INTRODUCTION

Carcinoid tumors are the most common malignancies of the appendix, accounting for 32-57% of all appendiceal tumors. Appendiceal carcinoid tumors are usually revealed incidentally at appendectomy, where their prevalence is 0.3-0.9% in patients undergoing an appendectomy.\(^1\) The pathologic characteristics of goblet cell carcinoid tumors, also known as adenocarcinoids, were first described by Gagne et al.\(^2\) in 1969. The term “goblet cell appendiceal carcinoids (GCAC)” was introduced by Subbuswamy et al.\(^3\) in 1974 because the predominant cell type was thought to be similar to the normal goblet cell of the epithelium of the intestinal tract, with Paneth’s and argentaffin cells being present in considerable numbers. The aggressiveness of the goblet cell carcinoid is still unclear,\(^4\) but it is probably more aggressive than the carcinoid and less so than a colorectal carcinoma.\(^5\) However, their management, especially whether appendectomy alone is an adequate treatment or a right hemicolectomy is indicated as for the appendiceal adenocarcinoma, is still a subject of debate.\(^8\)
Chemotherapy is the usual treatment option for the metastatic disease, but more data are required for if an optimal regimen is to be determined. Recently, we discovered one case of a GCAC that was diagnosed incidentally at appendectomy.

**CASE REPORT**

A 48-yr-old man with no remarkable past medical history was admitted to the Department of General Surgery because of right lower quadrant abdominal pain that had started 2 days earlier. The patient's abdomen was not distended, but tenderness and rebound tenderness were observed around right lower quadrant abdominal area. Vital signs revealed a fever of 38.2°C, a blood pressure of 140/80 mmHg, a pulse rate of 118/min, and a respiration rate of 20/min. A complete blood count showed hemoglobin of 14.4 g/dL, a white blood cell count of 12,630/μL (segmented neutrophil 87.6%, lymphocyte 7.6%, monocyte 2.6%, eosinophil 1.0%, basophil 0.5%), and a platelet count of 232,000/μL. Computed tomography of the abdomen revealed acute appendicitis with an appendicolith, about 14 mm in diameter (Fig. 1), and a laparoscopic appendectomy was performed. The type of appendicitis was gangrenous, and there were no obvious signs of malignancy. However, the pathologic diagnosis revealed a goblet cell carcinoid. Sections disclosed portions of the appendix showing infiltration by the tumor and composed of small, rounded nests of signet ring-like cells resembling normal intestinal goblet cells. This tumor showed predominant submucosal growth and had invaded through the entire appendiceal wall. Mitosis was counted.

![Fig. 1. Computed tomography of the abdomen revealed acute appendicitis with an appendicolith, about 14 mm in diameter.](image1)

![Fig. 2. Microphotograph shows infiltration by tumor tissue composed of small, rounded nests of signet ring-like cells resembling normal intestinal goblet cells. This tumor shows predominant submucosal growth and has invaded through the entire appendiceal wall. Mitosis is counted to 5/10 HPF (H&E stain, ×100).](image2)

![Fig. 3. Special stain findings were positive for PAS and Alcian blue.](image3)
to 5/10 HPF (Fig. 2). Special stain findings were positive for PAS, Alcian blue, and Mucicarmine (Fig. 3). Immunohistochemical findings were positive CEA, Chromogranin, Synaptophysin, and CD56 (Fig. 4). A subsequent laparoscopic right hemicolectomy was performed (Fig. 5). The mucosal surface showed no mass-like lesion. The cut surface revealed wall thickening, measuring about 2 cm in length, in the cecum. Sections from the cecum showed infiltration of tumor tissue resembling normal intestinal goblet cells. This tumor was extended into the subserosal layer. Vascular and lymphatic emboli were not identified. Mitotic figures were rarely seen. Regional lymph nodes showed metastasis in 1 out of the 14 retrieved lymph nodes. The patient received capecitabine.
After completion of 5 cycles, he refused an ongoing use of capecitabine due to worsening of underlying psoriasis during chemotherapy. He currently shows no recurrence 12 mo, after the original treatment.

**DISCUSSION**

GCAC are rare tumors and have an uncertain biological behavior and their features are different from those of classic appendiceal carcinoids. The mean age for diagnosing GCAC is 58.8 yr, with equal representation in both sexes. GCAC are rarely diagnosed preoperatively and are usually diagnosed intraoperatively or during pathologic examination of the specimen following an appendectomy for acute appendicitis. Seventy percent of GCAC are located in the distal part (tip) of the appendix. However, Toumpanakis et al. reported that 60% of the tumors were found at the base of the appendix. The metastatic potential of GCAC is high. At least 20% of tumors are reported to be metastatic at presentation. Transcoelomic intraperitoneal spread, including to the ovaries, is the most common finding, and lymphatic metastases appear more common than hematogenous spread. Hepatic metastases are rarely noted. In metastatic GCAC, FDG-PET scanning may be helpful in the differential diagnosis of new lesions demonstrated by conventional imaging. The pathogenesis of GCAC is not entirely clear. Some authors attribute the development of these tumors to the occurrence of p53 mutations and especially to G:C to A:T transition while other studies suggest that an allelic loss of chromosomes 11q, 16q, and 18q is frequent in GCAC.

As neuroendocrine tumors, GCAC express several neuroendocrine markers in tumor tissue, including chromogranin A, synaptophysin, and NSE. No definitive staging system has been validated for GCAC. The malignant potential of GCAC is evaluated similar to that of appendiceal carcinoids; this is done by using tumor size and mitosis rate. Many studies recommend a right hemicolectomy based solely on a pathologic diagnosis of a goblet cell carcinoid. Others support Warkel recommendations that more formal oncologic resections be performed based on pathologic evidence of invasion or spread. Bucher et al. reported that an appendectomy alone is curative for patients presenting with a small adenocarcinoid (<=1 cm) not expanding beyond the appendix and with a low mitosis rate. By contrast, adenocarcinoids >1 cm in size, with a mitosis count of >2/10 HPF, and/or spreading beyond the appendiceal adventitia should be treated with a right hemicolectomy. Also, if involvement of the appendiceal base or occult intraperitoneal spread cannot be excluded, the consensus has moved toward performing a right hemicolectomy.

Aggressive debulking of tumor lesions may improve symptom control and survival in patients with intraperitoneal spread. A bilateral oophorectomy has also been advocated in a female patient. Literature available on adjuvant chemotherapy for adenocarcinoids is limited. A regimen of 5-FU and streptozotocin or a cisplatin-based chemotherapy is recommended in case reports on a patient showing spread to both ovaries and another report has shown an encouraging result from Folfox chemotherapy for a metastatic case.

The malignant potential of an appendiceal adenocarcinoid has been reported to be between that of a carcinoid and a colonic adenocarcinoma. Some oncologists advocate a standard colorectal chemotherapy regimen. Our patient had capecitabine as adjuvant first-line monotherapy, which is FDA-approved for stage III colorectal cancer. The overall reported five-year survival of GCAC is about 60-84%. In patients with metastases the prognosis is poor, especially when ovaries are involved, with a mean survival of 7-12 mo.

**REFERENCES**

6. McCusker ME, Cote TR, Clegg LX, Sobin LH. Primary malignant neoplasms of the appendix: a population-based study from the surveillance,