Severe gastrointestinal endometriosis and low-grade appendiceal mucinous neoplasm: Is there a link?

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Abstract

Significance: Low-grade appendiceal mucinous neoplasms (LAMN) are well-differentiated tumors that can cause dilation of the appendix leading to rupture, or can progress outside the appendix in a malignant process. These are rare conditions, seen only in 0.2% of appendectomy specimens and are often incidentally detected in asymptomatic patients. Endometriosis of the gastrointestinal tract, largely of the small intestine and mesentery, may be an associated condition. Combination of both conditions in young females is remarkably rare. *Case Presentation:* A 32-year-old woman presented with acute abdominal pain and vomiting with tenderness over the right lower quadrant. She had no fever, weight loss or altered bowel habits. CEA was normal while CA-125 was significantly elevated. *Management:* Imaging studies revealed an ileocecal mass causing partial small intestinal obstruction and a dilated appendix. She underwent right hemicolectomy and appendectomy. Pathology revealed endometriosis of the onemtum, ileum, appendix, ascending and transverse colon. LAMN with extension to the mesoappendix was also reported. *Recommendation:* Endometriosis of the gastrointestinal tract may cause worsening gut obstruction and appendiceal neoplasms. Diagnosis and resection must be done early due to the risk of perforation as well as underlying malignancy. Appendiceal LAMN should be considered a differential diagnosis in cases of severe abdominal pain in a young woman with an appendiceal mass on CT scan.

Keywords: case report, low-grade appendiceal mucinous neoplasm, LAMN, endometriosis, gut obstruction

Background

Extrapelvic endometriosis is an uncommon entity. It affects slightly older population, leading to the assumption that it takes several years for pelvic endometriosis to spread outside of the pelvis. Endometriotic lesions have been reported in every part of the female human body, including the gastrointestinal tract, the lungs, the reproductive organs, and the urinary system.[1] The gastrointestinal tract is the most common location of extrapelvic endometriosis, having been reported in up to four percent of women diagnosed with endometriosis.[2] In gastrointestinal endometriosis, the sigmoid colon is the most commonly involved, followed by the rectum, ileum, appendix, and cecum. Gastrointestinal endometriosis is usually asymptomatic, but if present, can mimic conditions such as inflammatory bowel disease, ileocolonic intussusception, irritable bowel syndrome, acute appendicitis, and colonic malignancies.[3] Acute bowel obstruction and perforation of the affected bowel can also occur, and represents an extremely infrequent entity that has been published in a few case reports.[4,5,6,7] Neither reports of similar cases, nor the prevalence of gastrointestinal endometriosis in the Philippines have been published as of date.

Diagnosis of gastrointestinal endometriosis based on history and physical examination alone is difficult. And there is no radiologic finding that is specific for the condition. So far, though with not enough supporting data, MRI is considered to be the most useful imaging tool for bowel endometriosis.[8] Laparotomy with histopathological confirmation of endometriosis remains the gold standard for its diagnosis.[9] Options for treatment of extrapelvic endometriosis include surgery and/or hormonal agents. If the bowel is involved, hormonal therapy may improve symptoms, but does not prevent the progression of the disease.[3] Surgical excision of endometriotic lesions is still preferred, especially when symptoms of obstruction, bleeding, and severe pain occur.

Endometriosis of the appendix by itself is a rare condition, reported at two percent of all gastrointestinal endometriosis, and is usually seen as an incidental finding intraoperatively.[3] Endometriosis leading to an obstructive mucocele of the appendix is an even rarer finding, having only been described in less than a dozen times in medical literature. Obstruction caused by endometriosis of the appendix may lead to entrapment of mucin, generating mucinous cysts that eventually combine to become LAMN. Psudomyxoma peritonei (PMP), another rare complication of abdominal mucinous tumors, is characterized by the dissemination of peritoneal mucinous deposits, with the potential to progress to severe ascites. The majority of PMP is derived from appendiceal tumors; as such, a pre-existing intraperitoneal mucinous neoplasm has been implicated as the primary cause of PMP.[10]

Low-grade appendiceal mucinous neoplasms are well-differentiated tumors that cause dilation of the appendix and can proliferate outside the appendix in a malignant fashion.[11] These are rare conditions, seen in 0.2% of appendectomy specimens and are often incidentally detected in asymptomatic patients.[12] Women are affected four times as often as men, with a peak age incidence of over 50 years. Cases can present with abdominal pain, weight loss, nausea and vomiting, palpable mass, and acute appendicitis. Endometriosis of the appendix causing LAMN is remarkably rare.

We report a case of endometriosis of the intestines and appendix causing gut obstruction and LAMN in a young female presenting with acute abdominal pain.

Case Presentation

A 32-year-old woman presented at the emergency room with a one-week history of progressive diffuse abdominal pain and non-bilous vomiting. There was no history of fever, weight loss or altered bowel habits. She had no previous surgeries, denied smoking and intake of hormone replacement therapy. Family history on her maternal grandfather was positive for colorectal cancer. On physical examination, there was tenderness in the right lower quadrant, but without rebound or guarding, and there were no palpable abdominal masses. Serum CEA level was normal while serum CA-125 was significantly elevated.

Abdominal radiographs (**Figure 1**) showed air-filled levels and gas-filled dilated small bowel loops, with the widest transverse diameter of five centimeters (cm).

Figure 1. (**a**) Admitting abdominal radiograph showing dilated bowel loops (arrow). (**b**) Next-day repeat imaging showing widest-diameter small bowel dilatation (white arrow) and air-fluid levels (blue arrow).

Computer tomography (CT) imaging revealed a fluid-filled appendix that was distended to 1.6 cm without evidence of acute appendicitis. The distal jejunal segments and the ileum were dilated to a maximum diameter of 4.8 cm. A short segment circumferential thickening with a length of 4.5 cm in the ileocecal region was also seen (**Figure 2**).

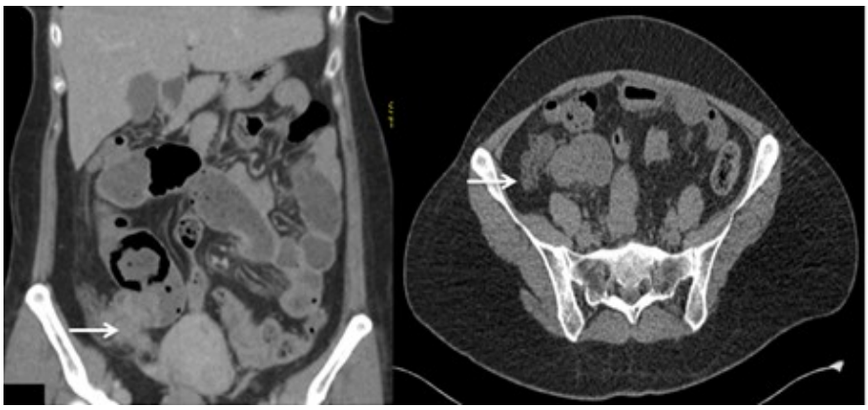

Figure 2. Images of CT scan in coronal view (left) and axial view (right) showing a thickened ileocecal valve and a dilated appendix (arrows).

The patient underwent surgical resection with an extended right hemicolectomy and adhesiolysis using an exploratory laparotomy approach. Upon opening of the abdominal cavity, there were multiple subcentimeter pelvic and peritoneal implants and the small bowel was dilated all the way to the ileocecal area. There was a puckering intraluminal ileocecal mass adherent to the right gutter causing dilation of the appendix, and a subcentimeter transverse colon mass adherent to the uterus, the former containing cheesy contents. Pathology demonstrated LAMN of the vermiform appendix with acellular mucin extending to the mesoappendix (**Figure 3**).

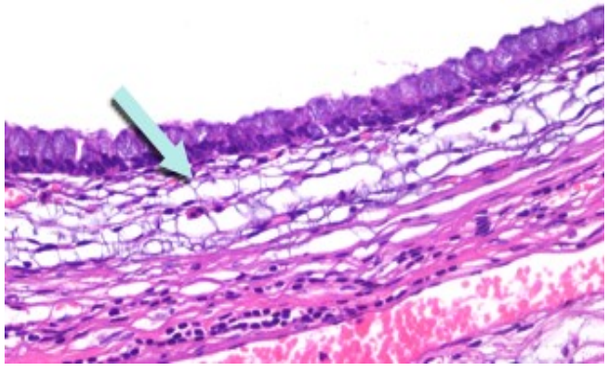

Figure 3. Histology of the LAMN in high power (x200 magnification) showing excess mucin accumulation and loss of lamina propia (arrow).

There was endometriosis in the ileum, appendix, ascending and transverse colon, omentum and one pericolic lymph node (**Figure 4**).

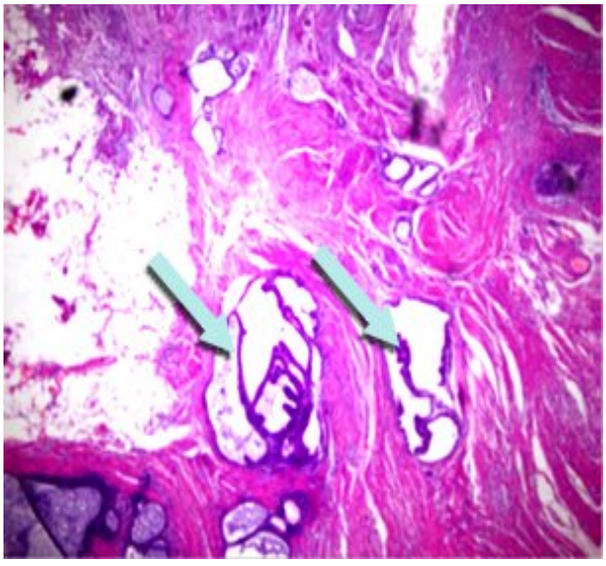

Figure 4. Histology of the colon in high-power (x200 magnification) showing presence of endometrial glands (arrows).

Immunochemistry stains of the small bowel were CK7 (+), CK20 (-), and ER (+) (**Figure 5**).

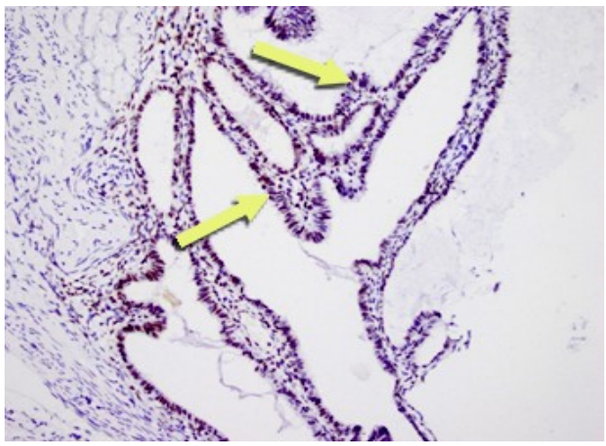

Figure 5. Immunochemistry stain of bowel tissue positive for estrogen receptors (arrows) consistent with endometriosis.

Patient recovery postoperatively was without any complications. She remained well since then.

Discussion

According to Hapke and Bigelow, gastrointestinal endometriosis may cause the development of an appendiceal tumor or mucocele due to the progression of smooth muscle hypertrophy in the muscularis propria, resulting in obstruction of the adjacent gland crypts. This obstruction will then cause the entrapment of mucin, producing mucinous cysts that eventually merge and grow. As the cysts grow through the appendiceal wall, they eventually perforate through the submucosal and serosal layers of the appendix.[13] Appendiceal mucoceles are also associated with tumors of the gastrointestinal tract, ovary, endometrium, and breast.[14] Colorectal carcinoma can be found in approximately 20% of patients with appendiceal mucoceles, but the association with LAMN and other appendiceal tumors is still unknown. In twelve reported cases of appendiceal mucocele due to endometriosis, the most common presenting symptom was chronic abdominal pain. Complications included appendiceal rupture, appendiceal intussusception, and ureteral obstruction. None of these cases reported had malignant transformation of the appendiceal mucoceles.

LAMN refers to a tumor with neoplastic adenomatous growth in the presence of low-grade cytologic atypia. Aside from causing intestinal obstruction and appendiceal rupture, these neoplasms can potentially cause PMP. Most cases of PMP are derived from appendiceal tumors, thereby, it can be said that LAMN is a precursor to PMP.[15] It is thus possible that endometriosis may affect the local tissue environment of an appendiceal mucocele, increasing the risk for neoplastic transformation. At present, it remains uncertain whether or not the presence of endometriosis will influence the development of malignancy from an appendiceal mucocele. The presence of endometriosis, however, increases the risk for other malignancies, particularly ovarian carcinoma.[15] An illustration of these associations is shown in **Figure 6**.

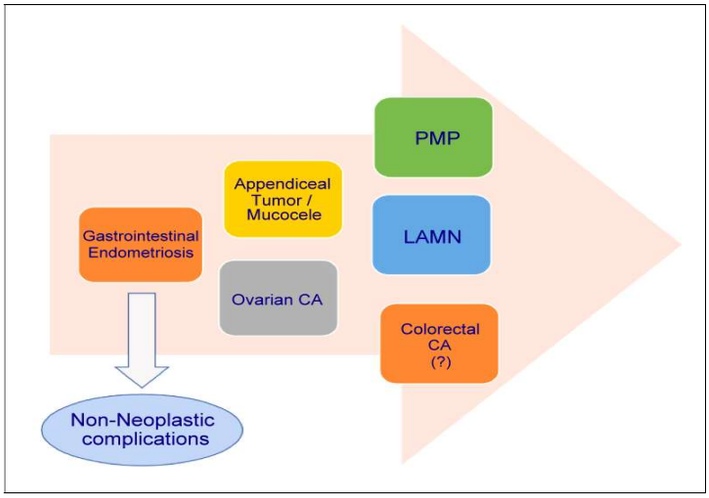

Figure 6. Possible complications of gastrointestinal endometriosis including neoplastic formations.
PMP = pseudomyxoma peritonei; LAMN = low-grade appendiceal mucinous neoplasms; CA = carcinoma

Conclusion

Endometriosis of the appendix is a rare condition, and for this to progress into LAMN is even rarer. Endometriosis of the gastrointestinal tract may cause worsening gut obstruction and may have the potential for neoplasm. Diagnosis and resection must be done early due to the risk of underlying malignancy and risk of perforation. Appendiceal LAMN should be included as a differential diagnosis in cases of severe abdominal pain in young women with appendiceal mass on CT scan. More research is needed to identify which type of appendiceal mucocele develops into neoplasm, and possible reasons for its potential for developing concurrent ovarian, colorectal carcinoma, and PMP.

Conflicts of Interest

The authors declare no conflicts of interest.

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