

Collision adenocarcinoma–carcinoid tumor of the rectum arising in ulcerative colitis



Nobuyoshi Yamazaki^a, Yuji Nishizawa^a, Motohiro Kojima^b, Nobuhiro Sugano^a, Akihiro Kobayashi^a, Masaaki Ito^{a,*}, Norio Saito^a

^a Department of Colorectal Surgery, National Cancer Center Hospital East, Kashiwa, Japan

^b Pathology Division, National Cancer Center Hospital East, Kashiwa, Japan

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ABSTRACT

A case of a collision carcinoma–carcinoid tumor of the rectum that arose in ulcerative colitis (UC). The patient was a 78-year-old man with a rectal tumor, who was diagnosed as having UC at 70 years of age. The tumor was diagnosed by endoscopy as a deep submucosal invasive rectal carcinoma. The patient underwent trans-anal local excision. Pathological examination of Hematoxylin–Eosin stained slides showed two different histological types: a conventional well differentiated tubular adenocarcinoma with submucosal invasion, and another that was composed of small cells with uniform nuclei and eosinophilic granular cytoplasm arranged in a trabecular pattern. Immunohistochemically, these cells were positive for chromogranin A and CD56. These cells exhibited a Ki-67 index that was less than 2% and mitosis in less than 1/10 HPF. These areas showed clear margins. Therefore, this tumor was considered to be a collision carcinoma–carcinoid tumor. Ultimately, the patient died 2 years after the local excision due to recurrence. Collision carcinoma–carcinoid tumors arising in ulcerative colitis are extremely rare. Collectively, it is considered that the behavior of the collision tumor is relatively aggressive. More careful surveillance of colorectal collision or composite carcinoma–carcinoid tumors is necessary, even when the carcinoma is early stage or the carcinoid is small.

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1. Introduction

It is well known that patients with long-standing ulcerative colitis (UC) are at increased risk of developing colorectal neoplasms, among which adenocarcinoma is the most frequent, followed by malignant lymphoma [1–3]. In addition, rectal carcinoid, which is classified as an neuroendocrine tumor (NET) G1, according to the World Health Organization [4], may also be associated with UC [4,5]. However, carcinoid tumors arising in UC are comparatively rare [6].

Tumors comprised of glandular (either an adenoma or adenocarcinoma) and carcinoid components are uncommon. Morphologically, these lesions have been differentiated into four subtypes: collision tumors; composite tumors; mixed tumors; amphicrine tumors [7]. Both collision and composite tumors occur more frequently in the stomach. On the other hand, in colorectal cancer, these tumors have been mentioned in several reports; in particular, collision tumors have only been noted in three reports [8–10].

To our knowledge, the present report describes the first case of a collision carcinoma–carcinoid tumor arising in UC. Herein, we report this case and review the relevant literature.

2. Case report

A 78-year-old Japanese male patient presented with no complaints. The patient had been diagnosed with UC at 70 years of age and the entire colon was involved. The patient had been treated with Mesalamine 1500 mg/day and Prednisolone 10 mg/day. In addition, due to a history of carotid artery sensing and atrial fibrillation, the patient had undergone anticoagulant therapy. Surveillance colonoscopy was performed at regular intervals, and ultimately showed a rectal tumor 1.5 cm in size that was located 7 cm from the anal verge. The tumor appeared extremely reddish, hard, and depressed. Microscopic examination with 0.05% crystal violet staining revealed a severe irregular-type pit pattern type V_i. We diagnosed the tumor as having invaded into the deeper submucosal layer. Histologically, the biopsy specimen revealed a well-differentiated tubular adenocarcinoma. Barium enema showed loss of haustrations. The primary tumor, swollen lymph nodes, and distant metastasis were not detected with computed tomography

* Correspondence to: Department of Colorectal Surgery, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa, 277-8577, Japan.

E-mail address: maito@east.ncc.go.jp (M. Ito).

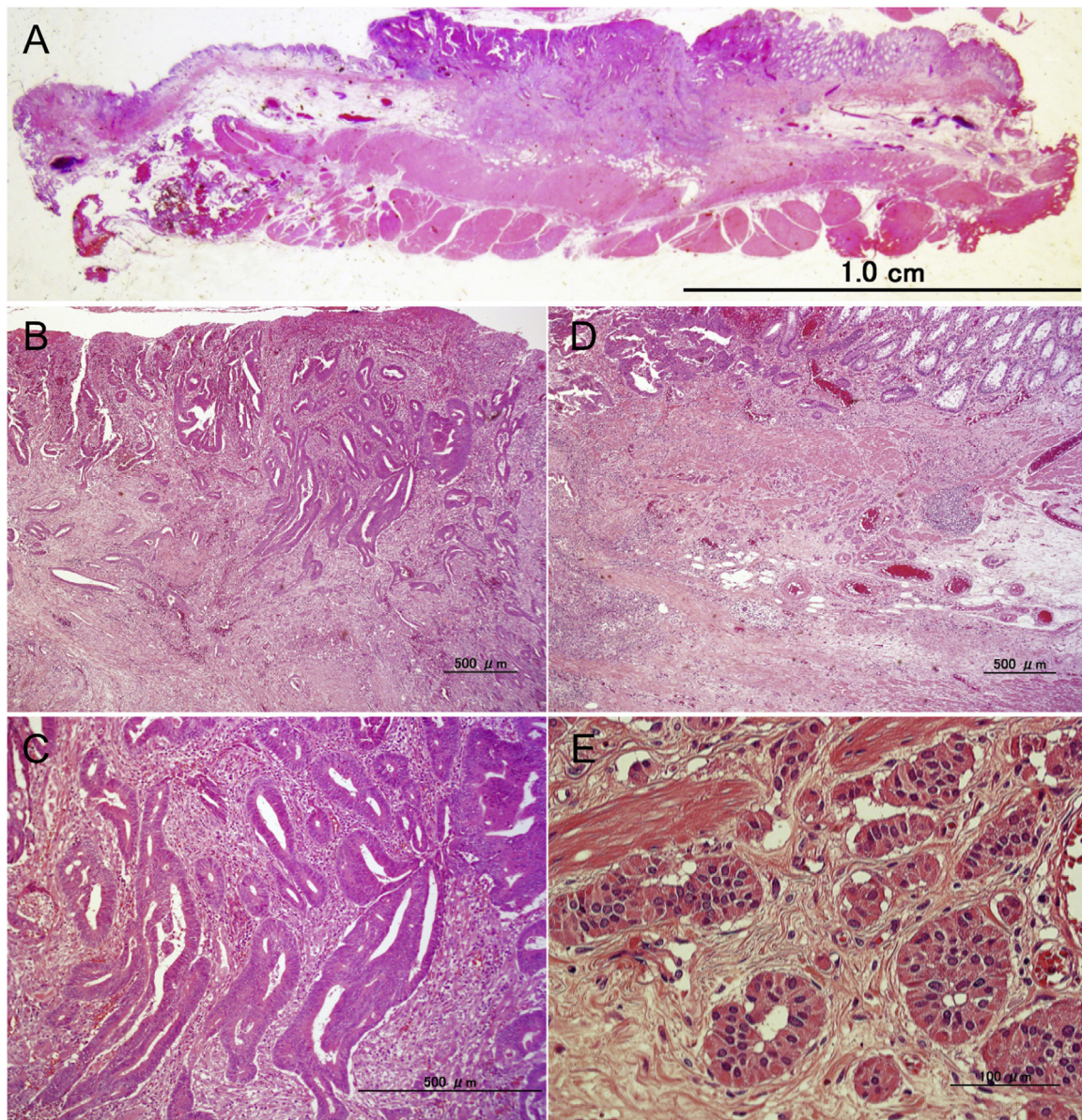


Fig. 1. Histological findings of the Hematoxylin–Eosin stained slides. The slide showed two different histological types (A: $\times 1$). One component was a conventional well-differentiated tubular adenocarcinoma (B: $\times 40$, C: $\times 200$). Another component showed small cells with uniform nuclei and granular eosinophilic cytoplasm, arranged in a trabecular pattern (D: $\times 40$, E: $\times 400$).

(CT). Routine hematological and biochemical investigations were within normal limits except for a decline in hemoglobin (10.8 g/dl) and elevated carcinoembryonic antigen (CEA; 6.9 ng/mL). Pathological investigation of the biopsy led to the diagnosis of well-differentiated adenocarcinoma. The tumor was staged as T1N0M0 (Stage I) according to the UICC TMN classification, 7th edition.

The patient underwent trans-anal local excision. Pathological examination of the Hematoxylin–Eosin stained slides showed two different histological types (Fig. 1A). One was a conventional well-differentiated tubular adenocarcinoma (Fig. 1B and C), which had a boundary. At the border of the adenocarcinomatous area, there was another component that was 2 mm in size (Fig. 1D). The component showed small cells with uniform nuclei and eosinophilic granular cytoplasm of the cube, arranged in a trabecular pattern (Fig. 1E). The nuclei showed very few signs of mitoses, < 2 per 10 high power fields (HPF). Immunohistochemically, these cells were positive for chromogranin A (Fig. 2A) and CD56 (Fig. 2B), but were negative for synaptophysin (Fig. 2C). In addition, these cells showed a Ki-67 index that was less than 2% (Fig. 2D), and mitosis

was less than 1 per 10 HPF. Thus, this component was diagnosed as carcinoid tumor that was NET G1 according to the WHO 2010 classification [4]. No intermingling was noted at the interface of these two components (Fig. 1D). This arrangement was diagnosed as a collision tumor of the colon, composed of an adenocarcinoma and a carcinoid tumor. Pathologically, the tumor showed sub-mucosal invasion to a depth of 2500 μm . Slight vascular invasion was present, and lymphatic invasion was not assessed using Elastica van Gieson stain or D2-40 stain. The horizontal and vertical surgical margins were negative for tumor.

After the local excision, no additional treatments were performed due to the wish of the patient and families. The patient underwent a CT scan, and tumor markers such as CEA and carbohydrate antigen 19-9 (CA19-9) were checked every 4 months. Total colonoscopy was performed in 12 months after local excision, and showed no change except for the scar of local excision. During the observation period, there was no increase in any tumor marker level, such as CEA was less than 5.0 ng/mL and carbohydrate antigen CA19-9 was less than 37.0 U/mL. Sixteen months after the

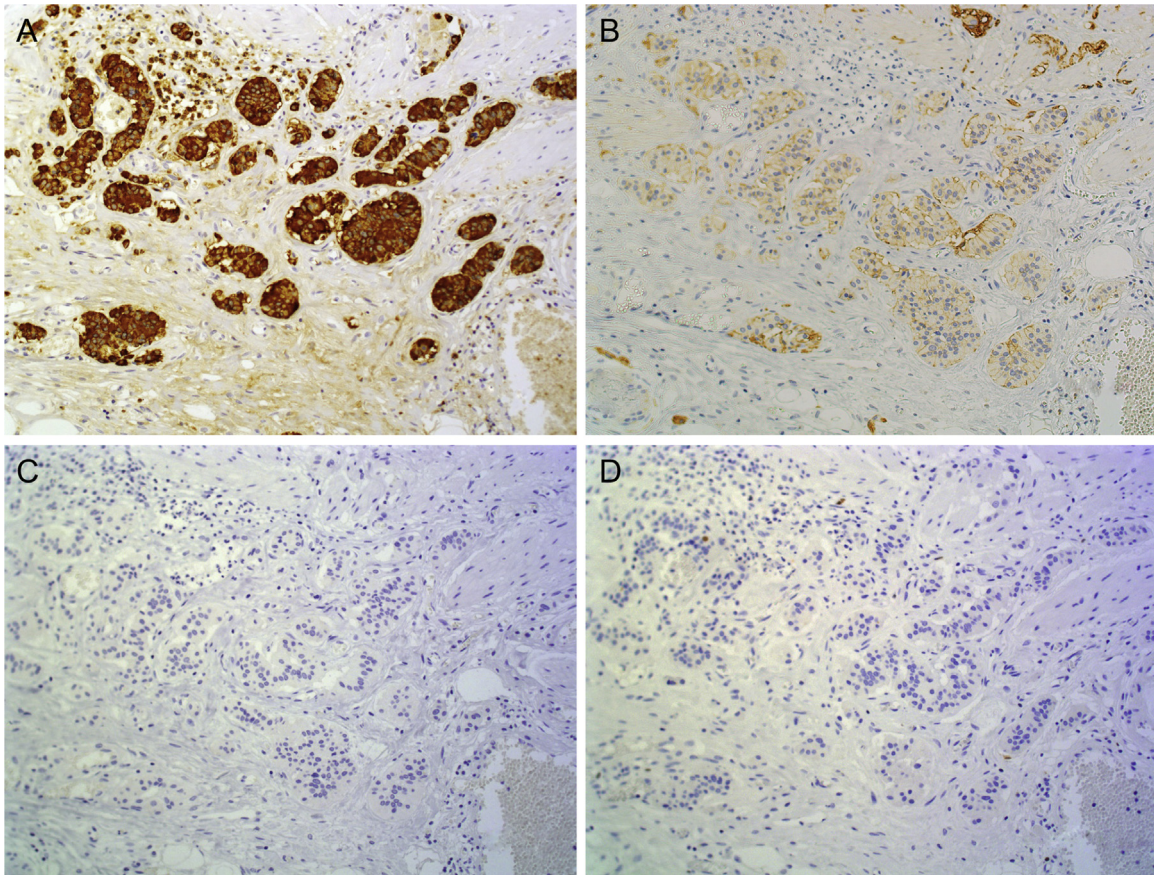


Fig. 2. Immunohistochemical findings in the part of the NET G1 Tumor cells of the part other than the adenocarcinoma were positive for chromogranin A (A) and CD56 (B), and negative for synaptophysin (C). These cells showed a Ki-67 index less than 2% (D).

local excision, pelvic CT and magnetic resonance imaging (MRI) showed a recurrence nodule, 3 cm in diameter, at the dorsal side of the rectum. 18F-Fluorodeoxy-glucose positron emission tomography showed enhancement, with a maximum standardized uptake value of 8.2 in the pelvic nodule. The patient underwent laparoscopic Hartmann's procedure. The pathological examination showed a moderately and poorly differentiated tubular adenocarcinoma. Most of the tumor was located within the muscular layer proper. Immunohistochemically, these cells showed no evidence of any component of neuroendocrine differentiation. Regional lymph node metastasis was not evident. Thus, we diagnosed this tumor as a local recurrence. Moreover, 2 months after Hartmann's operation, CT scan showed multiple nodules in the liver and bilateral lung field. We diagnosed these nodules as multiple liver and lung metastases. Ultimately, the patient died 2 years after the first surgery.

3. Discussion

In the present case, adenocarcinoma and a typical carcinoid tumor were found concurrently in a rectal tumor. Usually, it is not easy to morphologically distinguish a collision tumor from a composite tumor. In composite tumors, two types of tissue exist within the same tumor, and are intermingled with each other in a similar proportion [11]. In collision tumors, the two elements are adjacent to one another without intermixture of individual cell types ("side by side" or "one upon another" pattern) [9,12–14]. In the present case, the tissue components apparently grew from side by side with a readily identifiable line of interface. Thus, this was compatible with a collision tumor.

The association between carcinoid and inflammatory bowel disease (IBD), both in UC and Crohn's disease, has been reported as a consequence of hyperplastic changes in neuroendocrine cells [6]. Rectal NETs are usually located as solitary nodules in the submucosal layer. In UC patients, most tumors arise from inflamed areas [5,15]. Almost all cases of rectal NETs in IBD are found incidentally after surgery for IBD [6]. In the present case, the carcinoid component was also found incidentally. Cases of colorectal carcinoid and colorectal adenocarcinoma arising in UC have been reported as another lesion that present synchronously [6,16–18], and as a composite tumor [11,19,20], but not as a collision tumor.

In a previous report, the biologic behavior of a composite carcinoma–carcinoid tumor of the rectum arising in UC was markedly more aggressive [20]. Although the tumors had not arisen in the UC, the colorectal composite carcinoma–carcinoid tumors were reported to have a more aggressive course than ordinary adenocarcinoma [21,22]. Even the rectal collision adenoma–carcinoid tumor developed recurrence of the carcinoid component [23]. In the present case, the adenocarcinoma was pathologically classified as a high-risk lesion for local recurrence in the submucosal invasive colorectal cancer because of submucosal invasion to a depth of 2500 μ m and vascular invasion [24]. While inflammatory bowel disease was excluded, the 5 year DFS and OS for high-risk lesions of submucosal invasive rectal cancer that underwent endoscopic resection alone were reported as 77.7% and 96.2%, respectively [25]. In the present case, only local resection was performed and lymph node dissection was not performed during the initial treatment. Thus, the results of endoscopic and local resection would be considered as equivalent. In addition, since the size of the carcinoid component was 2 mm, it was evaluated as having a lower risk of metastasis in the present case [4]. Thus, it was

considered that the behavior of the collision tumor was relatively aggressive, as in the previous reports [20–22]. Thus, more careful surveillance or the consideration of additional treatment, i.e., radiation therapy or surgical resection, is necessary for colorectal collision or composite carcinoma–carcinoid tumors, even if the carcinoma is early stage or is a small lesion.

In conclusion, we report a collision carcinoma–carcinoid tumor arising in a patient with longstanding UC, along with a review of the relevant literature.

Conflict of interest

The authors declare that they have no conflict of interest.

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