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Single Case

Perforated Goblet Cell Carcinoid of the Appendix

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Keywords
Goblet cell carcinoid · Appendix · Acute appendicitis · Perforation

Abstract
Goblet cell carcinoid (GCC) of the perforated appendix is rare, and its pathological features and prognosis remain poorly described. A 71-year-old woman was admitted to our hospital for right lower abdominal pain, vomiting, and high-grade fever. She was diagnosed with acute appendicitis and underwent emergency laparoscopic appendectomy. Intraoperative examination revealed an enlarged and perforated appendix. Histopathological examination revealed GCC of the appendix with subserosal invasion. She underwent laparoscopic ileocecal resection with lymph node dissection (D3) following appendectomy. Histopathological findings showed no residual tumor or lymph node metastases. To the best of our knowledge, this report is a valuable addition to the GCC literature, describing a case of GCC of the appendix presenting as perforated appendix.

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Introduction

Goblet cell carcinoid (GCC) is a rare tumor of the appendix with histological features of both adenocarcinoma (AC) and neuroendocrine tumor [1]. In the 2010 WHO classification, mixed adenoneuroendocrine carcinoma is defined as a tumor with both AC and neuroendocrine carcinoma components, each comprising at least 30% of the lesion. Considered as a subgroup of mixed adenoneuroendocrine carcinoma [2], GCC is rarely diagnosed preoperatively, but usually intraoperatively or on pathological examination after appendectomy for acute appendicitis [3].

GCC is estimated to account for 10% of all appendiceal neuroendocrine tumors [4]; it is found in 0.3–0.9% of post-appendectomy specimens and accounts for 35–58% of all appendiceal tumors and approximately 14% of all appendiceal malignancies [5]. Five-year survival rates for GCC are reported to range between 58 and 84% [6], with peritoneal carcinomatosis being the most common cause of death [5].

Again, GCC of the perforated appendix is rare, and its pathological features and prognosis remain poorly elucidated. We herein report a case of GCC of a perforated appendix.

Case Presentation

A 71-year-old woman was admitted to our hospital for right lower abdominal pain, vomiting, and high-grade fever. Physical examination findings included: height, 145 cm; weight, 48 kg; fully conscious; blood pressure, 165/60 mm Hg; heart rate, 92/min; oxygen saturation of the peripheral artery, 93%; and body temperature, 39.2°C. Laboratory findings included: white blood cell count, 6.3 × 10^9/L; and C-reactive protein, 2.5 mg/dL. Computed tomography revealed an enlarged appendix, appendiceal wall enhancement, and peri-appendiceal fat stranding (Fig. 1).

The patient was diagnosed with acute appendicitis and underwent emergency laparoscopic appendectomy. Intraoperative examination showed an enlarged and perforated appendix, with turbid ascites found in the Douglas fossa and the right colon fossa. Macroscopically, the resected appendix was a 45 × 25 mm lesion with a negative margin (Fig. 2). Histopathologically, the lumen near the entrance of the appendix was filled with degenerative necrotic material, with the peripheral lumen showing purulent inflammation, the inflammatory cell infiltration exceeding the serosa, and complicated acute appendicitis. In addition, extensive tumor cell infiltration was observed from the mucosal to the subserosal layer, with tumor invasion to the perineural space and lymphatic vessels. The tumor was composed of small, rounded nests of signet ring-like cells resembling normal intestinal goblet cells, except for nuclear compression (Fig. 3a). Immunohistochemically, tumor cells were positive for chromogranin A (Fig. 3b), synaptophysin, CD56 (Fig. 3c), MUC1-014E, CAM5.2, serotonin (Fig. 3d), CEA (Fig. 3e), CK20 (Fig. 3f), and CDX2; however, they were negative for somatostatin (Fig. 3g) and CK7 (Fig. 3h). Ki-67 was positive in 10% of tumor cells (Fig. 3i). The tumor of the appendix was therefore diagnosed as GCC of the appendix with subserosal invasion.

The patient underwent laparoscopic ileocecal resection with lymph node dissection (D3) 1 month after appendectomy. Histopathological findings showed no evidence of residual tumor or lymph node metastases. Tegafur/uracil was administered as adjuvant chemotherapy

for 1 year. She was diagnosed with early gastric cancer 5 years after appendectomy and underwent laparoscopic cardiac gastrectomy for pathologically confirmed AC, type 0-IIb, measuring 20 × 15 mm, por+tub2, pT1b (SM). Regular follow-up computed tomography examinations revealed no recurrence or metastasis of GCC for 6 years after appendectomy.

Discussion and Conclusion

Our case has two important clinical implications.

The first implication of our case is that GCC may present as acute perforated appendicitis. GCC of the appendix with perforation is rare, and its pathological features and prognosis remain poorly described in the literature. GCC is a rare tumor involving the appendix almost exclusively [5]. Tang et al. [6] classified GCC into three groups: (A) typical GCC, (B) AC ex GCC, signet ring cell type, and (<c) AC ex GCC, poorly differentiated carcinoma type. Of these, the present lesion fulfilled the definition of group B (i.e., AC ex GCC, signet ring cell type). In addition, GCC is reported to share the immunohistochemical features with classical well-differentiated neuroendocrine tumor (WDNET) and conventional AC of the appendix [5]. To date, the frequency of the epithelial marker CEA/CK20/CK7 expression in GCC, WDNET, and conventional AC is reported to be 100/100/33–75%, 0–26/0–32/0–11%, and 100/100/14–53%, respectively. In addition, the frequency of the endocrine marker chromogranin A/synaptophysin expression in GCC, WDNET, and conventional AC is reported to be 85–100/88–100%, 100/100%, and 0/0–29%, respectively. The tumor in the present case was shown to be positive for CEA, CK20, chromogranin A, and synaptophysin and was therefore diagnosed as GCC.

The second implication of our case is that the patient had no recurrence or metastasis for 6 years postoperatively despite having a high-risk tumor. To date, only 19 cases of perforated GCC of the appendix have been reported (Table 1) [3, 7–12]. Of the 10 patients whose prognosis was reported, 3 had recurrence, 3 died of recurrence, and 4 had no recurrence, with the follow-up of the 4 patients with no recurrence being 5 months [12], 9 months [7], 1.3 years [8], and 4.5 years [7]. Pham et al. [13] reported that stage is the most important prognostic factor, with 5-year survival rates in stage I–IV being 100, 76, 22, and 14%, respectively. In addition, they proposed as criteria for additional resection (1) T3/4 disease, (2) direct cecum extension, and (3) clinically positive mesenteric nodes [13]. Thus, diagnosed as having stage II disease, our patient underwent an additional resection according to their criteria. Furthermore, Tang et al. [6] recommend chemotherapy in patients with high-stage GCC and localized perforation. While the role of chemotherapy remains controversial in GCC, consensus guidelines recommend 5-FU-based chemotherapy in GCC in reference to that in colorectal cancer [4]. Thus, tegafur/uracil was administered in the present case.

In conclusion, GCC may present as acute perforated appendicitis and call for careful follow-up, given its risk of recurrence.

Statement of Ethics

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

Conflict of Interest Statement

The authors have no conflicts of interest to disclose in association with this study.

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Author Contributions

K. Kubo, N. Kimura, M. Suzuoki, S. Matsuda, M. Tsuda, M. Ohara, and M. Kato carried out and confirmed the diagnosis, provided the details of the case, and contributed to the design of the report. K. Kubo, N. Kimura, and M. Kato drafted the manuscript. All authors read and approved the final version of the manuscript.

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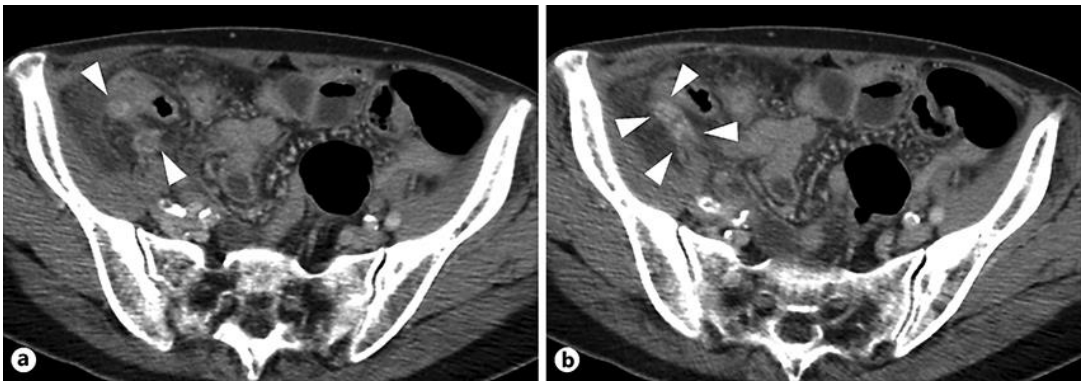

Fig. 1. **a**, **b** Computed tomography revealed an enlarged appendix, appendiceal wall enhancement, and peri-appendiceal fat stranding.

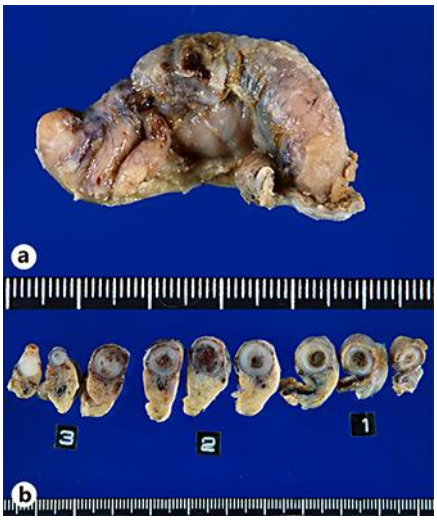

Fig. 2. **a**, **b** Macroscopic view of the resected specimen, which was a 45 × 25 mm lesion with a negative margin.

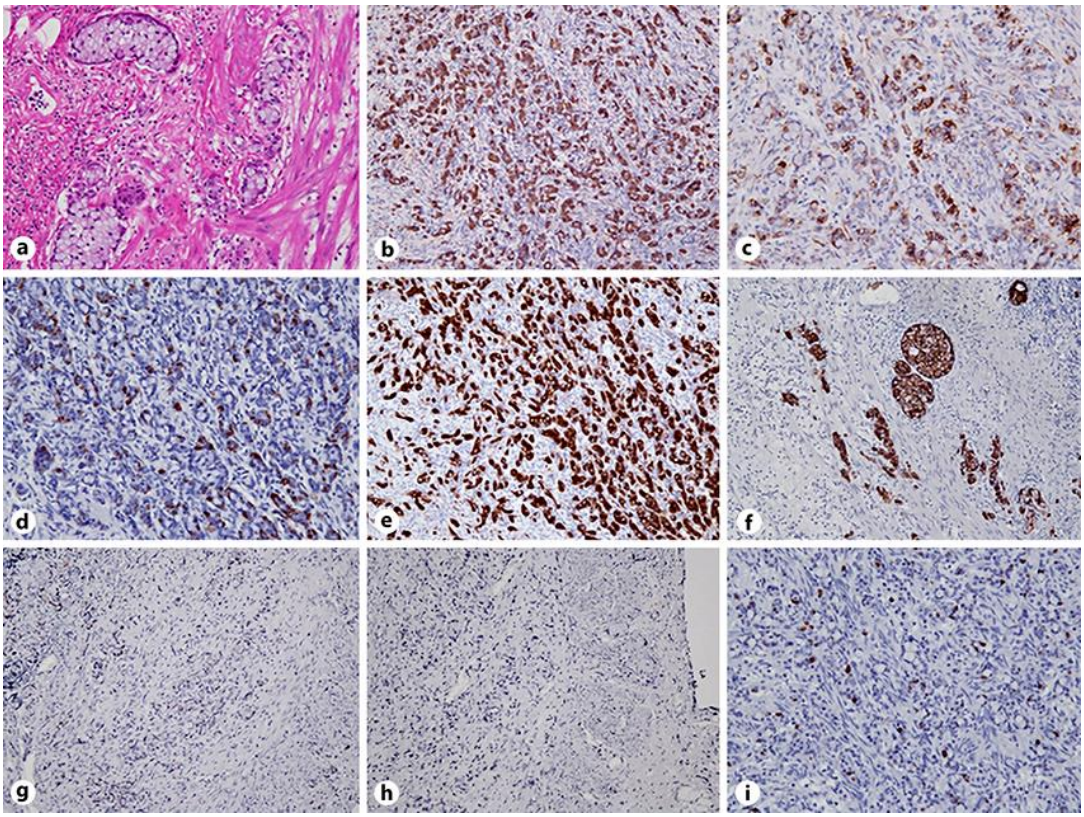

Fig. 3. Histopathological examination of the appendix lesion. **a** H&E staining showed tumor cells containing a large amount of mucin-like signet ring cell carcinoma. ×100. **b–h** Immunohistochemical staining indicated that tumor cells were positive for chromogranin A (**b**), CD56 (**c**), serotonin (**d**), CEA (**e**), and CK20 (**f**); however, they were negative for somatostatin (**g**) and CK7 (**h**). ×100. **i** Ki-67 was positive in 10% of tumor cells. ×200.

Table 1. Cases reported to date of perforated goblet cell carcinoid of the appendix

No.	Ref. No.	Year	Age, years	Sex	Surgical procedure	Adjuvant CTx	Prognosis
1	[7]	1974	57	M	appendectomy followed by right hemicolectomy	(–)	no recurrence for 4.5 years
2			45	M	appendectomy followed by right hemicolectomy	(–)	no recurrence for 9 months
3	[8]	2001	82	F	appendectomy followed by right hemicolectomy	NA	no recurrence for 1.3 years
4			61	M	appendectomy followed by right hemicolectomy	NA	DOD after 19.2 years
5			68	F	appendectomy followed by right hemicolectomy	NA	DOD after 5.4 years
6	[9]	2003	41	M	appendectomy followed by right hemicolectomy	(–)	recurrence after 32 months
7			56	M	appendectomy	(–)	NA
8			74	M	appendectomy	(–)	NA
9			49	F	appendectomy	(–)	NA
10			40	M	appendectomy and regional LND	(–)	NA
11			38	M	appendectomy	(–)	recurrence after 22 months
12			23	F	appendectomy	(–)	recurrence after 36 months
13	[10]	2005	39	F	appendectomy followed by right hemicolectomy	NA	NA
14	[3]	2007	NA	NA	appendectomy followed by right hemicolectomy	(–)	NA
15			NA	NA	appendectomy followed by right hemicolectomy	(+)	DOD after 14 months
16			NA	NA	appendectomy followed by right hemicolectomy	(–)	NA
17	[11]	2013	NA	NA	NA	NA	NA
18			NA	NA	NA	NA	NA
19	[12]	2018	68	F	ileocecectomy	NA	no recurrence for 5 months
20	our case	2020	71	F	appendectomy followed by ileocecectomy	(+)	no recurrence for 6 years

CTx, chemotherapy; DOD, death of disease; LND, lymph node dissection; NA, not available.