## Abstract

Appendiceal mucinous neoplasms can involve peritoneal pseudomyxoma or invasion of adjacent organs. This report describes a rare case in which a giant appendiceal mucinous carcinoma expansively developed in the retroperitoneum without perforating the abdominal cavity.

### Case presentation

The patient was a 55-year-old woman with no relevant history who was admitted to our hospital after imaging examinations revealed a retroperitoneal tumor. The clinical diagnosis was a retroperitoneal tumor involving the hedge mucin. The patient underwent right hemicolecotomy and partial resection of the duodenum and right abdominal wall to ensure complete tumor resection. Histopathological findings suggested that the tumor was a mucinous carcinoma arising from the appendix. The postoperative course was uneventful. Although adjuvant chemotherapy was performed for 6 months, peritoneal recurrence developed 7 years and 4 months postoperatively. Nine years have passed after surgery and the patient is alive under receiving chemotherapy.

### Conclusion

Detailed pathological examinations revealed that the tumor originated from the appendix. The characteristics of mucinous carcinoma contributed to the extensive growth of the tumor.
The title of the article

Giant mucinous carcinoma originating from the appendix: A case report

A short running headline

Appendiceal mucinous carcinoma

Name of each author

Makoto Takeda PhD. *1

Yoshinori Onuki PhD. *2

Kosuke Oishi M.D. *3

Osamu Kubota PhD. *4

Takashi Uchiyama PhD. *4

Yoshifumi Arai PhD. *5

Hiroya Takeuchi PhD. *1

Name of department and institution

*1: Department of Surgery, Hamamatsu University School of Medicine

*2: Department of Surgery, Municipal Kosai Hospital, Japan.

*3: Department of surgery, Fujieda Municipal General Hospital, Japan.
*4: Department of Surgery, Kikugawa General Hospital, Japan.

*5: Department of Pathology, Toyohashi Municipal Hospital, Japan.

MT contributed to the study concept and design, data collection, and analysis and interpretation of data. YO, KO, OK, TU, and YA were involved in the decision to publish or preparation of the manuscript. YA contributed to pathological examinations and interpretations. HT contributed to the study supervision. All authors read and approved the final manuscripts.

- Name, address and email of corresponding author

Name: Makoto Takeda M.D., PhD.

Address: Department of Surgery, Hamamatsu University School of Medicine

1-20-1 Handayama, Higashi-ku, Hamamatsu 431-3192, JAPAN

TEL: 81-53-435-2279, FAX: 81-53-435-22731632,

E-mail: mtakeda@hama-med.ac.jp

- Disclaimers

All the authors state that they have no potential conflict of interest to disclose.
Abstract

Introduction

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Case presentation

The patient was a 55-year-old woman with no relevant history who was admitted to our hospital after imaging examinations revealed a retroperitoneal tumor. The clinical diagnosis was a retroperitoneal tumor involving the hedge mucin. The patient underwent right hemicolectomy and partial resection of the duodenum and right abdominal wall to ensure complete tumor resection. Histopathological findings suggested that the tumor was a mucinous carcinoma arising from the appendix. The postoperative course was uneventful. Although adjuvant chemotherapy was performed for 6 months, peritoneal recurrence developed 7 years and 4 months postoperatively. Nine years have passed since the surgery and the patient is alive and receiving chemotherapy.

Conclusion

Detailed pathological examinations revealed that the tumor originated from the appendix. The
characteristics of mucinous carcinoma contributed to the extensive growth of the tumor.

Keywords: appendix, mucinous carcinoma, giant tumor
Background

Appendiceal mucinous neoplasms (AMNs) are usually relatively indolent and rarely develop metastases outside the peritoneal cavity. As AMNs do not have specific clinical manifestations, the diagnosis of AMNs may be delayed. For patients with AMNs, the most common clinical presentation is right lower abdominal quadrant pain secondary to distention of the appendix by mucin in the early stage of the disease (1). Carr et al. reported that 32% of patients with appendiceal neoplasms received a preoperative diagnosis of acute appendicitis, while 23% were incidentally diagnosed (2).

We experienced a case in which right hemicolecotmy was required to remove a giant tumor containing mucin. Although pathological examinations revealed that the tumor was a mucinous carcinoma, it was difficult to elucidate the tumor origin, as the appendix itself had been replaced by the tumor and could not be found. The patient had not previously undergone an appendectomy; therefore, we suspected that the tumor originated from the appendix. Herein, we discuss the tumor origin and the reasons why the tumor became so large.

Case presentation

The patient was a 55-year-old woman who presented with pain in her right loin. She had not undergone any laparotomy. Physical examination revealed that her abdomen was not distended;
however, there was a palpable tumor in her right flank, which was tender. The patient had elevated
tumor marker levels, with an anti-p53 antibody concentration of 0.68 U/ml (<1.30 U/ml), soluble IL-
2 receptor antibody concentration of 546 U/ml (<519 U/ml), carcinoembryonic antigen
concentration of 46.6 ng/ml (<5 ng/ml), and CA19-9 concentration of 78.7 U/ml (<37.0 U/ml). A
computed tomographic scan of her abdomen detected a large mass in her right retroperitoneal region
behind the ascending colon that extended from the cecum to the hepatic flexure and was about 12 cm
in diameter. The mass was suspected to have invaded the duodenum and ascending colon (Fig. 1).

The patient did not present with small bowel obstruction. A barium enema and colonoscopy
examination found that the ascending colon was being compressed in the exterior to interior
direction, and that the tumor had invaded the colonic lumen (Fig. 2A, 2B). Therefore, it was
impossible to examine the whole tumor beyond the hepatic flexure. As the tumor was protruded
and vulnerable, it was not biopsied in order to avoid massive hemorrhage.

Magnetic resonance imaging revealed that the tumor displayed low signal intensity on T1-weighted
images and high signal intensity on T2-weighted images. The edge of the tumor was clear, with strong
enhancement on contrast-enhanced magnetic resonance imaging (Fig. 3A, 3B, 3C). Fluorine-18-
fluorodeoxyglucose positron emission tomography and computed tomography revealed that the tumor
contained regions of strong accumulation and areas of weak accumulation, with a maximal standardized uptake value of 5.6 in the early phase and 7.4 in the late phase (Fig. 3D). Neither distant metastasis nor peritoneal dissemination were detected by these imaging modalities. Based on these examinations, the clinical diagnosis was a retroperitoneal tumor involving the hedge mucin; the differential diagnoses were a mucinous carcinoma, liposarcoma with mucinous changes, or gastrointestinal tumor with necrotic changes.

Without following an Enhanced Recovery After Surgery (ERAS) protocol, we planned to either completely resect the tumor or to perform an enterocystostomy if it was impossible to resect tumor. To avoid injuring the right ureter, a ureteric stent was placed prior to laparotomy. During laparotomy, we found that the tumor was surrounded by the right abdominal wall, second part of the duodenum, ascending colon, and right psoas, without liver metastasis or peritoneal dissemination. The mass had clearly invaded the ascending colon and was adhered to the second part of the duodenum, right abdominal wall, and right psoas. We partially resected the peritoneum of the adhered abdominal wall and the fascia of the psoas to prevent tumor exposure. We dissected the middle colic artery, middle colic vein, ileocolic artery, and ileocolic vein along the superior mesenteric vein. The side wall of the second part of the duodenum was resected. Finally, we performed right hemicolectomy with D3
dissection. We performed a functional end-to-end anastomosis for the ileum and transverse colon. 

Primary closure and an ileum patch were done for the side wall resection of the duodenum. Mucus leakage was not caused by operative manipulation. The intraoperative blood loss was 1534 ml, operation time was 484 minutes, and intraoperative red blood cell transfusion volume was 560 ml.

Macroscopically, the tumor was located in the retroperitoneum, adhered to the terminal ileum and ascending colon (Fig. 4A, 4B). Histopathological examination revealed that the tumor was a low-grade mucinous carcinoma (Fig. 4C), which grew expansively outside of the ileocolonic wall without vascular invasion or lymph node metastasis. Tumor invasion was limited in the surrounding structures and focally protruded on the mucosal surface of the ascending colon (Fig. 5A, 5B). The mucinous carcinoma was surrounded mainly by fibrous connective tissue but partly by dilated incomplete intestinal structures, such as mucosal, submucosal, and muscular layers, which were not connected with pre-existing ileocolonic walls (Fig. 4D, 4F). These intestinal structures were confirmed immunohistochemically, using antibodies against cytokeratin 20 and α-smooth muscle actin (Fig. 5C, 5D, 5E, 5G, 5H). The intestinal structures adjacent to the ascending colon in the retroperitoneum might have derived from the vermiform appendix, as no normal appendiceal components were identified in the ileocecal region by detailed radiological, surgical, or histopathological examinations. Mucinous
neoplastic epithelium was also found in the mucosa of the dilated intestinal structures outside of the colon (Fig. 5E). Based on the abovementioned findings, we considered that the advanced AMN was a low-grade mucinous carcinoma in the retroperitoneum (T4b, N0, M0, G1, Stage IIc: AJCC seventh edition). The operation achieved R0 resection.

The patient’s hospital stay was 44 days and the postoperative course was uneventful. Adjuvant chemotherapy using the FOLFOX regimen was performed for 6 months after discharge. Peritoneal recurrence developed 7 years and 4 months postoperatively. At the present time (9 years postoperatively), the patient is alive and receiving chemotherapy.

Discussion

Primary appendiceal adenocarcinoma is a very rare malignant neoplasm that is detected in 0.05–0.2% of all appendectomy cases. The diagnosis is often unexpected, and is found in approximately 1% of all appendectomy specimens (1, 3). Adenocarcinomas represent approximately two-thirds of these cases and can be subdivided into three histological subtypes: mucinous, non-mucinous (or colonic), and signet-ring cell (3). The signet-ring cell type is rare, while the colonic type is the most common. Although signet-ring cell adenocarcinomas are known to have a worse prognosis, the prognosis of the mucinous and non-mucinous histological subtypes has not been well studied (3).
The appropriate terminology for AMNs is controversial (4). Mucinous appendiceal adenocarcinomas can be classified as well, moderately, or poorly differentiated, although the histological criteria for these classifications are not well established. Well-differentiated adenocarcinomas often consist of cystic mucin pools lined by neoplastic epithelium with minimal nuclear atypia (5). The characteristics of mucinous carcinoma include a tendency for extensive invasion. When mucinous carcinoma invades the submucosa, it spreads among the sparse connective tissue and occasionally morphologically resembles a submucosal tumor. This is because early and expansive invasion is a feature of mucin-secreting tumors, and tenacious mucus overcomes the tissue resistance and facilitates local spread (6,7). As a result, mucinous adenocarcinomas tend to exhibit advanced invasion regardless of their size, and are difficult to diagnose (6,8). In our case, the tumor was a mucinous carcinoma with low-grade atypia and focal invasion of the stroma. Hence, in our opinion, the tumor had expansively and slowly enlarged, maintaining the parts of each digestive layer.

One of the differential diagnoses in the present case was mucinous carcinoma arising from the appendiceal diverticulum. Although there are reports that diverticular disease of the appendix may be associated with malignancy, a recent paper suggested that diverticular disease of the appendix is not associated with malignancy (9). In the present case, immunohistochemistry of the cut tumor surface
confirmed the presence of another digestive lumen structure surrounding the tumor in addition to the initial colonic lumen structure. Appendix diverticulosis is generally a pseudodiverticulum. However, the other digestive lumen structure surrounding the tumor contained each complete layer (mucosa, submucosa, muscularis propria, subserosa, and serosa). Although the present patient had never undergone an appendectomy, the appendix could not be detected in the resected specimens. Therefore, we concluded that the tumor origin was likely to be the appendix.

Our patient presented with a high CA19-9 level. However, a recent review did not report any evidence of an elevated CA19-9 level in patients with AMNs (10). CA19-9 elevation may be a useful tumor marker for the diagnosis of AMNs.

In general, because the incidence of nodal spread of well-differentiated localized appendiceal tumors is less than 2%, most of the published surgical literature suggests that simple appendectomy is sufficient for tumors exhibiting only local disease. Right hemicolecction should be considered to clear the tumor margins in patients who have previously undergone appendectomy, and for tumors involving the peri-appendiceal area, tumors that are 2 cm or larger, tumors with high-grade histology, or tumors that invade the muscularis propria (1). Even if the mass was a metastatic tumor that had spread to the appendix, right hemicolecction is an appropriate treatment (11). In our case, right
hemicolecctomy was performed to ensure that there was no residual tumor.

In the present case, the detailed pathological examination proved that the tumor origin was the appendix. We concluded that the very slow growth, which is characteristic of mucinous adenocarcinomas, contributed to the presence of the giant tumor.

List of abbreviations

AMN: appendiceal mucinous neoplasm

Consent for publication

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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Figure legends

Fig. 1: Computed tomographic images of the tumor.

The tumor (*) was localized in the dorsal aspect of the ascending colon (B: arrow), the ventral aspect of the right psoas muscle, the caudal aspect of a horizontal portion of the duodenum (C, D: arrowhead), and the right abdominal wall. The inner parts of the lesion were not enhanced by contrast medium, whereas the marginal regions were enhanced.

Fig. 2A: Barium enema examination. The ascending colon was being compressed in the exterior to interior direction (arrows). 2B: Colonoscopy examination. The tumor had invaded the ascending colon and was exposed in the hepatic flexure (arrow).

Fig. 3: Preoperative imaging of the mass. 3A: T1-weighted magnetic resonance imaging, 3B: T2-weighted magnetic resonance imaging, 3C: enhanced T1-weighted magnetic resonance imaging, 3D: fluorine-18-fluorodeoxyglucose positron emission tomography and computed tomography.
Fig. 4: Macroscopic and microscopic images of the resected specimen.

(4A) The retroperitoneal tumor had invaded the lumen of the ascending colon. (4B) Examination of each cut surface (I, II, III, IV, V) revealed that the tumor contained abundant mucin, was mainly located under the colonic wall, and had clear margins. The tumor measured 11.5×8.5×12 cm. (4C) High-powered microscopic examination revealed proliferation of low-grade mucinous neoplastic epithelium and intense mucin production.

Fig. 5: Histologic and immunohistochemical examinations of the cut surfaces of the tumor.

(5A, 5B; HE stain) The tumor filled the retroperitoneum and was surrounded by organized fibrous tissue or focally accompanied by nonneoplastic intestinal wall, probably derived from the appendix, which was not directly connected with pre-existing colonic structures. In the regions of the colonic lumen that the tumor had invaded, normal mucosal and muscular layers were observed next to the margins of the tumor. (5C, 5E, 5H) Both pre-existing intestinal mucosa and retroperitoneal tumor overlaying mucosa were stained by antibodies against cytokeratin 20 (CK20, brown color), and the muscularis mucosa and muscularis propria were stained by antibodies against α-smooth muscle antigen (α-SMA, blue color). I, IV, VII mucosa, II, V, VIII muscularis mucosa, III, VI, IX muscularis propria. I–III were from the ascending colon. IV–VI were probably derived from the appendix. VII–IX
were from the ileum. (5D–5H) Immunohistochemical staining demonstrated the presence of CK20 and α-SMA in each layer. In Fig. 5D and 5G, the continuous yellow, red, and orange lines indicate the mucosa, muscularis mucosa, and muscularis propria of the colon, respectively. The dotted lines of the same color indicate the mucosa, muscularis mucosa, and muscularis propria of the adhered ileum, respectively. The broken lines of the same color indicate those probably derived from the appendix. (5F, 5G, 5H) The tumor that was located dorsal to the initial colon was surrounded by mucosa, muscularis mucosa, and muscularis propria. (5H) The tumor was surrounded by mucosa and muscular propria, probably derived from the appendix with double staining of CK20 and α-SMA.
