Diarrhea Concealing a Duodenal-Cecal Fistula Secondary to Appendiceal Mucinous Neoplasm

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ABSTRACT

Primary mucinous adenocarcinoma of the appendix is a rare gastrointestinal malignancy. Fistulous tract formation is a complication that is cited in literature. An 85-year-old man with multiple comorbidities presented with several weeks of persistent non-bloody diarrhea. Laboratory work-up was non-diagnostic. Abdominal imaging with barium contrast showed an enterocolonic fistulous tract extending from the duodenum to the cecum involving an enlarged appendiceal mass. Subsequent biopsy confirmed mucinous appendiceal neoplasm with peritoneal spread to the liver and mesentery. This is the first report describing an enterocolonic fistula formation resulting from this malignancy.

INTRODUCTION

Primary appendiceal neoplasms are rare, accounting for less than 0.5% of all gastrointestinal (GI) malignances.[1-3] The most common clinical presentation is acute appendicitis.[4] Typically, this type of tumor is incidentally diagnosed at the time of operation or once it has progressed with mucinous implants in other abdominal organs or the peritoneum leading to mucinous ascites, known as pseudomyxoma peritonei. Isolated case reports have been published describing fistula formations on the skin, bladder, vagina, and colon secondary to this rare malignancy. This is the first report of mucinous appendiceal neoplasm presenting with an enterocolonic fistula.

CASE REPORT

An 84-year-old man presented to the hospital after 3 weeks of diarrhea. He appeared healthy and had stable vital signs. He had an unremarkable abdominal exam, including the absence of tenderness to palpation, palpable masses, and peritoneal signs. He was able to ambulate without assistance and did not exhibit any weakness, tremors, abnormal reflexes, or neurological deficits.

The patient had a history of chronic myelogenous leukemia in molecular remission, interstitial lung disease, coronary artery disease, chronic kidney disease, hypertension, and lumbar back disease. He reported liquid bowel movements occurring two to four times per hour with occasional stool incontinence. He described a concomitant 4.5-kg weight loss in the month prior to presentation. A full review of systems was otherwise negative, including the absence of hematochezia, melena, nausea, vomiting, abdominal pain, fevers, chills, or appetite change. He reported no recent travel, unusual food ingestion, or new environmental exposures. He lived with his wife, who did not have similar symptoms.

One year prior to this presentation the patient had a surveillance colonoscopy, which was performed despite his relatively advanced age as he was otherwise healthy and had a personal history of high-risk polyps. Remarkable findings on that colonoscopy included two 3–4 mm sessile polyps in the ascending and sigmoid colon,

Figure 1. Focal erythematous patch at the appendiceal orifice seen on colonoscopy 1 year prior to presentation.

diverticulosis, and a focal patch of erythematous mucosa at the appendiceal orifice (Figure 1). The polyps were removed with cold biopsy forceps and pathologic examination showed colonic mucosa with focal hyperplastic changes. Biopsies from the abnormal mucosa at the appendiceal orifice revealed a mildly active focal chronic colitis. At that time, clinical suspicion for inflammatory bowel disease was low because laboratory workup did not show elevated inflammatory markers or abnormal blood counts, and the patient was asymptomatic, specifically denying diarrhea, blood in stool, or weight loss.

**Figure 2.** Endoscopic view of appendiceal lumen showing ulcerated mucosa.

Figure 3. Computed tomography of the abdomen demonstrating a midline appendiceal mass extending superiorly and communicating with the proximal bowel.

A detailed infectious workup was unremarkable including negative results for stool cultures, *Clostridium difficile* toxin, Giardia, parasite exam, and cytomegalovirus culture. Inflammatory stool markers including leukocytes, lactoferrin, and calprotectin were unremarkable. Calculated stool osmotic gap was elevated at 156 mOsm/kg. Stool pH was low at 4.5. Both neutral and split fecal fat products were elevated.

The patient was taking imatinib for 5 years to treat chronic myelogenic leukemia with no prior adverse effects. Nonetheless, given the potential side effect profile, the medication was discontinued. He was taking doxycycline for a dermatological condition, but this too was discontinued. Despite these medication changes and the regular use of loperamide, the patient had no relief in the frequency or volume of liquid bowel movements.

The current presentation with diarrhea was the first time in the ensuing year that the patient reported any symptoms to suggest a need for repeat colon evaluation. Diagnostic colonoscopy was notable for severely ulcerated nonbleeding mucosa within an enlarged appendiceal orifice (Figure 2). Biopsies obtained from this region at the time of the colonoscopy were nondiagnostic, showing only necrotic tissue.
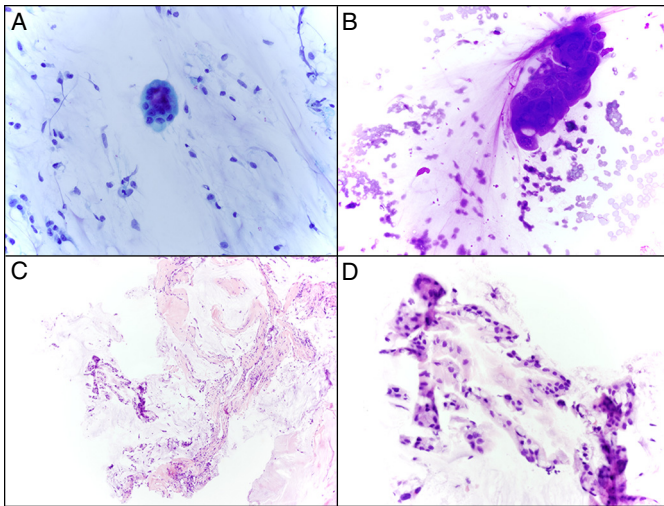
Figure 4. Cytopathology and histopathology of the peritoneal implant showing clusters of epithelial cells of low-grade mucinous neoplasm in a thick mucinous background. (A) Papanicolaou stain, 400x. (B) Diff-quick stain, 400x. (C) Hematoxylin and eosin stain, 100x. (D) Hematoxylin and eosin stain, 400x.

Subsequent evaluation with computed tomography imaging revealed a midline abdominal mass measuring 7.6 cm in its largest dimension. It appeared to lie inferiorly to the duodenum and superiorly to the colon (Figure 3). There were fluid collections adjacent to the liver as well as the mesentery. Interventional radiology performed fine-needle aspirations and core biopsies of the peritoneal lesions. The histopathology and cytopathology findings were consistent with a low-grade mucinous neoplasm originating from the appendix with pseudomyxoma peritonei syndrome (Figure 4).

The computed tomography scan further suggested communication between the appendiceal mass and the proximal small intestine and colon. This abnormal anatomy explained the patient's persistent diarrhea. A small-bowel follow-through demonstrated a fistulous communication from the third portion of the duodenum to the cecum (Figure 5).

The duodenal-cecal fistula allowed contents to bypass nearly the entire small intestine, which explained the elevation of the stool osmotic gap. Small bowel fistula formation additionally increases the risk for small intestinal bacterial overgrowth and fat malabsorption. Therefore, the low stool pH and increased fecal fat products can be explained by the patient's unusual anatomy.

Medical oncology and surgical oncology were consulted to discuss treatment options. Due to the patient's advanced age and comorbidities as well as the relatively slow growth of this type of tumor, the patient opted to forgo both surgical intervention and treatment with chemotherapy. He was managed symptomatically with antidiarrheal agents and antibiotics for bacterial overgrowth.
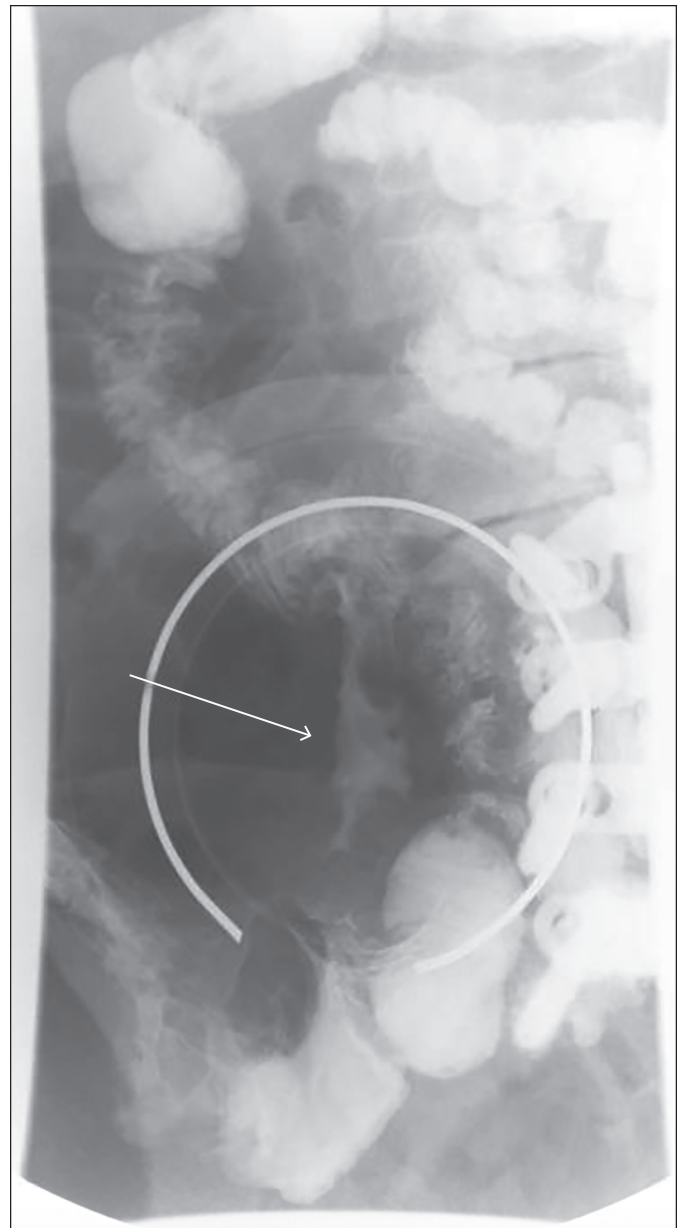
Figure 5. Small bowel follow-through demonstrating a fistulous tract extending from the third part of the duodenum to the cecum.

DISCUSSION

Malignancies of the appendix are rare, with a reported incidence of 0.12 cases per 1,000,000 people per year based on population data from the SEER program.[1-3] Primary neoplasm of the appendix constitutes less than 0.5% of all GI neoplasms,[2] and the most common histologic type is mucinous neoplasm, accounting for more than one-third of these cases.[1]

The diagnosis of appendiceal mucinous neoplasm is challenging, and preoperative diagnosis is rarely made. Abdominal imaging may show a right lower quadrant soft-tissue mass with curvilinear mural calcification, but this finding is evident in less

than half of cases.[4] The diagnosis is often made at the time of operation because the most common clinical presentation is luminal obstruction leading to acute appendicitis.[5,6] Other reported presentations include appendicular abscess, palpable abdominal mass, intestinal obstruction, and intussusception.[4] Pseudomyxoma peritonei may be seen as the disease progresses with mucocele rupture or transmural extension.[7]

Mucinous appendiceal neoplasm follows an indolent and progressive course, eventually leading to mortality secondary to lymph node and solid organ metastasis. Implantation of mucinous material into the peritoneum is an uncommon condition known as pseudomyxoma peritonei.[4] Fistula formation as a complication of primary mucinous appendiceal neoplasm is rare. A number of case reports have been published within the past several decades describing various types of fistulous tracts. The most common organs involved include skin,[8-12] bladder,[13-20] vagina,[21,22] and colon.[23,24] In the majority of the cases reviewed, patients were symptomatic from the fistula formation, and this eventually led to the diagnosis of appendiceal mucinous neoplasm upon further investigation via imaging, endoscopy, or surgical exploration. History of abdominal surgery was a prevailing risk factor for development of a fistulous tract in these case reports and is known to be the most common cause for fistulas in the GI tract, accounting for up to 85% of cases.[25] Other causes for spontaneous fistula formation in the GI tract include inflammatory diseases (including inflammatory bowel disease, diverticular disease, appendicitis, and peptic ulcer disease), infection, malignancy, and radiation exposure. Medications with antiangiogenic properties, including tyrosine kinase inhibitors like imatinib, have been reported to cause decreased blood supply to large tumors resulting in tumor necrosis, perforation, and fistula formation.[26] The incidence of this phenomenon is unknown given its relatively rare occurrence.

The recommended treatment for mucinous appendiceal neoplasm varies on the extent of the malignancy. Patients with low-grade histology have a predicted 5-year survival rate of 75%.[4] The recommended treatment for mucinous appendiceal neoplasm is a right hemicolectomy.[5] Mucinous ascites (pseudomyxoma peritonei) is a late finding, presence of which necessitates more aggressive therapy with surgical debulking followed by intraperitoneal and/or systemic chemotherapy.[6]

DISCLOSURES

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