Is T3 appendiceal goblet cell adenocarcinoma still an oncological riddle for acute care surgeons? A case report

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Abstract

Appendectomy for acute appendicitis is one of the most commonly performed surgical procedures nowadays. Here we present the case of a 48-year-old man who was admitted to our emergency department with abdominal pain suggestive of acute appendicitis. Then, the patient underwent a laparoscopic appendectomy, and the histological examination of the surgical specimen revealed an unexpected occult neoplasm: goblet cell adenocarcinoma (GCA). After a multidisciplinary evaluation, a right colectomy was performed with good oncological and clinical outcomes at the 1-year follow-up evaluation. To date, either non-operative strategies or surgical radicalization treatment have been proposed for this condition. Therefore, the choice of the proper therapeutic algorithm is still a challenge for surgeons. This case report is an addition to the existing literature to hold surgeons’ attention when managing such cases: multidisciplinary evaluation and patient-targeted therapies are the key steps to achieving good oncological and surgical outcomes.

Introduction

Acute appendicitis is one of the most common causes of acute abdominal pain and appendectomy is one of the most performed surgical procedures in the world every year.1 Histological examination of surgical specimens could find an unexpected occult tumoral disease such as GCA.2-4 GCA is a rare neoplasm with specific histological and clinical features characterized by both exocrine and neuroendocrine differentiation.2,3 Due to this dual nature, GCA is more aggressive than other carcinomas of the gut and has a greater risk of loco-regional and peritoneal spreading that significantly affects patient survival.4 Histological features of this tumor allow many management strategies according to different interpretations of the risk of tumoral spreading. To date, no standard of care for this condition has been established. Appendectomy alone, right colectomy or cytoreductive surgery, and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) are feasible treatment options according to the grade and stage of the disease.5 Here, we present the case of a T3, stage II GCA to underline the need for multidisciplinary management to overcome the current concerns in the management of locally advanced appendiceal GCA.

Case report

A 48-year-old man was admitted in March 2022 to our emergency department complaining of pain in the right lower abdomen that had started two days before in the mesogastrium and fever (39°C). Past medical history was unremarkable. Physical examination showed abdominal tenderness in the right iliac fossa and both positive Rovsing’s and Blumberg’s signs. Blood examination showed a CRP of 12.85 mg/dL and a white blood cell count of 12,500/mm³. Laboratory tests also showed a positive leukocytosis and CRP. The patient underwent an appendectomy which was followed by a laparoscopic right colectomy with good oncological and clinical outcomes at the 1-year follow-up evaluation.
15.9×10³/L (53% polymorphonuclear neutrophils). An Appendicitis Inflammatory Response (AIR) score of 8 was calculated according to WSES guidelines. An abdominal POCUS showed a thickened appendix wall (5 mm) without abdominal free fluid. A CT scan was then performed showing an appendix with a thickened wall (8 mm) and a luminal diameter of 8 mm. Other CT findings were the presence of coprolites inside the appendix, fat stranding of the mesentery, and loco-regional lymph node enlargement (Figure 1).

An exploratory laparoscopy made the diagnosis of gangrenous appendicitis with minimal local exudate and regional pelvic peritonitis according to Gomes et al. The intraoperative evaluation confirmed the absence of an appendicular abscess and perforation. An appendectomy was performed. The specimen was handled safely to avoid any rupture and then removed with the use of a sample bag. The recovery was uneventful, and the patient was discharged on postoperative day 2. Histological examination of the appendix showed an unexpected G2, pT3, KRAS-, BRAF- Goblet Cell Adenocarcinoma with perineural invasion and clear resection margins. A colonoscopy and a thoracoabdominal CT scan were performed without any suspicious finding of synchronous primitive or metastatic disease. According to AJCC, the patient was diagnosed with a stage II neoplasm. A multidisciplinary team with the presence of a surgeon, an oncologist, and a pathologist decided to perform a right colectomy. The decision was shared with the patient who agreed with the treatment plan. A laparoscopic right colectomy was then performed about a month after the appendectomy. The recovery was uneventful, and the patient was discharged on postoperative day 5 with a return to daily activities. Histological examination of the specimen showed the absence of any residual neoplastic tissue in the right colon; no metastases were found in the 16 regional lymph nodes removed. According to the histological findings, the multidisciplinary team decided to avoid adjuvant chemotherapy and to proceed with a periodic clinical and radiological follow-up. After 1 year, the CT scan did not find any recurrence. The patient reported his satisfaction with the therapeutic pathway.

Discussion

GCA is a rare primary appendiceal neoplasm that is usually incidentally discovered following an appendectomy performed for acute appendicitis. This condition set up a double challenge for surgeons: the choice of proper treatment for appendicitis in the acute care setting and the even trickier management of a tumoral disease. We managed the case of a patient complaining of abdominal pain with an intermediate risk for acute appendicitis according to the result of the AIR score. A CT scan showed the presence of an appendicolith. This is a recognized independent risk factor for non-operative management (NOM) failure. Thus, even if in this clinical scenario and the result of the AIR score could leave the choice between NOM versus operative management to the surgeon, the presence of a CT-detected appendicolith made it necessary to perform an appendectomy. In the absence of any appendicolith, the patient would have been admitted for starting a conservative treatment, thereby delaying a surgical intervention, and leaving the diagnosis of a tumoral disease unrecognized. Acute appendicitis is often the only early clinical manifestation of appendiceal tumors, as happened in our experience. With the benefit of insight, the choice to proceed to a laparoscopic appendectomy turned out to be beneficial for the patient. As rarely happens, the histological examination of the specimen indeed uncovered an occult GCA. This diagnosis is often unexpected because the diagnostic investigation required to detect an appendiceal neoplasm is both not feasible in the emergency setting and unnecessary due to their rarity. GCA is a neoplasm with specific histological features that can exhibit both mucinous and neuroendocrine differentiation. Due to this dual nature, GCA is characterized by a wide range of possible clinical evolutions with a greater risk of loco-regional diffusion and peritoneal spreading mostly in the case of high-grade and locally advanced tumors. Although surgery plays a key role in the treatment of early-stage and organ-confined tumors, long-term survival and local recurrence are primarily determined by GCA grade and stage. The patient had a G2, T3, stage II GCA. A right colectomy seems to be mandatory according to guidelines to treat a T3 GCA but, to date, there is no consensus about the standard of care for a tumor at this stage. Real benefits from radicalization surgery and other procedures (i.e., CRS- HIPEC) still stand unexplored due to the rarity of GCA and the lack of prospective studies. According to the literature, negative surgical margins and harvesting more than 12 lymph nodes are related to improved survival. However, a recent systematic review found that T3 GCAs were N0 in 81-87% of cases. In 2021, a retrospective analysis confirmed a survival benefit for patients with a T3 GCA after a hemicolectomy with a 5-year survival rate of 85.4% in the hemicolectomy group vs 82.0% in the non-hemicolectomy group (p = 0.028). According to the literature, recurrences can also occur in patients after a radical resection: two retrospective cohort studies in 2015 found a recurrence rate of 20%-29% for patients who underwent a hemicolectomy, and a multicenter study in 2018 found a recurrence rate of 16% in patients who underwent a hemicolec­tomy and CRS-HIPEC in eight patients with localized disease presenting these criteria of high risk for peritoneal metastases: in their experience, the 5-year overall survival was 100% with a median follow-up time of 3.5 years. However, in this case, none of these criteria was present. To date, it is still unclear whether a hemicolec­tomy alone is enough to treat T3 GCA or whether CRS-HIPEC is a therapeutic option in patients without metastatic disease at onset since many of these patients may experience a disease relapse even after a hemicolec­tomy. In this case, a laparoscopic right colectomy was performed safely with a fast recovery and an uneventful postop-

Figure 1. CT scan performed at the onset of symptoms showed a thickened appendix wall with coprolites and edema of the mesentery.
ervative period. Moreover, hemicolectomy alone was effective in treating the patient’s disease without any recurrence at 1-year follow-up. CRS-HIPEC seems to improve survival, but the procedure-related complications are a major concern: a recent systematic review by Wajekar et al. reported morbidity rates between 12%-60% and a mortality rate of 0.9%-5.8%. For this reason, the use of CRS-HIPEC is currently reserved for selected patients within clinical trials at referral high-volume centers. Our experience, although a case report, demonstrates how difficult it is to define a proper therapeutic strategy in patients affected by a locally advanced appendiceal GCA without clinical and histological high-risk recurrence features. When managing such cases, a multidisciplinary evaluation can properly assess the safety and effectiveness of the different management strategies to improve patient survival.5,11

Conclusions

Appendectomy is one of the most commonly performed procedures in the emergency setting. Although rare, the sudden finding of a rare and potentially wide-spread neoplasm could represent a challenge for acute care surgeons. The presence of an underlying GCA does not change the surgical strategy in the emergency setting but a further proper assessment of the condition is mandatory to improve patients' survival. To date, different approaches have been proposed for the treatment of this condition when it presents as a T3, advanced, but organ-confined neoplasm. In our experience, right colectomy was found to be safe and effective without any recurrence at 1-year follow-up. Real benefits occurring from more invasive treatments (i.e. CRS-HIPEC) are still to be cleared. Thus, the choice of the proper treatment algorithm still represents a riddle for surgeons because a variety of treatments is affordable. In our experience, multidisciplinary management was a crucial step to properly define a tailored treatment strategy, however, further prospective studies and disease-specific consensus guidelines are required to achieve high-quality statements in the completion treatment of appendiceal GCA.

References