충수돌기 술잔세포 유암종

박선진 · 최성일 · 송정윤 · 김용호

경희대학교 의과대학 외과학교실

Goblet Cell Carcinoid of the Appendix

Sun Jin Park, M.D., Sung Il Choi, M.D., Jeong Yoon Song, M.D., Yong Ho Kim, M.D.

Department of Surgery, Kyung Hee University College of Medicine, Seoul, Korea

A goblet cell appendiceal carcinoid (GCAC) is an uncommon tumor. It shares the histologic features of both adenocarcinoma and conventional carcinoids. The metastatic potential of GCAC is higher than that of classic appendiceal carcinoids. Their management, whether an appendectomy alone is an adequate treatment or whether a right hemicolectomy is indicated, is still under debate. The metastatic potential of GCAC is similar to that of classic appendiceal carcinoids and depends on the tumor size and the mitosis rate. Therefore, some authors advocate a simple appendectomy, not expanding beyond the appendix adventitia, for selected patients with tumors less than 1 cm in diameter with a low mitosis rate (<2/10 HPF). Otherwise, a right hemicolectomy is indicated for all other patients to reduce the risk of developing metastatic disease. Chemotherapy is the usual treatment option for metastatic disease, but more data are required if an optimal regimen is to be determined. Finally, colonoscopy plays an important role in patients with an appendiceal adenocarcinoma because of their high risk of developing a colorectal adenocarcinoma. Recently, we discovered one case of a GCAC that was diagnosed incidentally at appendectomy. A 48-yr-old man visited the emergency department with the symptom of right lower quadrant abdominal pain. Acute appendicitis was suspected after evaluation, and a laparoscopic appendectomy was performed. The type of appendicitis was gangrenous, and there were no obvious signs of malignancy. However, a pathologic diagnosis of a goblet cell carcinoid was made. A laparoscopic right hemicolectomy was subsequently performed. The patient received 5 cycles of chemotherapy applied to the goblet cell carcinoid and has shown no other remarkable indispositions during the last 12 mo.

Keywords: Goblet cell carcinoid; Appendix

중심단어: 충수돌기, 술잔세포 유암종

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 un-

dergoing 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.⁵⁻⁷ 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.^{8,9}

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Correspondence to : Yong Ho Kim, M.D.

Department of Surgery, Kyung Hee University College of Medicine,
Kyung Hee University Medical Center, 1 Hoegi-dong,
Dongdaemun-gu, Seoul 130-702, Korea
Tel : +82.2-958-8246, Fax : +82.2-966-9366
E-mail : kyjho@khmc.or.kr

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Chemotherapy is the usual treatment option for the metastatic disease,¹⁰ 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 hemog-

lobin of 14.4 g/dL, a white blood cell count of 12,630/ μ L (segmented neutrophil 87.6%, lymphocyte 7.6%, monocyte 2.6%, eosinophil 1.0%, basophil 0.5%), and a platelet count of 232,000/ μ L. 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.

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, $\times 100$).

Fig. 3. Special stain findings were positive for PAS and Alcian blue.

to 5/10 HPF (Fig. 2). Special stain findings were positive for PAS, Alcian blue, and Mucicarmino (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 by 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.

Fig. 4. Immunohistochemical findings were positive for CEA, chromogranin, and CD56.

Fig. 5. Gross finding of the right hemicolectomy specimen. (A) Mucosal surface shows no mass-like lesion. The serosal surface shows a whitish area. (B) The cut surface reveals wall thickening, measuring about 2 cm in length, in the cecum.

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.^{10,11} 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.¹² However, Toumpanakis et al.¹⁰ 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.¹⁰ Hepatic metastases are rarely noted.¹³ In metastatic GCAC, FDG-PET scanning may be helpful in the differential diagnosis of new lesions demonstrated by conventional imaging.¹⁰ 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 transition¹⁴ while other studies suggest that an allelic loss of chromosomes 11q, 16q, and 18q is frequent in GCAC.¹⁵

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.^{12,16} Others support Warkel recommendations that more formal oncologic resections be performed based on pathologic evidence of invasion or spread.^{1,13} Bucher et al.¹⁷ 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.^{3,12,17,18} Also, if involvement of the appendiceal base or occult intraperitoneal spread cannot be excluded, the consensus has moved toward performing a right hemicolectomy.^{1,8,10}

Aggressive debulking of tumor lesions may improve symptom control and survival in patients with intraperitoneal spread.⁴ A bilateral oophorectomy has also been advocated in a female patients.^{19,20} 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,^{20,21} and another report has shown an encouraging result from Folfex chemotherapy for a metastatic case.²²

The malignant potential of an appendiceal adenocarcinoid has been reported to be between that of a carcinoid and a colonic adenocarcinoma.⁵⁻⁷ Some oncologists advocate a standard colorectal chemotherapy regimen.¹⁰ 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%.²³ In patients with metastases the prognosis is poor, especially when ovaries are involved, with a mean survival of 7-12 mo.^{10,24}

REFERENCES

- Goede AC, Caplin ME, Winslet MC. Carcinoid tumour of the appendix. *Br J Surg* 2003;90:1317-22.
- Gagne F, Fortin P, Dufour V, Delage C. Tumors of the appendix associating histologic features of carcinoid and adenocarcinoma. *Ann Anat Pathol (Paris)* 1969;14:393-406.
- Subbuswamy SG, Gibbs NM, Ross CF, Morson BC. Goblet cell carcinoid of the appendix. *Cancer* 1974;34:338-44.
- Mahteme H, Sugarbaker PH. Treatment of peritoneal carcinomatosis from adenocarcinoid of appendiceal origin. *Br J Surg* 2004;91:1168-73.
- Hirsch I, Kasper HU, Brabender J, Holscher AH, Dienes HP. Adenocarcinoid of the appendix vermiformis. *Pathologie* 2005;26:231-5.
- McCusker ME, Cote TR, Clegg LX, Sobin LH. Primary malignant neoplasms of the appendix: a population-based study from the surveillance,

- epidemiology and end-results program, 1973-1998. *Cancer* 2002;94:3307-12.
7. Rutledge RH, Alexander JW. Primary appendiceal malignancies: rare but important. *Surgery* 1992;111:244-50.
 8. Stinner B, Rothmund M. Neuroendocrine tumours (carcinoids) of the appendix. *Best Pract Res Clin Gastroenterol* 2005;19:729-38.
 9. Byrn JC, Wang JL, Divino CM, Nguyen SQ, Warner RR. Management of goblet cell carcinoid. *J Surg Oncol* 2006;94:396-402.
 10. Toumpanakis C, Standish RA, Baishnab E, Winslet MC, Caplin ME. Goblet cell carcinoid tumors (adenocarcinoid) of the appendix. *Dis Colon Rectum* 2007;50:315-22.
 11. Aizawa M, Watanabe O, Naritaka Y, Katsube T, Imamura H, Kinoshita J, et al. Adenocarcinoid of the appendix: report of two cases. *Surg Today* 2003;33:375-8.
 12. Park K, Blessing K, Kerr K, Chetty U, Gilmour H. Goblet cell carcinoid of the appendix. *Gut* 1990;31:322-4.
 13. Anderson NH, Somerville JE, Johnston CF, Hayes DM, Buchanan KD, Sloan JM. Appendiceal goblet cell carcinoids: a clinicopathological and immunohistochemical study. *Histopathology* 1991;18:61-5.
 14. Ramnani DM, Wistuba II, Behrens C, Gazdar AF, Sobin LH, Albores-Saavedra J. K-ras and p53 mutations in the pathogenesis of classical and goblet cell carcinoids of the appendix. *Cancer* 1999;86:14-21.
 15. Stancu M, Wu TT, Wallace C, Houlihan PS, Hamilton SR, Rashid A. Genetic alterations in goblet cell carcinoids of the vermiform appendix and comparison with gastrointestinal carcinoid tumors. *Mod Pathol* 2003;16:1189-98.
 16. Gouzi JL, Laigneau P, Delalande JP, Flamant Y, Bloom E, Oberlin P, et al. Indications for right hemicolectomy in carcinoid tumors of the appendix. The French Associations for Surgical Research. *Surg Gynecol Obstet* 1993;176:543-7.
 17. Bucher P, Gervaz P, Ris F, Oulhaci W, Egger JF, Morel P. Surgical treatment of appendiceal adenocarcinoid (goblet cell carcinoid). *World J Surg* 2005;29:1436-9.
 18. Warkel RL, Cooper PH, Helwig EB. Adenocarcinoid, a mucin-producing carcinoid tumor of the appendix: a study of 39 cases. *Cancer* 1978;42:2781-93.
 19. Butler JA, Houshiar A, Lin F, Wilson SE. Goblet cell carcinoid of the appendix. *Am J Surg* 1994;168:685-7.
 20. Mandai M, Konishi I, Tsuruta Y, Suginami N, Kusakari T, Iwasaki T, et al. Krukenberg tumor from an occult appendiceal adenocarcinoid: a case report and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 2001;97:90-5.
 21. Hirschfield LS, Kahn LB, Winkler B, Bochner RZ, Gibstein AA. Adenocarcinoid of the appendix presenting as bilateral Krukenberg's tumor of the ovaries. Immunohistochemical and ultrastructural studies and literature review. *Arch Pathol Lab Med* 1985;109:930-3.
 22. Garin L, Corbinais S, Boucher E, Blanchot J, Le Guilcher P, Raoul JL. Adenocarcinoid of the appendix vermiformis: complete and persistent remission after chemotherapy (folfox) of a metastatic case. *Dig Dis Sci* 2002;47:2760-2.
 23. Berardi RS, Chen H. Goblet cell carcinoid of the appendix. *Int Surg* 1989;74:109-10.
 24. Baker PM, Oliva E, Young RH, Talerman A, Scully RE. Ovarian mucinous carcinoids including some with a carcinomatous component: a report of 17 cases. *Am J Surg Pathol* 2001;25:557-68.