JAMA Clinical Challenge

Abdominal Pain and an Appendiceal Mass

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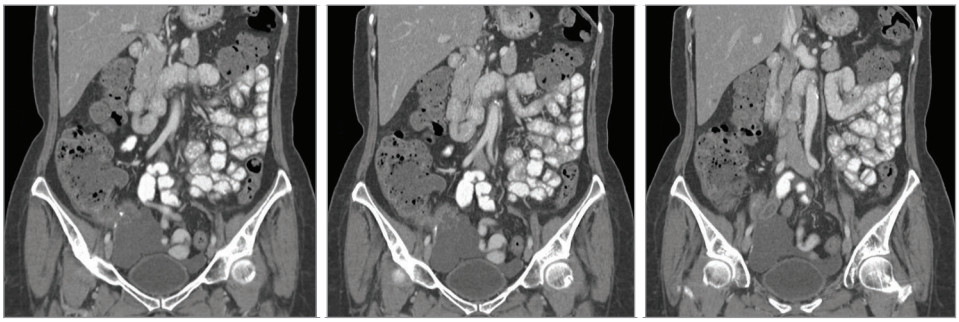

Figure 1. Computed tomography imaging on presentation.

A 68-year-old woman with a history of uterine carcinoma (unknown histology) diagnosed and treated 30 years prior with hysterectomy and adjuvant chemotherapy in another country presented with 2 months of generalized abdominal pain and distention. She had no fevers, nausea, vomiting, diarrhea, constipation, blood in the stool, or weight loss. She was not taking any medications. On examination, her temperature was 36.9 °C; heart rate, 72/min; blood pressure, 132/68 mm Hg; and body mass index, 25 (calculated as weight in kilograms divided by height in meters squared). Results of complete blood cell count and serum chemistries were unremarkable, with no leukocytosis and normal differential count. Abdominal examination demonstrated mild distention without fluid wave and mild right lower abdomen and suprapubic tenderness. Computed tomography (**Figure 1**) and magnetic resonance imaging demonstrated pelvic ascites and an enhancing lesion at the base of the cecum. Two attempts at ultrasound-guided paracentesis were nondiagnostic because of acellular specimens. Serum CA-125 level was normal; carcinoembryonic antigen (CEA) level was 18 ng/mL (reference, <5 ng/mL).

WHAT WOULD YOU DO NEXT?

A. Perform laparoscopic appendectomy and peritoneal biopsy

B. Order repeat image-guided paracentesis/cytology

C. Order colonoscopy with biopsy

D. Order broad-spectrum antibiotics to cover gram-negative and anaerobic enteric species

Diagnosis

Appendiceal mucinous neoplasm (AMN)

What to Do Next

A. Perform laparoscopic appendectomy and peritoneal biopsy

The key to the likely diagnosis in this case is the presence of an appendiceal mass with a subacute presentation of symptoms. Of the choices listed, appendectomy with peritoneal biopsy is the most appropriate next step, as it will provide a definitive diagnosis. Repeat aspiration with cytology (choice B) is unlikely to yield the diagnosis, as the fluid is typically hypocellular and too viscous to aspirate. Colonoscopy (choice C) may demonstrate an extrinsic bulge at the appendiceal orifice, but biopsies of the appendiceal mucosa are not generally feasible via colonoscopy. Treatment with antibiotics (choice D) is inappropriate given the subacute presentation, lack of infectious symptoms, and imaging concern for neoplasia.

This patient underwent an exploratory laparoscopy with appendectomy and omental biopsy. Findings showed a ruptured AMN with pseudomyxoma peritonei (PMP). Pathology demonstrated low-grade appendiceal mucinous neoplasm (LAMN), a negative proximal margin, and cellular mucin involving the omentum (**Figure 2**).

Discussion

The differential diagnosis of a cystic or mass lesion of the appendix includes acute or chronic appendicitis, mucinous tumor (AMN, sessile serrated adenoma), benign simple cyst (mesenteric, enteric duplication), mesodermal tumors (leiomyoma, neuroma, lipoma), neuroendocrine tumor (formerly carcinoid), goblet cell adenocarcinoma, adenocarcinoma, and mixed-histology cancers. Any of these lesions can present symptomatically, often mimicking appendicitis, and can thus be difficult to diagnose preoperatively. Increasingly, lesions of the appendix are identified on workup of nonspecific

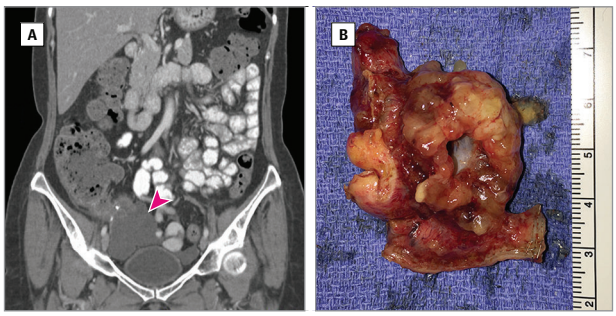

Figure 2. A, Computed tomography image on presentation (same as Figure 1, left panel), showing pelvic ascites and enhancing lesion in the right lower quadrant at the base of the cecum (arrowhead). B, Surgical specimen of low-grade appendiceal mucinous neoplasm. Scale increments = 1 cm.

symptoms (as in this case) or incidentally on cross-sectional imaging performed for other reasons.[1]

In the setting of acute appendicitis, urgent appendectomy is warranted. For subacute and incidental presentations, establishing a diagnosis prior to definitive treatment is important, as treatment varies depending on the diagnosis. Diagnostic workup includes serum chemistries, blood cell counts, and cross-sectional imaging. Typical imaging findings of AMNs include a markedly dilated and fluid-filled appendix, minimal or absent surrounding inflammatory stranding with or without abdominal or pelvic free fluid, and infiltration of the omentum, depending on the presence of PMP. Solid tumors (neuroendocrine tumor, goblet cell adenocarcinoma, adenocarcinoma) may be associated with mesenteric adenopathy and evidence of carcinomatosis (ascites, omental caking, peritoneal nodularity).

At laparoscopy, a detailed survey of the entire abdomen and pelvis is performed to evaluate the extent of peritoneal involvement, followed by a biopsy of omentum or peritoneal tissue along with appendectomy. Serum tumor markers including CEA, CA-125, and CA19-9 are prognostic when PMP is present but are not necessary prior to establishing the diagnosis. An elevated CEA level can predict recurrent PMP when there is subclinical histologic extravasation of mucin from a grossly unruptured LAMN.[2]

Appendiceal tumors are an incidental finding in approximately 1% of acute appendicitis specimens, and treatment and prognosis are highly dependent on tumor histology and stage.[3] AMNs have an incidence of 3/1 000 000[4] and their clinical behavior varies, from nonruptured LAMNs with no risk for lymph node metastasis, dissemination, or recurrence following appendectomy to high-grade mucinous adenocarcinomas typified by aggressive local tissue infiltration and widespread metastasis. As a result, the treatment of AMNs is decided by pathologic determinants and the presence and extent of peritoneal dissemination.

For PMP from a ruptured LAMN, cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemoperfusion (HIPEC) are definitive therapy[5]; systemic chemotherapy is contraindicated. Posttreatment surveillance is indicated, and recurrences are typically managed with repeat CRS-HIPEC. Perioperative morbidity such as anastomotic leakage, intra-abdominal abscess, and wound complications is considerable (8%-41%),[6,7] but mortality is rare (approximately <2%) at experienced centers.[7] For appendiceal mucinous adenocarcinomas and goblet cell adenocarcinomas with high-grade histology, systemic multiagent chemotherapy is first-line therapy and CRS-HIPEC is applied selectively. In choosing the correct treatment, a definitive histologic diagnosis is necessary prior to more aggressive therapies such as chemotherapy or right hemicolectomy. In general, initial right hemicolectomy is not warranted because appendectomy is less morbid and potentially curative for many lesions (AMNs, many neuroendocrine tumors, benign cysts, leiomyomas.) If indicated, hemicolectomy can be safely performed at a second operation.

Patient Outcome

The patient underwent CRS-HIPEC at a second operation with an uneventful recovery. Four years after surgery, she is asymptomatic and clinically free of disease. She continues to have annual clinical follow-up, serum CEA measurement, and surveillance imaging.

ARTICLE INFORMATION

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Submissions: We encourage authors to submit papers for consideration as a JAMA Clinical Challenge. Please contact Dr McDermott at mdm608@northwestern.edu.

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