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CASE REPORT

Incidentally discovered low-grade appendiceal mucinous neoplasm: a precursor to pseudomyxoma peritonei

Vennila Padmanaban[1], William F. Morano[1], Elizabeth Gleeson[1], Anshu Aggarwal[1], Beth L. Mapow[2], David E. Stein[1] & Wilbur B. Bowne[1]

[1]Department Of Surgery, Drexel University College Of Medicine, Philadelphia, Pennsylvania, USA
[2]Department of Pathology & Laboratory Medicine, Drexel University College of Medicine, Philadelphia, Pennsylvania, USA

Correspondence
Wilbur B. Bowne, Department Of Surgery, Drexel University College of Medicine, 245 N. 15th Street, Suite 7150, Philadelphia, PA 19102, USA. Tel: 215-762-1647; Fax: 215-762-8389; E-mail: wilbur.bowne@drexelmed.edu

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Key Clinical Message

Appendiceal mucoceles (AMs) infrequently arise from an underlying malignancy. Treatment has progressed toward a less aggressive approach over time; they can be managed by appendectomy-only unless pathology reveals malignancy. The ultimate goal of management is to prevent AM rupture, avoiding the syndrome of pseudomyxoma peritonei.

Keywords

Appendiceal mucinous neoplasm, appendix, mucinous cystadenoma, mucocele, pseudomyxoma peritonei.

Introduction

Appendiceal mucocele (AM), first described in 1842 by Rokitansky, is a rare dilation of the appendiceal lumen secondary to the accumulation of mucinous secretions [1]. The incidence is 0.2–0.3% of all appendectomies and most often presents as an incidental finding in asymptomatic patients [2]. Appendiceal mucoceles have a predilection for females above the age of 50 and merit inclusion in the differential diagnosis of acute or chronic right lower quadrant abdominal pain [2–4]. Less frequently, patients may present with acute appendicitis or abdominal fullness with an associated mass in the iliac fossa. Although typically nonspecific, patients may experience nausea, vomiting, changes in bowel habits or complete obstipation, and weight loss. The presence of symptoms may be associated with AM rupture and underlying malignancy [4, 5].

There are four types of AMs, defined by the cause of obstruction, both benign and malignant: retention cysts, epithelial hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma. The latter two represent neoplastic processes, with cystadenomas typically referred to as low-grade appendiceal mucinous neoplasms (LAMNs) [6]. Complications of mucoceles include intussusception into the cecum, ureteral obstruction, volvulus and small bowel obstruction, or rupture with eventual presentation as acute abdomen [7, 8]. The appendix may also torse or become gangrenous [9]. The most feared complication, occurring secondary to natural or iatrogenic rupture, is pseudomyxoma peritonei (PMP), an accumulation of mucinous ascites within the abdomen and pelvis. PMP is poorly understood; however, it is known to develop insidiously as a result of mucin-producing, neoplastic, epithelial goblet cells forming mucinous implants throughout the abdominopelvic peritoneum [5, 6, 10]. PMP commonly recurs after surgical removal and is associated with significant morbidity and mortality [10]. Definitive therapy for AMs is controversial, although requires surgery. There is presently a lack of consensus regarding the appropriate management, extent of surgery, and type of surgery (open vs. laparoscopic). Here, we

present the case of an incidentally discovered appendiceal mucocele in a 66-year-old woman, whom subsequently underwent open ileocecectomy. The patient's diagnosis and course of treatment underscores the various unresolved questions in today's inconsistent practice for treating AMs.

Case Presentation

A 66-year-old Caucasian woman presented to an outside hospital for mild weight loss and fatigue. The patient denied abdominal pain or other symptoms. Laboratory results, including BMP and CBC, were within normal limits. She underwent a noncontrast CT of the abdomen and pelvis, which revealed an appendiceal mass. She subsequently underwent abdominal ultrasound, which displayed a complex cystic mass suspicious for AM. At this point, the patient was referred to our institution for surgical intervention. Further contrast-enhanced cross-sectional imaging verified findings consistent with an AM (Fig. 1).

Laparotomy revealed a distended appendix (8 × 4 cm), which was consistent with the clinical diagnosis of an AM, with no evidence of gross perforation (Fig. 2). Close inspection of the small bowel and peritoneum showed no evidence of periappendiceal or peritoneal mucin or epithelial implants or lymphadenopathy. The mucin-filled appendix was grossly intact. Subsequently, an ileocecectomy with ileocolic anastomosis was performed. The patient's postoperative course was uneventful, and she was subsequently discharged and symptom-free at outpatient follow-up.

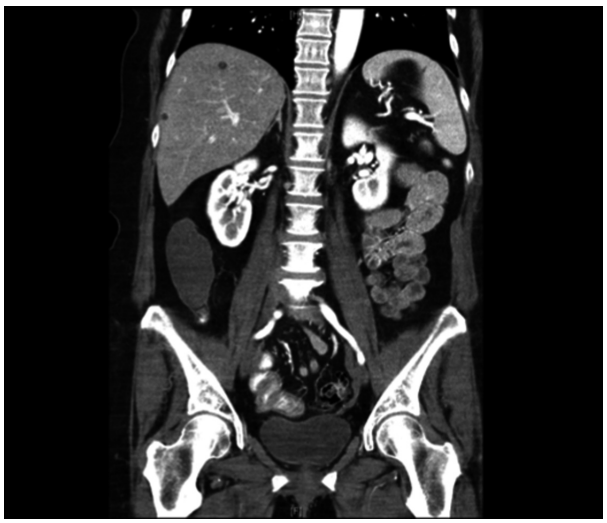

Figure 1. Contrast-enhanced computed tomography image of the abdomen and pelvis showing a well-circumscribed, fluid-dense cystic mass measuring 8.5 × 4.3 × 4.1 cm and absence of findings associated with PMP.

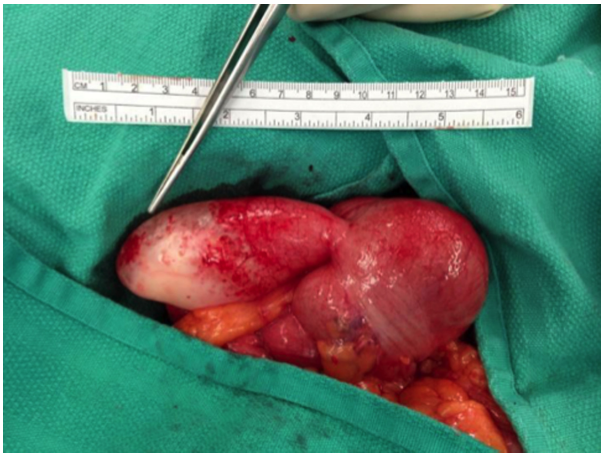

Figure 2. Forceps identifying the distended distal appendix (9 × 4.2 cm) visualized on the operative field.

On pathology, the resected specimen consisted of a segment of the terminal ileum (2.3 × 2.2 cm) and a segment of cecum (7.5 × 7 cm). The specimen showed a pink, tan, smooth, and glistening serosa with unremarkable mesenteric fat. The appendix (9 × 4.2 cm) was opened distally to reveal abundant mucinous material (Figs 3–5). The appendiceal mesentery showed multiple, pink-tan lymph nodes without disease involvement (largest at 0.7 cm in greatest dimension). Histological examination showed a low-grade appendiceal mucinous neoplasm (LAMN) diffusely involving the appendix without evidence of microinvasion, rupture, or lymph node metastasis.

Discussion

Appendiceal mucoceles are misdiagnosed in half of all cases, often as acute appendicitis, a retroperitoneal tumor, or adnexal mass when discovered on radiology,

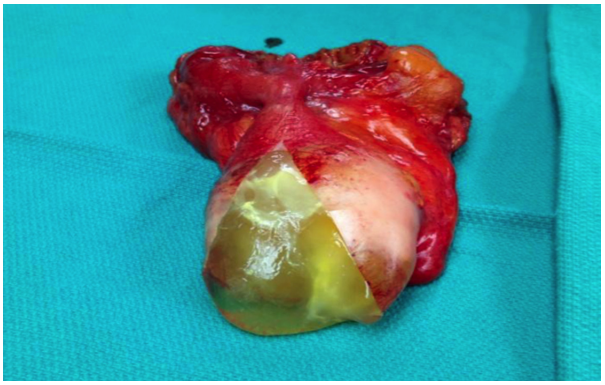

Figure 3. Resected specimen with incised appendix revealing viscous, mucoid material.

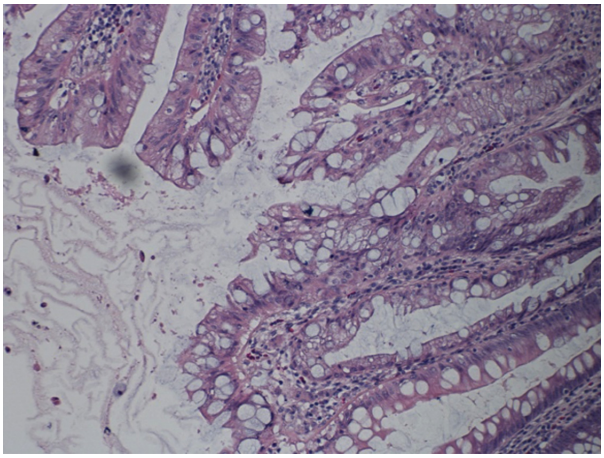

Figure 4. Section of the appendiceal margin showing goblet cells and lumen distended by mucin (H&E, 10x).

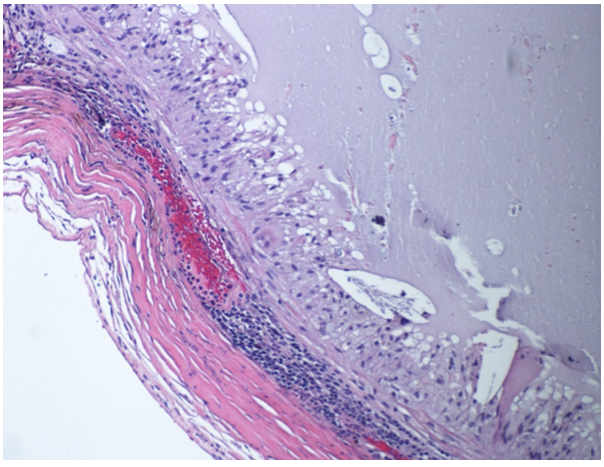

Figure 5. Section of the thinned appendiceal wall secondary to luminal distension by mucin with hyalinization. (H&E, 10x).

endoscopy, or in the operating room [1]. Frequent misdiagnoses occur secondary to variations in diagnostic imaging [11]. Proponents for ultrasound (US) suggest using this modality to distinguish AMs from the more prevalent condition acute appendicitis defined by US criteria with an appendiceal outer diameter 15 mm or greater and possible visualization of mucinous effusion. Contrast-enhanced CT imaging is most commonly used modality for preoperative diagnosis. CT findings suggestive of a mucocele include an appendiceal lumen >1.3 cm, with cystic dilation, and wall calcification [2, 9]. Specifically, mucinous cystadenomas may present with cystic masses, low contrast attenuation, irregular wall thickening, and absence of inflammation [12]. While the literature is lacking with regards to use of preoperative colonoscopy, its use may reveal a pathognomonic "volcano sign," so-called to describe an encroaching mass which obstructs the appendiceal opening with a central crater that produces mucin [13].

The World Health Organization (WHO) classifies mucoceles into four histological groups. Simple or retention mucoceles may exhibit normal epithelium and mild dilation due to obstruction of appendiceal outflow, often by a fecalith. The second group of mucoceles has hyperplastic epithelium with mild luminal distension. The third and most common group is benign mucinous cystadenoma (or LAMNs), classified by the presence or absence of epithelial atypia and moderate distension. The fourth group represents mucinous cystadenocarcinoma, demonstrating invasion into the appendiceal wall, in addition to features of LAMNs [7]. Mucoceles may also be classified by size, as it has been reported that those <2 cm are rarely malignant, while sizes >6 cm are more often associated with cystadenoma and cystadenocarcinoma, as well as a higher rate of perforation [12]. Both ruptured benign and malignant neoplasia can produce mucinous peritoneal spread leading to diagnosis of PMP [14]. PMP resulting from rupture of benign AMs has a 91–100% 5-year survival rate, while the prognosis for malignant forms is poor with a 5-year survival rate of 25% [7, 15, 16]. The syndrome of PMP may necessitate an aggressive, complex surgical procedure that involves extirpation of mucinous material, debulking, and peritonectomy with heated intraperitoneal chemotherapy (HIPEC) [3, 17, 18].

At present, there is debate concerning the use of laparoscopic versus open resection, with current literature deliberating the advantages and disadvantages of both approaches. Most literature suggests a low incidence of malignant mucinous cystadenocarcinoma, however, when selecting a laparoscopic versus open procedure, careful consideration must be given to minimize rupture and mucinous seeding [4, 14]. Pneumoperitoneum and removal of the specimen through the abdominal wall increase the risk of dissemination and port site seeding [14]. Fujini et al. recommend laparoscopic technique, citing benefits such as decreased risk of seeding, magnification of the surgical field, and quicker recovery, emphasizing the ease of conversion to open surgery if necessary [19]. Indications for conversion to an open surgery include traumatic grasping and rupture of the mucocele [20].

Open surgery confers the potential benefits of direct inspection and palpation of the abdominal cavity for mucinous tumors [21]. Additionally, it may facilitate exploration of the cavity for fluid and mucin in the peritoneal cavity, the presence of which requires complete removal and cytological examination and inspection of the ovaries, if applicable [22, 23]. Conversely, open appendectomy may subject the appendix to more trauma

and intra-abdominal manipulation leading to ileus [24]. Long-term results are similar for both approaches, although success is contingent on the surgeon's laparoscopic experience [25]. The surgical approach to AMs should rest upon the surgeon's experience with open versus laparoscopic techniques, with a goal of avoiding iatrogenic violation of the AM and mucin spillage at all costs.

Historically, most diagnoses of mucocele were managed with right hemicolectomy with intent that an oncologic resection would confer a survival advantage. However, recent evidence suggests that appendectomy-only is curative for benign, grossly intact mucoceles [8]. Ileocecectomy is recommended when there is risk of injury to the ileocecal valve, either by traumatic manipulation or from the protrusion of the tumor into the cecal lumen [25]. To determine whether right hemicolectomy is necessary, González-Moreno and Sugarbaker recommended use of a sentinel node approach, with frozen section examination of lymph nodes within the appendiceal mesentery found along the appendiceal artery. In the absence of metastatic disease to the lymph nodes, a right colectomy is not indicated [26]. Generally, as in the above case, lymph node metastases secondary to appendiceal mucinous neoplasms are rare, occurring in only 4.2% of patients with a mucinous malignancy [22, 23, 25]. Dhage-Ivatury and Sugarbaker have established an algorithm for surgical management of mucoceles, including perforated and nonperforated, as well as scenarios for involvement of the base of the appendix, and the presence of positive mesoappendiceal and ileocolic lymph nodes. Surgical treatment ranges from appendectomy to right hemicolectomy.

Postoperatively, minimal duration of follow-up is 5–10 years involving thorough physical examination, annual CT scan, and monitoring CEA and CA 19-9 tumor markers, as elevated levels may suggest recurrence [20]. Additionally, although CEA levels are often elevated in colonic malignancy, they are not routinely drawn when an AM is discovered [11]. In our case, a CEA level obtained preoperatively was within normal limits at 2.10 ng/mL (0–2.5 ng/mL). The utility of trending CEA levels for diagnosis and prognosis of appendiceal mucoceles is largely unexplored. A report in 2013 by M.E.C. McFarlane and colleagues showed two instances of elevated CEA levels in mucinous cystadenoma, a rare finding. Although CEA levels are not often requested, elevation is more frequently reported in malignant cystadenocarcinoma [11].

This case highlights the need for a more defined treatment algorithm for the management of AMs. Due to the concern for malignancy, our patient underwent an extended colonic resection, as have a number of similar patients presented in various published case reports and reviews in the world literature. Pathology in our case was consistent with an intact AM resulting from a benign etiology; therefore, ileocecal resection was likely unnecessary. At our institution, we now routinely perform appendectomy-only for AMs and reserve right hemicolectomy only for histologically proven mucinous cystadenocarcinoma based upon a large, retrospective review of literature including all case reports between 1995 and 2015, which demonstrated mucinous cystadenocarcinoma in only 4.2% of patients with an intact AM [27].

Conclusion

In conclusion, AMs are rare and often-incidental findings. This diagnosis should always be considered when cystic lesions of the right lower quadrant are discovered. Surgical resection of a mucocele is required due to the potential for rupture and progression to PMP. The management of these lesions has evolved over time; appendectomy-only appears to be a reasonable treatment option, especially considering the largely benign nature of these lesions. Laparoscopy may be used for removal; however, care should be taken to avoid iatrogenic rupture of an intact mucocele and prevention of PMP.

Conflict of Interest

None declared.

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