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CASE REPORT

Goblet Cell Adenocarcinoma of the Appendix: A Case Report and Review of the Literature

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ABSTRACT

Goblet cell adenocarcinoma (GCA) of the appendix is a rare and aggressive neoplasm characterized by goblet-like mucinous cells. Due to its rarity, there is limited data on its clinical course and management. Typically diagnosed incidentally or when mimicking acute appendicitis, GCAs require careful management to mitigate the risk of disseminated disease. This report discusses a case involving a 64-year-old man diagnosed with low-grade GCA, including the diagnostic workup, treatment approach, and outcomes. The management strategies parallel those for colorectal cancer, with potential benefits from cytoreductive surgery and intraperitoneal chemotherapy. The aim of this report is to enrich the knowledge base and offer insights into optimal management strategies.

Keywords: Appendectomy, carcinoma of the appendix, goblet cell adenocarcinoma, goblet cell carcinoma

Introduction

Primary appendiceal neoplasms are rare, accounting for only 1% of gastrointestinal tumors, with an incidence of fewer than 0.05 cases per 100,000 annually.[1] These tumors include colonic-type adenocarcinomas, carcinoids, mucinous neoplasms, signet ring cell carcinomas, and goblet cell adenocarcinomas (GCAs), which constitute 14-19% of cases.[2,3] GCA is an amphicrine neoplasm characterized by goblet-like mucinous cells with neuroendocrine features and behaves aggressively like an adenocarcinoma variant.[2,3] The incidence of GCA exhibits no gender bias, and is typically diagnosed between the ages of 50 and 60.[1]

Patients with appendiceal GCA often present with symptoms that mimic acute appendicitis or indicate advanced disease. Up to one-third of cases are incidentally discovered during an appendectomy. Considering a right hemicolectomy is crucial; however, due to the rarity of the disease, there is no clear consensus on its management. This report discusses a case of appendiceal GCA and current management strategies.

Case Report

A 64-year-old man with no prior surgical history or comorbidities presented to the emergency department complaining of right lower quadrant (RLQ) abdominal pain and vomiting. During the physical examination, the patient exhibited focal peritonitis in the RLQ. A computed tomography (CT) scan of the abdomen and pelvis revealed evidence of acute appendicitis. A laparoscopic appendectomy was performed based on this diagnosis.

Pathologic analysis of the specimen revealed a 1.5 cm diameter low-grade GCA (Figure 1) invading through the muscularis propria. Moreover, the tumor extended to the lateral surgical margin, and there was perineural invasion but no lymphovascular invasion. Furthermore, tumor cells stained strongly positive for chromogranin A (CgA) and focally positive for synaptophysin. Consequently, the specimen was classified as GCA, pathologic stage pT3NxMx.[4]

One week after the operation, plasma carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels were 3.96 ng/mL (0-5) and 17 U/mL (0-34), respectively.

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Additionally, abdominal-pelvic magnetic resonance imaging (MRI) revealed lymph nodes measuring 13 mm in size adjacent to the right iliac vein and minimal fluid in the perihepatic and perisplenic areas.

Subsequently, a right hemicolectomy was performed, and a pathologic examination revealed low-grade GCA infiltration in the right colon, with multiple foci on the serosal surface. The tumor had invaded the visceral peritoneum. Notably, of the 14 resected mesenteric lymph nodes, two were reported as metastatic. However, the surgical margins were tumor-free. Immunohistochemistry for synaptophysin and CgA was focally positive (Figure 2). The final pathologic staging of the tumor was pT4N1Mx.[4]

Following the hemicolectomy, plasma CEA and CA19-9 levels were 3.2 ng/mL (0-5) and 12 U/mL (0-34), respectively, with similar values measured during follow-up.

Postoperatively, adjuvant chemotherapy was discussed in a multidisciplinary tumor board. As a result, the patient received modified folinic acid, fluorouracil, and oxaliplatin every 2 weeks. Six months of chemotherapy were completed, and consecutive CT scans revealed no signs of recurrent disease. Furthermore, a subsequent colonoscopy performed 1-year after the initial diagnosis did not identify any malignant lesions. The patient has remained disease-free for 1.5 years during ongoing surveillance. Informed consent was obtained from the patient for this case report.

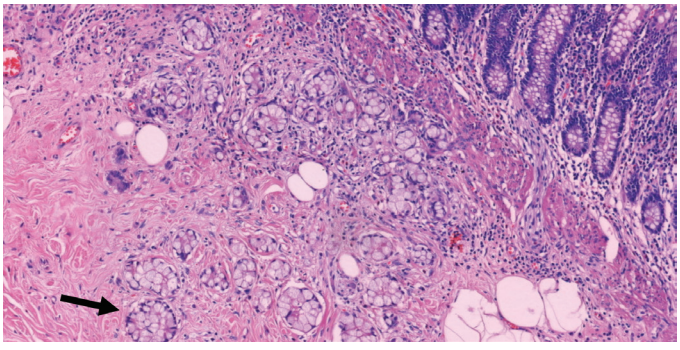

Figure 1. Low-grade goblet cell carcinoma of the appendix showing cohesive clusters of tumor cells with goblet-like mucinous cells (x15, Hematoxylin and eosin)

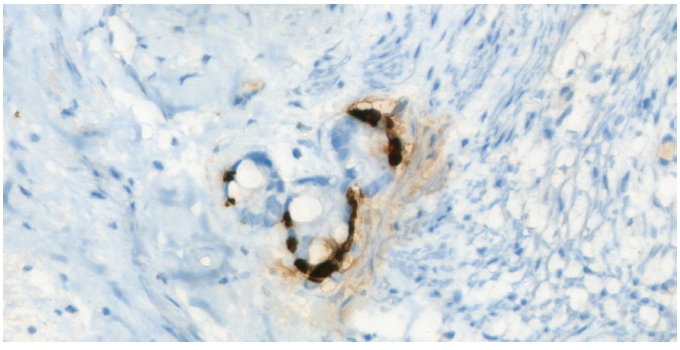

Figure 2. Chromogranin positivity in some of the tumor cells (x58, anti-chromogranin A)

Discussion

We presented a case involving a 64-year-old man initially diagnosed with acute appendicitis, who subsequently underwent a right hemicolectomy after a diagnosis of GCA was confirmed.

GCAs are classified as mixed adenoneuroendocrine carcinomas, displaying both neuroendocrine and glandular features. Histologically, they are characterized by goblet-shaped epithelial cells that contain mucin, often clustered in the lamina propria or submucosa of the appendix. These cells are distinctively marked by positive Periodic acid-Schiff staining, which helps differentiate them from appendiceal neuroendocrine tumors (NETs). Immunohistochemical markers such as CgA and synaptophysin show substantial expression, whereas CEA expression helps distinguish GCAs from appendiceal NETs. Cytokeratin (CK) staining for CK20 and CK19 also aids in differentiating them from adenocarcinomas.[5]

Due to the similarity of symptoms to various abdominal pathologies and gynecological malignancies, diagnosing appendiceal neoplasms can sometimes be challenging. Cases are typically diagnosed pathologically following an appendectomy. In some patients, preoperative CT imaging may raise suspicions of an appendiceal tumor. In such cases, or when an appendiceal tumor is suspected intraoperatively, diagnoses and surgical approaches can be refined through frozen-section analysis. For patients diagnosed with GCA, conducting abdomen-pelvis CT or MRI scans is advisable to ascertain the absence of locoregional or distant metastases.

In up to 80% of cases, CEA and CA19-9 levels are elevated. However, it is important to note that, unlike appendiceal NETs, serum levels of CgA hold no diagnostic value for GCA, as evidenced by our patient's case.

The prognosis of GCA is generally worse than that of appendix NETs but better than that of adenocarcinomas. The 5-year survival rate for GCA is approximately 90% for stage 1 and 2, 55-57% for stage 3, and 19% for stage 4 disease.[6] Among appendiceal tumors, GCAs have the lowest incidence of regional nodal metastases. Moreover, GCAs can also disseminate intraperitoneally, even without nodal metastases, a pattern similar to colorectal cancer (CRC), in which peritoneal tumor deposits are also observed.

Numerous cases of GCA are incidentally identified post-appendectomy, raising questions about the necessity for additional resection, such as right hemicolectomy. While randomized trials are lacking, studies have explored the potential benefits of right colectomy, especially in patients

with T3-T4 tumors.[7] Given the increased risk of metastases, a complete right hemicolectomy is recommended if the patient can tolerate further surgery. The American Society of Colon and Rectal Surgeons advocates for right hemicolectomy as the standard surgical treatment for GCA.[8]

The role of adjuvant chemotherapy for GCA has not been definitively established in randomized studies due to the rarity of this disease. Although the results regarding the survival benefit of adjuvant chemotherapy in non-metastatic GCA are conflicting,[9,10] similar to colon cancer, fluorouracil-based chemotherapy is recommended in the adjuvant setting.[8,11]

Treatment strategies for advanced appendiceal GCAs parallel those used for advanced CRC, involving fluoropyrimidine-based regimens. However, the specific roles of biologic agents such as bevacizumab and those targeting the epidermal growth factor receptor remain uncertain.[11] Notably, chemotherapy appears to yield superior responses in appendiceal GCAs compared with other adenocarcinomas of the appendix.[7] Limited data indicate that patients with isolated peritoneal spread might achieve prolonged survival through cytoreductive surgery coupled with hyperthermic intraperitoneal chemotherapy.[12,13]

Regarding post-treatment surveillance, given the aggressive nature of GCA, surveillance strategies similar to those used for CRC are recommended.[11]

GCA, a rare appendiceal tumor, combines adenomatous and neuroendocrine features. It is commonly diagnosed post-appendectomy, and early-stage cases often require a right hemicolectomy due to the risk of metastasis. Although the evidence is limited, adjuvant chemotherapy is typically recommended for localized disease. Continued research may lead to standardized treatment approaches, improving patient outcomes.

Ethics

Informed Consent: Informed consent was obtained from the patient for this case report.

Authorship Contributions

Surgical and Medical Practices: B.B.K., C.A., B.S., G.U., Concept: C.A., G.U., Design: C.A., B.S., Data Collection or Processing: B.B.K., B.S., G.U., Analysis or Interpretation: B.B.K., B.S., G.U., Literature Search: B.B.K., G.U., Writing: B.B.K., C.A., B.S., G.U.

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