A 40-Year-Old Man with Intermittent Right Lower Quadrant Pain and Increasing Abdominal Girth

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CASE PRESENTATION

Initial Presentation and History

A 40-year-old man presented with a 4-month history of intermittent right lower quadrant abdominal pain associated with increasing abdominal girth, early satiety, loose stools, unintentional weight loss of 20 lb, and generalized fatigue. He denied episodes of nausea, vomiting, melena, hematochezia, or fever. The patient's past medical history was significant only for an inguinal hernia repair 10 years earlier. He worked as a groundskeeper and reported being in excellent physical condition. He acknowledged that he had previously been a heavy drinker of alcohol, but he quit consuming alcohol 6 months prior to presentation. He denied illicit drug or tobacco use, medication use, recent travel, or a family history of significant medical conditions.

Physical Examination

On physical examination, the patient had normal vital signs. He appeared to be in no physical distress but did exhibit bitemporal wasting. Sclerae were anicteric, lungs were clear to auscultation, and heart rhythm and sounds were normal. Bowel sounds were present and normal. The patient's abdomen was moderately distended and dull to percussion, with mild tenderness evoked upon palpation of the right lower quadrant. Rebound and guarding were absent, but a fluid wave and shifting dullness were both present. Two enlarged lymph nodes were palpated in the right inguinal region. Brown, hemoccult-negative stool was present in the rectal vault.

Diagnostic Studies

Laboratory studies and complete blood count were ordered. Hemoglobin was 10.8 g/dL (normal, 13.5–17 g/dL), iron was 15 µg/dL (normal, 60–150 µg/dL), and total iron binding capacity was 206 µg/dL (normal, 250–400 µg/dL), which was indicative of mild iron-deficiency anemia. The white blood cell count, platelet count, transaminases, bilirubin, amylase, lipase, coagulation studies, and urinalysis were all within normal limits. Albumin was slightly low at 3.3 g/dL (normal, 3.9–5.0 g/dL). Levels of carcinoembryonic antigen (CEA) and cancer antigen (CA) 19-9 were elevated at 91.5 ng/mL (normal, 0–5 ng/mL) and 470.0 ng/mL (normal, 0–15.8 ng/mL), respectively. A plain radiograph of the abdomen was unremarkable. Computed tomography (CT) showed extensive septated ascites throughout the abdomen, with scalloping of the liver margin and omental thickening. Also noted was a thickened tubular structure in the area of the appendix (**Figure 1**).

Bedside paracentesis was attempted but no abdominal fluid was recovered, most likely due to the viscosity of the fluid. Ultrasound-guided paracentesis using a 20-gauge needle was then attempted, which again failed to obtain fluid despite the position of the needle being confirmed in the ascites. Finally, an omental biopsy was successfully performed by an interventional radiologist. The fluid from this procedure revealed numerous neoplastic cells floating in pools of mucin (**Figure 2**).

WHAT IS YOUR DIAGNOSIS?

(A) Acute appendicitis
(B) Carcinoid tumor of the appendix
(C) Cirrhosis with ascites
(D) Disseminated echinococcal disease
(E) Pseudomyxoma peritonei

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ANSWER

The correct answer is (E), pseudomyxoma peritonei (PMP).

DISCUSSION

The patient's presentation, physical examination, laboratory data, and imaging studies were all consistent with a presumptive diagnosis of PMP. Although disseminated echinococcal disease can cause septated ascites, a primary cystic lesion (hydatid cyst) is usually seen in the liver.[1] The patient's laboratory study results and the presence of septated ascites fluid were not consistent with the diagnosis of cirrhosis, nor did his liver appear to be cirrhotic on imaging.[2] Acute appendicitis would demonstrate an inflamed appendix on CT imaging, and is associated with fever, an elevated white blood cell count, and a more abrupt time course.[3] A carcinoid tumor of the appendix can present with many of the constitutional symptoms experienced by the case patient in addition to an enlarged appendix on imaging.[4] However, it is not associated with septated ascites or scalloping of the liver margin. Finally, the presence of mucinous ascites with neoplastic cells confirms the diagnosis of PMP.[5]

CLINICAL COURSE OF THE CASE PATIENT

The case patient underwent an exploratory laparotomy, which revealed massive amounts of gelatinous material throughout the abdomen (**Figure 3**). Tumor cells were affixed to the stomach, liver, small bowel, and peritoneal walls, and an appendiceal mass was palpated. The appendiceal mass was resected via an ileal cecectomy with primary anastomosis. In addition, omentectomy and splenectomy were performed. Due to the extent of PMP, complete cytoreduction was not possible. Pathologic examination revealed a well-differentiated, low-grade mucinous cystadenocarcinoma of the appendix (**Figure 4**). Mucin was noted to be exuding through a perforation in the appendiceal wall. The patient underwent perioperative intraperitoneal chemotherapy (PIC) with 5-fluorouracil and mitomycin-C.

Two years after his initial presentation, the patient continued to be asymptomatic and reported feeling well. However, follow-up CT scans demonstrated recurrence of abdominal fluid collection. CEA and CA 19-9 levels, which had significantly decreased after surgery and PIC, were rising again. The patient was scheduled for close follow-up, as he eventually will require repeat debulking surgery and possibly additional chemotherapy.

PSEUDOMYXOMA PERITONEI

PMP (literally, "false mucinous tumor of the peritoneum") is a rare condition that was first described by Werth[6] in 1884. PMP has an estimated incidence of 1 case per million persons annually.[7] The characteristic feature of PMP is large quantities of mucinous ascites, which is often referred to as "jelly belly."[7,8] PMP is the clinical term used to describe this condition, but it does not specify the underlying lesion responsible for the mucinous ascites. In most cases, the lesion is a slow-growing but progressive appendiceal neoplasm. As the tumor enlarges, it obstructs the lumen of the appendix, thus causing perforation.[5] As a result, mucin-producing neoplastic cells are disseminated throughout the peritoneal cavity where they produce copious amounts of mucin, which accumulates due to gravity in various areas of the abdomen. Most of these tumors are minimally aggressive, rarely metastasize, and tend to remain confined to the peritoneum.[5] If not treated, patients slowly develop terminal starvation due to abdominal distention and increased tumor volume.[5]

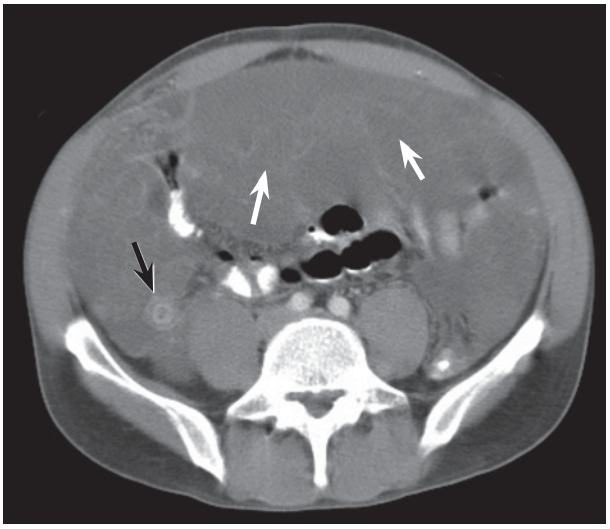

Figure 1. Computed tomography demonstrating massive amounts of septated ascites (*white arrows*) and a tubular appendiceal structure (*black arrow*).

Although PMP is most commonly associated with an appendiceal tumor, it may also arise from other sites. Recent studies have shown that ovarian lesions, previously thought to be even more common than appendiceal lesions, are likely due to metastatic spread from an appendiceal primary site.[8,9] Rare cases have also been reported to arise from tumors in the colon, rectum, pancreas, stomach, small bowel, gallbladder and bile ducts, lung, breast, fallopian tubes, urachus, and urinary bladder.[10]

As PMP is a clinical term, various classification systems have been devised to categorize this entity by its

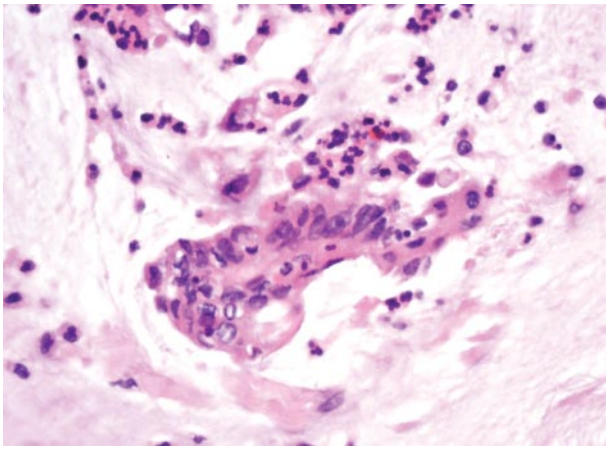

Figure 2. Neoplastic cells isolated from abdominal fluid (obtained via paracentesis) floating in pools of mucin (hematoxylin and eosin, 400×).

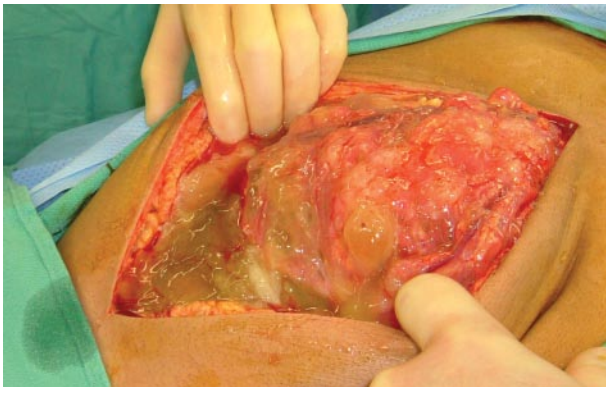

Figure 3. Laparotomy revealing large quantities of intraperitoneal mucinous material ("jelly belly").

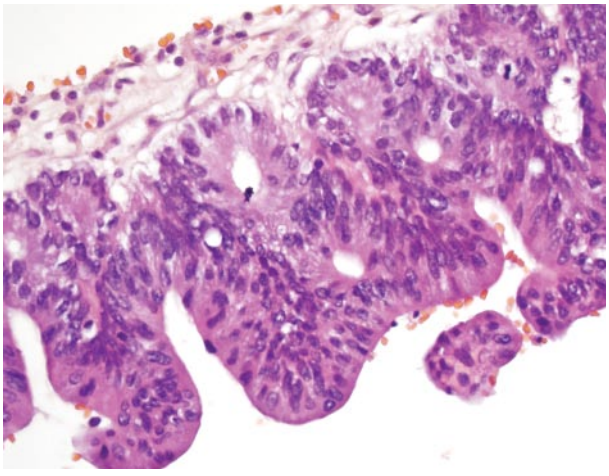

Figure 4. Histopathology showing a well-differentiated mucinous cystadenocarcinoma of the appendix (hematoxylin and eosin, 400×).

pathologic findings. In a landmark paper, Ronnett et al[11] described 3 categories: disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis (PMCA), and peritoneal mucinous carcinomatosis-intermediate (PMCA-I). DPAM is characterized by PMP containing epithelial cells with little cytologic atypia or mitotic activity, whereas PMCA contains more abundant mucinous epithelial cells with the architectural and cytologic features of carcinoma. PMCA-I, as the name suggests, is an intermediate group that contains peritoneal lesions most consistent with DPAM but has focal areas of mucinous carcinoma consistent with PMCA. Ronnett et al[11,12] found that this classification system predicted mortality, with DPAM having the best survival, followed by PMCA-I and PMCA. Bradley et al[13] applied this classification to their patient cohort and found that PMCA-I patients had the same survival as DPAM patients. As a result, they suggested merging DPAM and PMCA-I into a single group and proposed a simplified classification system with 2 categories: high-grade mucinous carcinoma peritonei (MCP-H) and low-grade mucinous carcinoma peritonei (MCP-L). These differing pathologic classifications have understandably created a great deal of confusion and contention in the medical literature.[14] Further adding to the confusion is a debate about whether the term PMP should be used only in reference to mucinous spread from low-grade appendiceal lesions (whether it is called DPAM or MCP-L) or in reference to the whole spectrum of lesions regardless of pathologic grade. Ronnett et al[12] have suggested limiting the term PMP to DPAM cases, given the more benign nature of this entity. However, this opinion has not been fully accepted, and it remains an area of debate.

Disease Manifestations and Diagnosis

Asymptomatic cases of PMP may be found incidentally during surgery and are estimated to occur in approximately 2 out of every 10,000 laparotomies.[9] When patients develop symptomatic disease, they most commonly present with suspected appendicitis (27%), increased abdominal girth (23%), an ovarian mass (20% of female patients), or a new hernia (14%),[15] which are not specific for PMP. On laboratory evaluation, patients often have elevated tumor markers. CEA is elevated in 56% to 75% of cases, and CA 19-9 is elevated in 58% to 67% of cases.[16,17] Normal levels at presentation may predict improved survival,[16] and elevated levels after treatment may predict recurrence and a worse outcome.[17]

In patients who present with increased abdominal girth and ascites and in whom PMP is suspected, an

abdominal CT scan is an important diagnostic tool.[18] As the amount of mucinous fluid increases in PMP, the attenuation of the fluid also increases. The pattern of fluid accumulation is predictable since it follows the normal flow of peritoneal fluid. Scalloping of the liver and other visceral surfaces, septae, curvilinear calcifications, and displacement of the small bowel are common features. Although an appendiceal lesion is evident on the CT scan of the case patient (Figure 1), such lesions are rarely identified.[14]

In a patient with typical symptoms and classic CT findings, a presumptive diagnosis of PMP may be conferred safely.[15,18] However, PMP can only be definitively established with a pathologic examination, either by paracentesis fluid analysis or at surgery. Paracentesis fluid typically shows bland neoplastic cells in mucinous material, which are often described by pathologists as floating in pools of mucin (Figure 2).[13,14]

Management

Classically, treatment for PMP is debulking surgery repeated as often as necessary to relieve obstructive symptoms.[5] However, this is rarely a definitive procedure and some residual disease is left behind, assuring that the patient will require repeated surgeries. Repeat surgeries become increasingly complicated given the altered anatomy, formation of adhesions, and recurrent nature of the disease. Ultimately, surgical intervention fails to be a viable option. Patients eventually die from intestinal obstruction, terminal starvation, or surgical complications, with a 5-year survival of less than 10% for high-grade PMP and approximately 50% for low-grade PMP.[5,13] Several uncontrolled, retrospective case series assessing the efficacy of systemic chemotherapy administered after surgical resection have failed to show a benefit.[9] In 1 case report, radiation therapy was used after surgical resection, but no other studies have evaluated this treatment modality.[9]

Some centers now attempt comprehensive treatment through the combination of cytoreductive surgery (CRS) and PIC.[19,20] The goal of CRS is to remove all visible lesions, tumor implants, and ascites, while also lysing all abdominal adhesions. This goal is accomplished by visceral resections and peritonectomy procedures.[19] These procedures allow for PIC, in which the chemotherapy is directly introduced into the peritoneal cavity via catheters implanted during surgery, to gain direct contact with any residual tumor cells. PIC is usually composed of 5-fluorouracil and mitomycin-C. Mitomycin-C is often heated as hyperthermia has been shown to potentiate chemotherapeutic penetration and cytotoxicity.[9] Although CRS-PIC is an intense therapeutic regimen, it does not appear to be associated with increased morbidity or a decreased quality of life.[5,21]

As PMP is a rare disease, all treatment studies, either with the classic debulking method or with CRS-PIC, have been observational without a comparison group. A recent meta-analysis of 863 patients undergoing combined CRS-PIC demonstrated improved survival as compared with historical controls.[5] One-year survival rates for low-grade PMP varied from 80% to 100%, with 5-year survival at 52% to 96%.[5] In another recent study involving 101 patients who were treated with CRS-PIC, 5-year survival was reported as 37.7% for high-grade PMP (23 patients) and 62.5% for low-grade PMP (78 patients).[12] Although these survival benefits with combination CRS-PIC are encouraging, they have been demonstrated in only a few centers. The question of its benefit remains controversial, and randomized controlled studies are needed.

CONCLUSION

PMP is a rare disease characterized by the accumulation of mucinous ascites in the abdomen, which usually originate from a slow-growing appendiceal neoplasm.[8] Patients most commonly present with either suspected appendicitis or increased abdominal girth.[15] The definitive diagnosis is made by pathologic examination; high-grade lesions are associated with poorer prognosis.[13,14] Treatment is surgical, with the newer combined approach of CRS-PIC possibly becoming the new standard of care. **HP**

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