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Primary Signet-ring Cell Carcinoma of the Cecum

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Abstract

Primary signet-ring cell carcinoma of colon is rare. We report a primary cecal signet-ring cell carcinoma of 50-year-old man. He was admitted to emergency department with a complaint of abdominal pain. Computed tomography (CT) images demonstrated irregular wall thickening involving cecum and proximal ascending colon. After right hemicolectomy, the large ulcerating mass revealed diffuse neoplastic proliferation of signet-ring cells in the whole layers of the cecum.

Key Words : Cecum, Colon, Signet-ring cell carcinoma

Introduction

Primary signet-ring cell carcinoma arises most frequently in the glandular cells of the stomach, but it may develop occasionally in the large bowel or elsewhere. We report a case of primary cecal signet-ring cell carcinoma.

Case Report

A 50-year-old man was admitted to the emergency department with the symptoms of abdominal distension and tenderness. The patient had alcoholic liver cirrhosis and history of esophageal varix bleeding and type 2 diabetes. In the abdominal simple X-ray, gas-filled small and large bowel loops were revealed (Fig. 1A). Abdominal computed tomography (CT) imaging demonstrated irregular wall thickening involving cecum and proximal ascending colon and a few slightly enlarged lymph nodes in right colic and ileocolic chains. Ascending colon cancer was suggested and CT stage was T4aN2Mx (Fig. 1B). Laboratory finding showed elevated levels of CEA (411.37 ng/mL) and CA19-9 (75.41 U/mL). Next

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day the patient underwent emergency right hemicolectomy due to perforation.

The gross finding of the ascending colon including cecum showed a large ulcerofungating mass, measuring 9.5×9.0×2.5 cm in dimensions (Fig. 2A). The cut surface of the tumor showed ill-defined, pale tan, firm and friable tissue, extending to the whole layers and perforating within tumor mass (Fig. 2B). The remaining mucosa of the colon showed edematous appearance without polypoid mass. Microscopically, there was diffuse proliferation of individual tumor cells with loss of normal mucosal glandular structure (Fig. 3A). Well-identified signet-ring cells exist as single cells or forming loose clusters in a background of mucoid material (Fig. 3B). There was no evidence of tumor metastasis in 27 regional lymph nodes. In immunohistochemical studies, CDX-2 was diffuse positive reaction in the signet-ring tumor cells as well as normal mucosal epithelial cells (Fig. 4A). Although most conventional adenocarcinoma of the colon shows negative for CK7 and positive reaction for CK20, this case showed diffuse strong positive for CK7 in contrast focal weakly positive for CK20 (Fig. 4B and 4C). Numerous lymphovascular invasions were distinct on D2-40 immunohistochemical stain (Fig. 4D).

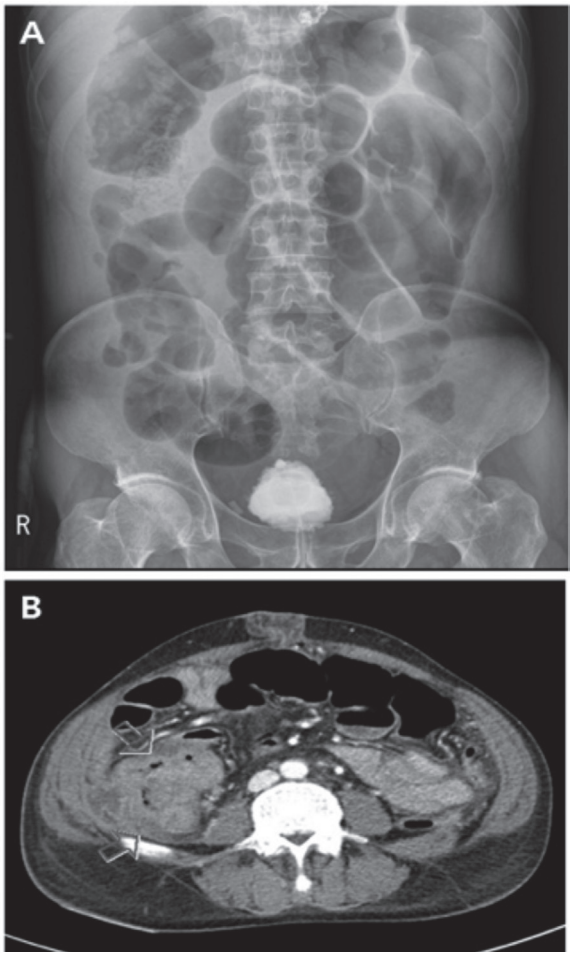

Fig. 1. A: Simple abdominal findings of gas-filled bowel loops. B: Ascending colon cancer is suggested in CT.

Discussion

Signet-ring cell carcinoma is a subtype of mucinous adenocarcinoma and composed of cells with a cytoplasmic droplet of mucus that compresses the nucleus to one side along the cell membrane (signet-ring cell). The infiltrating cells may be arranged individually or aggregated in loose clusters, and they spread diffusely throughout the bowel wall (linitis plastica type) [1]. More than 96% of signet-ring cell carcinomas arise in the stomach, and the rest occur in other organs, including the colon, rectum, gallbladder, pancreas, urinary bladder, and breast [2]. Primary signet-ring cell carcinoma of the colon and rectum, as first described by Laufman and Saphir in 1951, is rare [3]. The incidence of signet-ring cell carcinoma in the colorectum is 0.1%-2.4% [3-7]. Mutations of K-ras and p53 gene have been reported in signet-ring cell carcinomas of the colon, but the frequency of K-ras gene mutation in signet-ring carcinomas is significantly lower than that of well and moderately differentiated carcinomas [8]. These results suggest

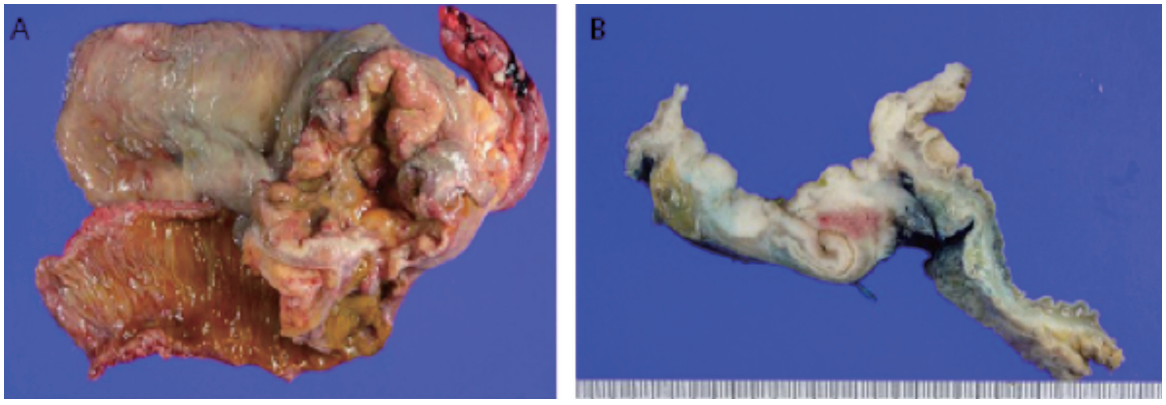

Fig. 2. A: A large ulcerofungating mass in cecum is seen, the tumor is 9.5 cm in maximum diameter. B: Cut section of tumor shows pale tan solid firm mass in the whole layers.

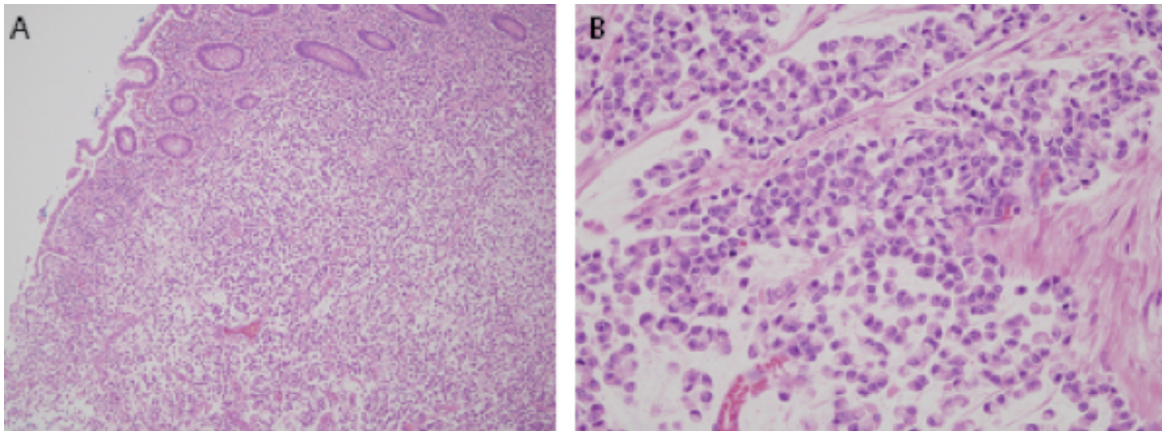

Fig. 3. A: Diffuse proliferation of individual tumor cells which efface normal mucosal structure (H&E, ×100). B: Well-identified signet-ring cells exist individually or aggregates in a background of mucus (H&E, ×400).

that the genetic background of signet-ring cell carcinomas might differ from that of well or moderately differentiated carcinomas of the colon and rectum. It is suggested that DNA-replication errors are at least partly involved in the carcinogenesis of signet-ring cell colorectal carcinoma [8]. Approximately 15% to 20% of colorectal adenocarcinomas arise from deficiencies in mismatch repair complex function, resulting in microsatellite instability (MSI) [9,10]. In comparison with typical glandular colorectal adenocarcinomas, signet-ring cell carcinoma is more often MSI-high. In addition, colorectal adenocarcinomas are typically positive for CK-20, CDX-2, and villin and negative CK-7 in immunohistochemistry. But colorectal signet-ring cell carcinoma may be different in the immunohistochemical stains. In one study, colonic signet-ring cell carcinoma showed CDX-2 (+), 89%, CK7 (+), 44% and CK20 (+), 78% [11]. This case showed diffuse positivity for CK7, CDX-2 and focal

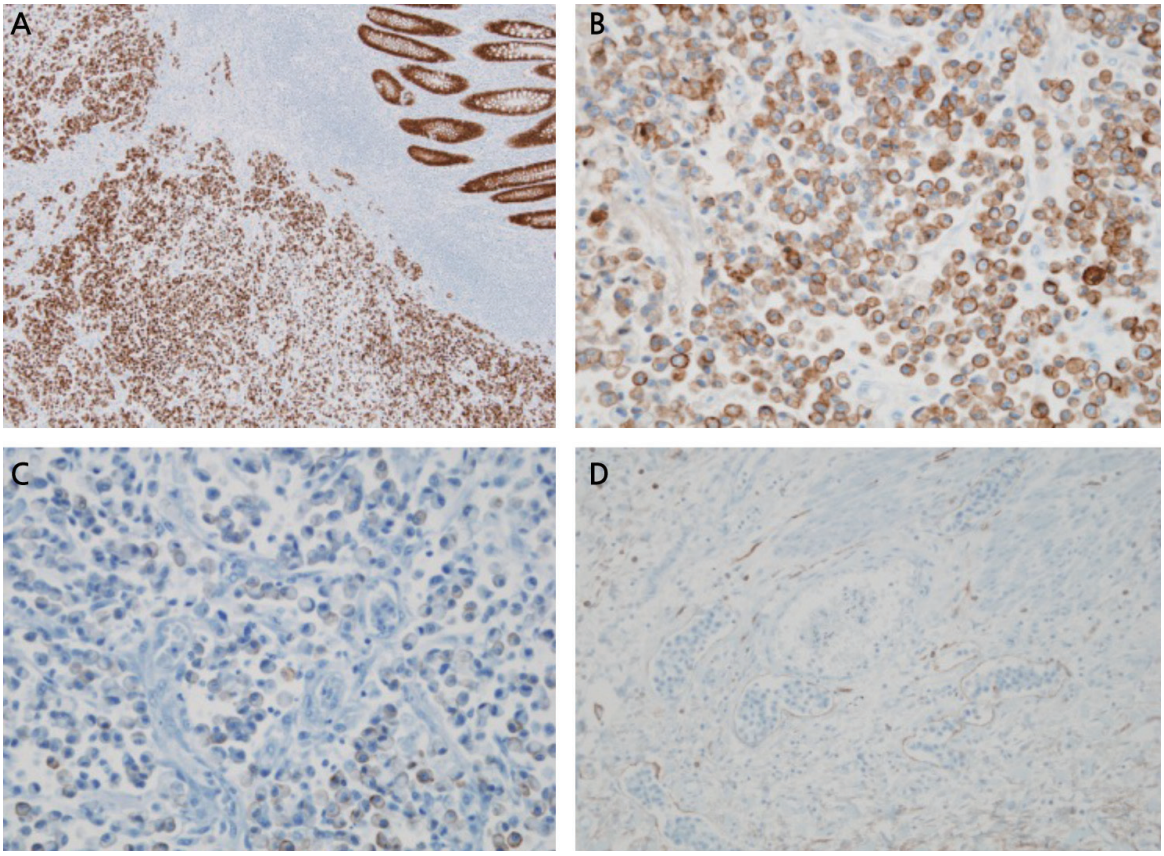

Fig. 4. Diffuse positivity for CDX-2 (A, ×100) and CK-7 (B, ×400) in tumor cells are seen. Focal weakly positive reaction for CK-20 is detected (C, ×400). Numerous lymphovascular invasion of the tumor cells are identified by D2-40 (D, ×200).

weakly positivity for CK-20. Signet-ring cell adenocarcinoma can aberrantly express CDX-2 and CK-20 due to MSI. CK-20 can be negative in up to 32% of MSI-high colon cancers, while CDX-2 has been reported to be negative in 22% of MSI-high tumors [12]. CK-7 can be expressed in up to about 13% of colorectal adenocarcinomas, and this includes both MSI-high and microsatellite stable tumors [12]. In addition, a higher percentage of signet-ring cell carcinomas are positive for MUC2 (100%) and MUC5AC (89%) and a lesser percentage are positive for E-cadherin (56%) [11]. Although our patient did not have inflammatory bowel disease (IBD), an association of IBD with signet-ring cell carcinoma up to 14% has been reported [13]. Psathakis *et al.* [14] reported two of 14 patients with signet-ring cell carcinoma, who had a long history of ulcerative colitis. Anthony *et al.* [6] reported two cases of Crohn's disease that developed signet-ring cell carcinoma. Signet-ring cell carcinomas of the colon and rectum are usually diagnosed at an advanced stage, because symptoms usually develop late [15]. The clinical features of signet-ring cell carcinoma and mucinous adenocarcinoma of the colorectum, including advanced stage at diagnosis, large tumor size, proximal location, young age,

propensity for lymphovascular invasion, and peritoneal seeding are known by other studies [2,4,16-19].

Signet-ring cell carcinoma is known to have a poor prognosis. Messerini *et al*. [16] reported the overall 5-year survival rate of signet-ring cell carcinoma of the colorectum, it was 9.1% and survival was influenced significantly by tumor stage. And in one study, the overall 1, 2, and 5 year survival rates of patients with signet-ring cell carcinoma were 77.8%, 26.7%, and 11.9%, respectively [7]. In that study, early diagnosed patient with signet-ring cell carcinoma at stage I+II showed better prognosis, 1, 2, and 5 year survival rates were 100%, 100%, and 50%, respectively, but the number of signet-ring cell carcinoma cases was too small to compare [7]. The relationship between signet-ring cell tumor histology and poor prognosis is still unclear because the number of cases was small and many patients were at an advanced stage and had poor differentiation [7]. We have followed up the patient for 4 months, CEA level decreased and the patient has had no specific complaint yet.

Conclusion

Primary signet-ring cell carcinoma of the colon is rare but has poor prognosis as 5-year survival rate is approximately 10%.

Early diagnosis of primary colorectal signet-ring cell carcinomas may be difficult because of late symptoms and a little different characteristic in contrast to conventional adenocarcinomas. Even though the variable difficulties in the early diagnosis of primary signet-ring cell carcinoma of the colon, we think if we diagnose it in early stage, it is more helpful to the patients.

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