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CASE REPORT

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Locally advanced perforated appendiceal cancer: Case report and review

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Abstract

Appendiceal cancers may be difficult to diagnose even after comprehensive investigation. This report of locally advanced perforated appendiceal adenocarcinoma attached to the terminal ileum, cecum, and rectosigmoid illustrates the management challenges that require comprehensive knowledge of pathologic variations and range from simple appendectomy to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.

KEYWORDS

appendiceal cancer, appendiceal neoplasm, appendix, cancer, case report

1 | INTRODUCTION

The incidence of appendiceal neoplasms is 1.2 cases per 100,000 persons per year in the United States and 1%–2% of appendectomies.[1] Management of appendiceal neoplasms is challenging partly due to classification complexity. Following SCARE criteria,[2] we present a patient with locally advanced and perforated appendiceal adenocarcinoma with no signs of peritoneal, solid organ, or nodal metastases and without evidence of pseudomyxoma peritonei. To address pathologic variations and treatment algorithm inconsistencies, we also review epithelial appendiceal neoplasms based on the World Health Organization classification, current nomenclature, and clinical presentations and provide a proposed algorithm for management.

2 | CASE REPORT

A 58-year-old healthy man with no family history of colorectal cancer or inflammatory bowel disease presented to our colorectal clinic with a 6-month history of bilateral lower abdominal pain radiating to the back, 5-pound weight loss, and irregular watery bowel movements. He has one alcoholic drink per day and denied tobacco and recreational drug use. There was no nausea, vomiting, melena, hematochezia, shortness of breath, chest pain, dysuria or previous abdominal surgeries. On presentation, his vitals were normal. Physical examination revealed no abdominal tenderness, distention, or palpable masses. Stool was hemoccult negative.

2.1 | Diagnosis

Prior to the colorectal surgery clinic visit, a stool DNA test was ordered by his primary care physician and was negative. Laboratory studies were remarkable only for a carcinoembryonic antigen (CEA) level of 5.9 ng/ml. CA-125 and CA 19-9 levels were not done. Based on clinical presentation, the patient was preemptively diagnosed with irritable bowel syndrome. Colonoscopy was then performed by the gastroenterologist and revealed a long rectosigmoid stricture that required a gastroscope to negotiate. The cecum and appendiceal orifice appeared normal. Biopsies of the rectosigmoid stenosis showed no significant pathologic abnormality and were nondiagnostic. Computed tomography (CT) imaging of the abdomen and pelvis demonstrated an irregular rim-enhancing heterogeneous mass measuring 6.7 × 2.8 cm, originating from the base of the cecum and extending across the midline and tethered to the rectosigmoid junction without evidence of fistula (Figure 1). CT-guided fine-needle aspiration was unsuccessful. The patient was then referred to the colorectal surgery clinic for further evaluation.

2.2 | Differential Diagnosis

Considering patient symptoms, CT imaging, and endoscopic findings, the differential diagnosis included possible colorectal malignancy, perforated appendix with pelvic abscess formation with involvement of the rectosigmoid junction, perforated colon cancer with abscess formation, or inflammatory bowel disease with fistula and abscess formation.

2.3 | Treatment

Unable to obtain a histologic diagnosis, the patient underwent an exploratory laparotomy for concern of possible malignancy and near-obstructing rectosigmoid stricture. An abscess cavity involving the terminal ileum, distal sigmoid, and proximal rectum was identified. Mobilization of the right colon revealed a pocket of purulent material posterior to the proximal ascending colon. En-bloc resection of the terminal ileum, right colon, sigmoid, and proximal rectum was performed with two primary anastomoses (ileocolic and colorectal) and without stomas.

2.4 | Outcome

Intraoperative pelvic fluid cultures grew Streptococcus viridans, and the patient was treated with appropriate antibiotics. Pathology showed perforated appendiceal moderately differentiated adenocarcinoma with abscess formation and direct invasion of the rectum without lymph node involvement—Stage IIC T4bN0Mx, 0/34 lymph nodes (Figures 2-4). Postoperative course was unremarkable, and the patient was discharged home without complications and meeting discharge criteria.

The patient was presented at the multidisciplinary tumor board, and 6-12 cycles of systemic FOLFOX chemotherapy were recommended because of high-risk features that included T4 depth of invasion, perforation and adherence to the rectosigmoid, concern for micrometastasis, and lymphovascular invasion. However, the patient refused chemotherapy and instead opted for routine surveillance with CEA levels and CT imaging. Postoperative CEA level one month after surgery was 1.7 (from 5.9 and currently 4.3). CT of the chest/abdomen/pelvis 6 months after surgery showed no evidence of recurrence or metastasis. The patient is now 12 months since surgery without evidence of recurrent disease and training for a half marathon.

3 | DISCUSSION

The World Health Organization classification scheme divides appendiceal neoplasms into epithelial tumors,

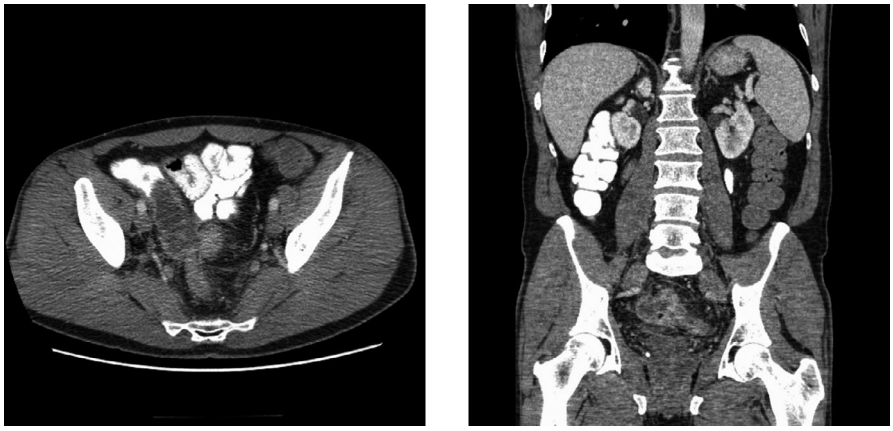

FIGURE 1 CT imaging of irregular pelvic mass arising from cecum with extension to the rectosigmoid junction

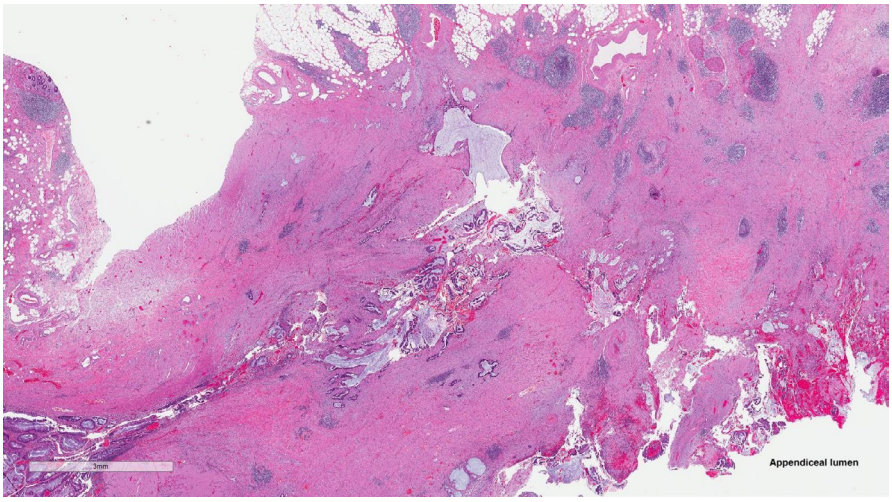

FIGURE 2 Adenocarcinoma invading through appendiceal wall (low power)

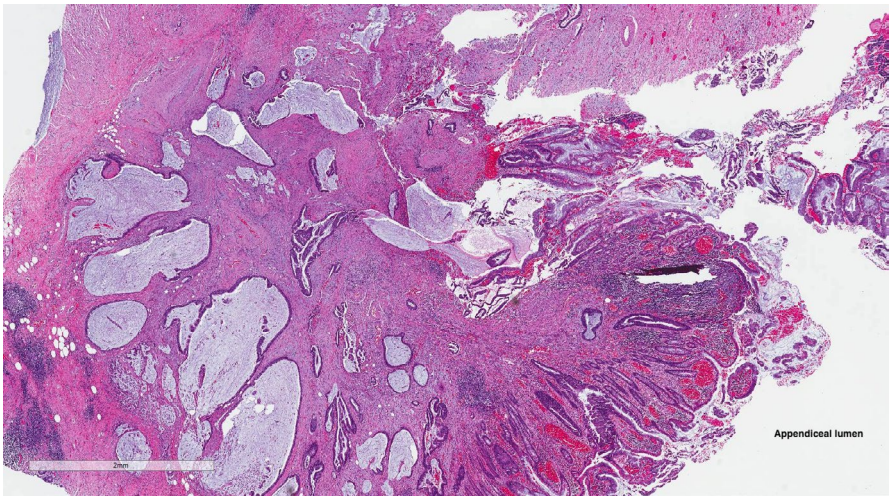

FIGURE 3 Adenocarcinoma invading through appendiceal wall (medium power)

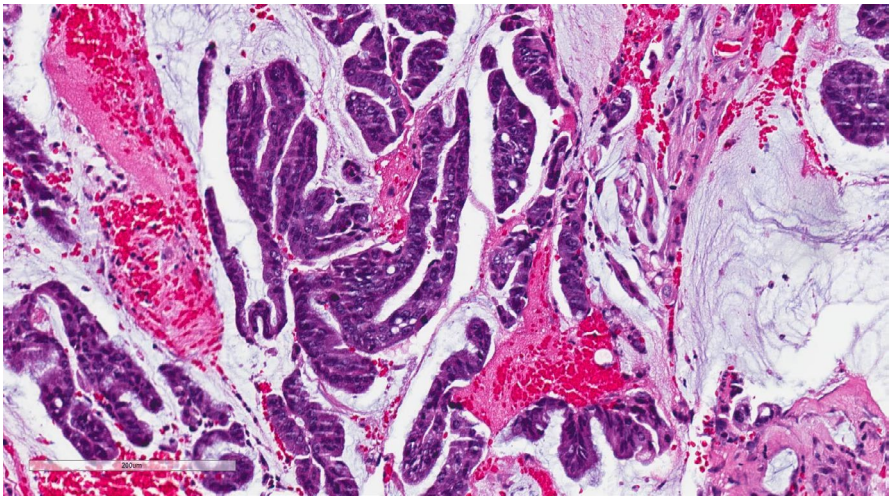

FIGURE 4 Adenocarcinoma invading through appendiceal wall (high power)

mesenchymal tumors, lymphomas, and secondary tumors. The epithelial tumors include premalignant lesions (adenomas and serrated lesions), carcinomas (mucinous adenocarcinoma, low-grade appendiceal mucinous neoplasm (LAMN), signet ring cell carcinoma, undifferentiated carcinoma), and neuroendocrine neoplasms.[2,3]

The diagnosis of appendiceal neoplasm may be challenging and requires thorough history and physical examination, laboratory studies, imaging (CT/MRI), endoscopy, and diagnostic tumor biopsy or surgery. Serum carcinoembryonic antigen (CEA) levels should be obtained as for colorectal cancers. Colonoscopy may show an

appendiceal orifice mass. Tumor markers CA-125 and CA 19-9 may be elevated in patients with appendiceal primary tumors and peritoneal disease.[4] Normal levels of CA-125 and CA 19-9 are associated with improved survival and decreased rates of recurrence.[5] CT of the chest, abdomen, and pelvis allows evaluation of the primary tumor and assessment of metastatic disease.[5] The diagnosis is often unknown prior to operative intervention for presumed appendicitis. Malignant neoplasia is identified in 2.3%–12.0% of patients having appendectomy for appendicitis. Risk factors for appendiceal cancer in this appendicitis group are older age and periappendiceal abscess.[2]

Risk factors that predispose locally invasive appendiceal adenocarcinoma to intraperitoneal dissemination and metastasis have been described.[6] One study showed that T4 depth of invasion, N2 nodal status, and mucinous tumor was associated with peritoneal metastasis.[6] Another study showed that the incidence of lymph node metastasis was associated with both larger tumor size and advanced T stage.[7] The patient described in this case report had a T4b neoplasm but had no lymph node metastases and has no evidence of metastatic disease to date.

Appendiceal adenocarcinomas occur in the 5th–7th decade with mean age 60 and are more common in men.[1] Patients may present with signs and symptoms of acute appendicitis. Adenocarcinomas may be mucinous or nonmucinous and are subclassified into adenocarcinoma not otherwise specified, mucinous adenocarcinoma, signet ring cell adenocarcinoma, and undifferentiated carcinoma.[3] Mucinous adenocarcinoma is the most common adenocarcinoma of the appendix—about 40% of all adenocarcinomas. They consist of malignant glandular mucinous epithelium within the wall of the appendix with infiltrative destructive invasion, high-grade cytologic atypia, and extracellular mucin in >50% of the neoplasm.[2,3]

Adenocarcinomas are associated with mutations of chromosome 18q, frequently have KRAS mutations, and histologically express p53, CD44, and CDX2.[3] Intraperitoneal dissemination of mucinous adenocarcinoma is similar to LAMN except that the malignant epithelium contains high-grade cytologic atypia and the mucin is more cellular.[3] Signet ring cell adenocarcinomas are rare and have a poor prognosis.[5] Nonmucinous adenocarcinomas, like that presented in this case report, behave like colonic adenocarcinomas.

Management of appendiceal neoplasms varies depending on the pathology. For appendiceal adenocarcinoma, treatment depends on whether the neoplasm has perforated and led to intraperitoneal dissemination. There is extensive literature describing ruptured appendiceal adenocarcinoma with widespread intraperitoneal mucinous ascites leading to pseudomyxoma peritonei (PMP) and peritoneal carcinomatosis. However, there are currently no standard guidelines for the management of locally invasive perforated appendiceal adenocarcinoma without PMP or intraperitoneal dissemination.[2,3]

For patients like the one presented in this case report with locally advanced perforated appendiceal adenocarcinoma without PMP or peritoneal carcinomatosis, en-bloc R0 resection, when possible, with postoperative systemic chemotherapy would likely be the best option. Surgeons should consider the clinical context of patient presentation with all available information, especially when histologic confirmation of malignancy is not possible, and be prepared for multivisceral resection when indicated.

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CONFLICT OF INTEREST

Samik H. Patel MD, Sharon Bihlmeyer, John C. Eggenberger MD, and Beth-Ann Shanker MD have no conflict of interest to report. Robert K. Cleary has no conflict of interest to report related to this research. He has received honoraria from Intuitive Surgical, Inc. for educational speaking.

AUTHOR CONTRIBUTIONS

Samik H Patel MD: substantially contributed to the design of the work and analysis and interpretation of data for the work; drafted the work or revising it critically for important intellectual content; and involved in final approval of the version to be published and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Sharon Bihlmeyer MD: substantially contributed to the interpretation of data for the work; drafted the work or revising it critically for important intellectual content; and involved in final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. John C Eggenberger MD: substantially contributed to the design of the work; drafted the work or revising it critically for important intellectual content; and involved in final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Beth-Ann Shanker MD: substantially contributed to the design of the work; drafted the work or revising it critically for important intellectual content; and involved in final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and

resolved. Robert K Cleary MD: substantially contributed to the design of the work and analysis and interpretation of data for the work; drafted the work or revising it critically for important intellectual content; and involved in final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

All of the data is included in this report.

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