Endometriosis of the appendix mimicking appendicitis: Histomorphology and case report

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INTRODUCTION

There are various possible causes of pain in the right lower quadrant of the abdomen. Common causes include appendicitis, diverticular disease, irritable bowel syndrome, and hernias. Ectopic pregnancy, ovarian mass, and pelvic inflammatory disease may also be suspected in women.1,2 Besides these, a much rarer cause is endometriosis of the appendix.

Endometriosis is the presence of ectopic endometrial tissue outside the uterus.3 While endometriosis is relatively common (affecting 10-15% of all women of reproductive age), appendiceal endometriosis is much rarer. Endometriosis of the appendix was identified in less than 1% of patients with pelvic endometriosis and 0.05-0.8% of appendectomy specimens.3-5 Endometriosis of the appendix has various clinical presentations, ranging from asymptomatic to acute appendicitis. Symptoms are caused by endometrial bleeding.4 Histopathological examination is required for a definitive diagnosis.6

CASE REPORT

A 42-year-old woman presented to the emergency department with severe right lower abdominal pain. The pain persisted for 4 days and gradually worsened. The patient also had a fever and nausea. The patient was menstruating at the time of presentation. She experienced periodic lower abdominal pain for more than 6 months but never consulted a doctor.

On physical examination, the patient was febrile (37.8°C). There was tenderness and guarding in the right lower quadrant. A complete blood count showed leukocytosis with increased neutrophils. The pregnancy test was negative. The initial diagnosis was appendicitis. An appendectomy was performed. After the procedure, she had a good clinical recovery without residual pain.

The excised appendix was sent to the laboratory for histopathological examination. The appendix specimen was 5.5 cm long, the proximal segment diameter was 0.5 cm, and the distal segment diameter was 1 cm (Figure 1). The cut section showed obliterated lumen, especially in the distal segment. There was no perforation.

A histopathological examination was performed with a hematoxylin–eosin stain. The proximal and medial sections contain normal layers of appendix tissue. In the distal section, multiple foci of endometrial stroma and glands were present in the muscularis propria and serosa (Figure 2 and 3) and reactive lymphoid hyperplasia was found in the mucosa. There was no sign of appendicitis. The diagnosis was established as endometriosis of the appendix.

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DISCUSSION

The wall of the appendix consists of the mucosa, the submucosa, the muscularis propria, and the serosa (visceral peritoneum). The mucosa comprises the lining epithelium, lamina propria, and muscularis mucosae. The lining epithelium consists of simple columnar epithelial cells with numerous goblet cells. The intestinal glands (crypts of Lieberkühn) in the lamina propria are less developed, shorter, and more spaced apart than those in the colon. One characteristic feature of the appendix is the abundant lymphatic nodules with germinal centers originating from lamina propria and may extend to the submucosa. The underlying submucosa contains connective tissue, blood vessels, and nerves. Two smooth muscle layers comprise the muscularis propria, the inner circular and outer longitudinal layers. The parasympathetic ganglia may be seen between those muscles. Serosa is the outermost layer, in which adipose cells can be seen.7

Appendicitis is a common cause of lower abdominal pain, with a lifetime risk of 6.7% in females.8 The Alvarado score is widely used to determine the likelihood of appendicitis in a suspected patient. It incorporates findings from the patient’s history, physical examination, and laboratory examination. The result is stratified into low-, moderate-, and high-risk categories.9,10 Clinically, this patient’s diagnosis was suspected to be appendicitis. The patient’s Alvarado score was within the high-risk category. Hence, an appendectomy was performed, and the tissue specimen was sent to the laboratory for confirmation.

Acute appendicitis is associated with increased intraluminal pressure and compromised venous outflow. This results in ischemia, bacterial overgrowth, and inflammation. Perivascular neutrophilic infiltrate and congested subserosal vessels may indicate early acute appendicitis.11 As the disease progresses, focal abscesses may form (acute supplicative appendicitis). Severe vascular compromise may lead to hemorrhagic ulceration and gangrenous necrosis (acute gangrenous appendicitis). To diagnose acute appendicitis, microscopic finding of neutrophilic infiltration in muscularis propria is needed.11 However, in this specimen, no evidence of appendicitis was found. Interestingly, when analyzing the distal section of the appendix, multiple glands and stroma resembling endometrial tissue were found. This indicates the presence of endometriosis.

The endometrium is the innermost layer of the uterine wall. The endometrium primarily consists of endometrial glands and stroma. The glands are lined by columnar cells with basally located nuclei. Minimal multilayering might be observable during the late proliferative phase. The stroma consists of cells with small cytoplasm (‘naked nuclei’ appearance). Mitotic figures might be observable throughout the proliferative phase.12 Endometrial tissue that presents in endometriosis most commonly includes both endometrial glands and stroma. However, stromal endometriosis may occur without the presence of glands. Appendiceal endometriosis is usually implanted in the serosa layer but can erode deeper and invade the muscularis propria. Mucosa is typically unaffected.11,13,14 Endometrial glands and stroma were found in this specimen’s serosa and muscularis propria. The cells did not show nuclear pleomorphism or abnormal mitosis. Reactive lymphoid hyperplasia, characterized by proliferating lymphocytes with active germinal centers, was found in the mucosa. The exact etiology of reactive lymphoid hyperplasia is unknown. It was likely a chronic inflammatory reaction due to antigenic stimulation.15,16

Endometriosis is homologous to endosalpingiosis and endocervicosis. Sometimes those entities are grouped as “Mullerianosis”. Endosalpingiosis is the presence of ciliated columnar epithelium with peg cells (fallopian tube-type epithelium) outside the fallopian tube. Endocervicosis is the presence of cervical mucinous epithelium outside the cervix. Variably sized mucous endocervical glands may also be observed. Sometimes, a tissue specimen may contain more than one entity.17-19 There was no evidence of endosalpingiosis and endocervicosis in this specimen, so we decided that endometriosis was more appropriate than Mullerianosis.

Pain in the lower abdomen can be
attributed to many causes. Even though appendicitis is a common etiology, endometriosis can cause abdominal pain. The endometrial tissue bleeds periodically due to ovarian and intrinsic hormonal stimulation. This leads to inflammation, pain, adhesion, and its related complications. Perforation of the appendix may occur. Fortunately, in this patient, there was no perforation. While endometriosis has a significant clinical impact, the risk of developing endometriosis-related cancer remains low. In this specimen, no atypia and pleomorphism were found. The pathogenesis of endometriosis is not well understood. The retrograde menstruation theory states that the foci of endometrial tissue from menstrual blood are spread through fallopian tubes due to retrograde flow. Some other theories include metaplasia, increased tissue response to estrogen, inflammation, immune dysfunction, extraterine stem cell differentiation, and genetics. The etiology of endometriosis might be multifactorial and involves a complex interaction between those factors. There might be several different pathways, which explains why one theory could not fully explain the occurrence of endometriosis in other locations.

Initial assessments may end up with many differential diagnoses. Appropriate diagnostic tests like pregnancy tests, urinalysis, and transvaginal and transabdominal ultrasound are recommended to rule out other causes of pelvic pain. Unfortunately, a reliable non-invasive test for endometriosis has yet to be found. Hence, postoperative histopathologic confirmation is required for a definite diagnosis.

CONCLUSION

Endometriosis of the appendix is a rare case. It can mimic appendicitis and is hard to detect preoperatively. A histopathology examination was recommended to confirm the diagnosis.

CONFLICT OF INTEREST

The authors report no conflicts of interest in this study.

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ETHICAL CONSIDERATION

The patient signed the informed consent and agreed that the medical data would be published as a case report in medical scientific journals.

AUTHOR CONTRIBUTION

All of the authors contributed equally to this study.

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