 cm in length at the rectosigmoid (RS) junction (Figure 1). Moreover, insufflation of the diseased colonic lumen was difficult. Interestingly, selective biopsy of the affected bowel segment yielded poorly differentiated adenocarcinoma with focal signet-ring cell differentiation (Figure 2). For staging of the colonic neoplasm, the patient underwent contrast-enhanced computed tomography of the entire abdomen, which revealed symmetric wall thickening of the RS junction with peritoneal invasion (Figure 3) and hepatic metastasis. The patient was administered combination chemotherapy using 5-fluorouracil and targeted therapy using an anti-epidermal growth factor (anti-EGF) antibody and subsequently underwent low anterior resection to relieve obstructive symptoms. Intraoperatively, we detected massive peritoneal carcinomatosis, metastatic retroperitoneal lymph node-induced compression, and partial left ureteral blockage, which were implicated in the causation of the patient's intrac-

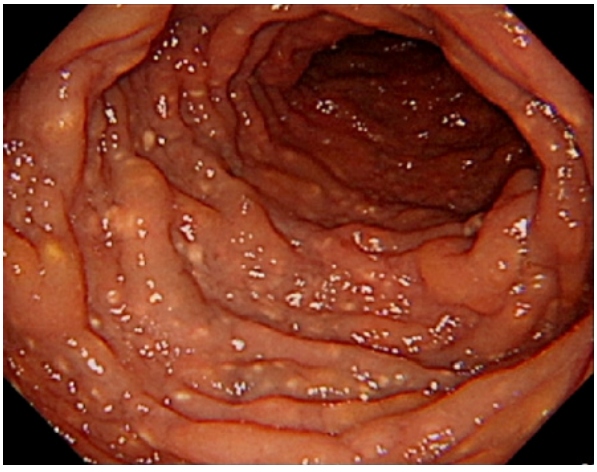

Figure 1. Colonoscopic image showing whitish shiny nodules overlying the darkened surrounding mucosa over a segment measuring 10 cm in length at the RS junction. Insufflation of the diseased lumen was difficult.
RS: rectosigmoid.

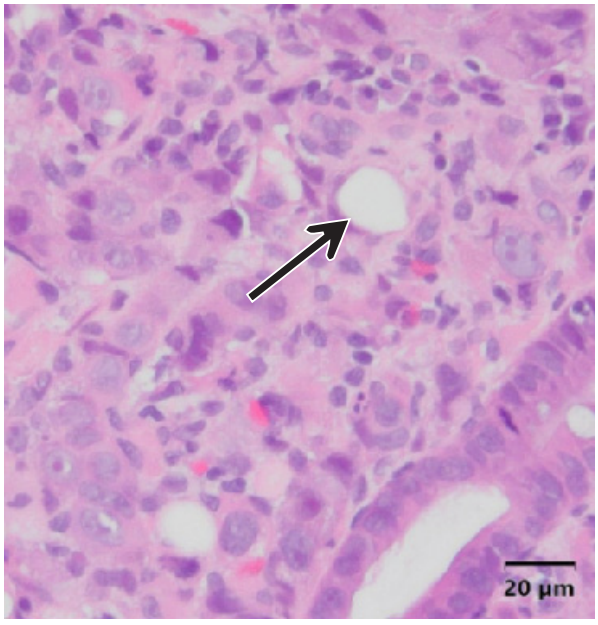

Figure 2. Histopathological findings (high-power field) showing malignant cells with large cytoplasmic mucin droplets pushing the nucleus to the periphery, with a focal signet-ring cell appearance (Arrow, ×400 magnification).

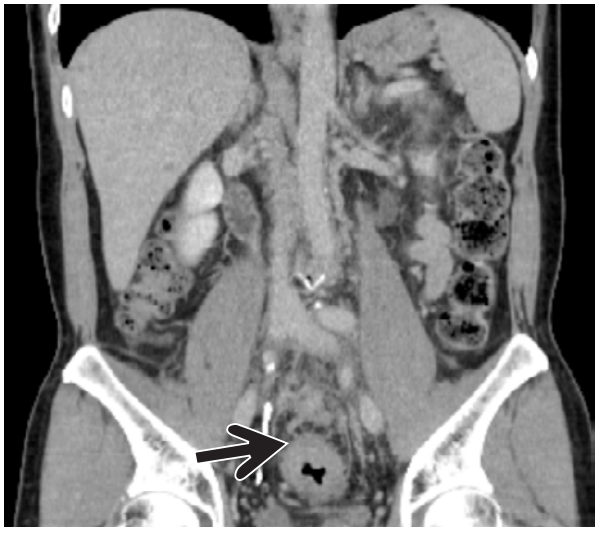

Figure 3. Contrast-enhanced CT scan showing segmental narrowing with symmetrical thickening of the bowel wall at the RS junction (arrow). Hepatic and peritoneal metastases are also observed.
CT: computed tomography, RS: rectosigmoid.

table LLQ pain. The patient continued to experience intermittent breakthrough pain, which necessitated frequent administration of analgesic medications, despite the aforementioned treatment. Post-operatively, the patient received second-line treatment using combination therapy with anti-EGF/BRAF/MEK target agents due to BRAF V600E mutation, and achieved partial response with gradual reduction in pain and hepatic metastasis.

Discussion

SRCC is a subtype of mucinous adenocarcinoma. Gastric SRCC is commonly reported in the literature; however, colorectal SRCC is extremely rare and accounts for 0.1%–2.6% of all cases of CRC.[1] Colonic PSRCC usually involves the ascending colon and is considered an aggressive malignancy, which is histopathologically characterized by the glandular lining of the gastrointestinal tract and cells with a signet-ring appearance on microscopic evaluation.[2] The signet-ring appearance of these cells is attributed to excess intracellular mucin deposition, which pushes the nuclei to the periphery.[3]

Primary colorectal SRCC differs from the adenocarcinoma variety in the following respects: (a) Patients often show a larger tumor burden and are diagnosed late during the advanced stage of the disease,[4] which may be attributable to the characteristics of colorectal SRCC, including younger age at onset, atypical and delayed clinical manifestations, and the high false-negative endoscopic biopsy rates.[5] (b) Most colonic PSRCCs are diagnosed during stages III or IV, with an overall median survival time of 12.7 months and a 5-year survival rate of 9.4%.[6] This lesion typically shows a fibrotic appearance and a predilection for peritoneal metastasis.[7] Few reports have described the endoscopic appearance of this tumor; however, magnifying endoscopy with narrow-band imaging (NBI) and crystal violet staining may be useful for early diagnosis. A previous study has reported a case of PSRCC observed using NBI magnifying endoscopy.[8] Endoscopically, the lesion typically presents with a sessile morphology that does not show the classic adenoma-carcinoma sequence and is therefore not easily detectable on colonoscopic screening.[9]

Similar to other colonic mucosal lesions, the differential diagnosis of PSRCC includes infectious colitis or inflammatory bowel disease. Despite its presentation at an advanced stage, surgery remains the definitive treatment for this malignancy. However, colonic PSRCC shows high recurrence rates and is invariably detected during the advanced stage; therefore, adjuvant chemotherapy may be required to reduce the relapse rate and improve survival.[10]

Conclusion

Colonic PSRCC is rare. Therefore, it is important to obtain all available clinical data for this potentially life-threatening disease to facilitate early diagnosis and prompt treatment. Further molecular characterization of this aggressive CRC subtype will improve diagnostic and therapeutic capabilities to ensure optimal care for patients.

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大腸戒環狀細胞腺癌：個案報告

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摘　要

大腸癌以腺癌為主要的病理型態，大腸戒環狀細胞線癌十分罕見，只佔大腸癌的不到百分之一；有界環狀細胞出現時，可視為預後不好的象徵，因為惡性度非常高，加上診斷時往往已經擴散轉移。本篇文章介紹一位48歲大腸戒環狀細胞線癌患者，其罕見的內視鏡發現，以及典型戒環細胞的病理學型態。