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CASE REPORT

Endometriosis of the Appendix: Two Rarely Encountered Cases and Review of the Literature

Apendiks Endometriozisi: Nadir Karşılaşılan İki Olgu ve Literatürün Gözden Geçirilmesi

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ABSTRACT
Endometriosis is defined as the presence of endometrial glands and stroma outside the uterine cavity and musculature. Appendiceal endometriosis was first described in 1860 by von Rokitansky. The pathogenesis of endometriosis is based on three main theories: Retrograde menstruation with implantation and failure of immunologic clearance, coelomic metaplasia, and hematologic or lymphatic metastasis. A 26-year-old female patient presenting with abdominal pain no known medical history and a 50-year-old female patient presenting with menstrual irregularity without any known medical problems are presented. Histopathological examination of their appendectomy specimens revealed foci of endometriosis. Appendiceal endometriosis, while relatively uncommon in patients with endometriosis, is rare in the general population. It not only may cause symptoms of acute and chronic appendicitis but is also known to cause cyclic and chronic right lower quadrant pain, melena, lower intestinal hemorrhage, and cecal intussusception. Appendicitis should be considered in the differential diagnosis. Recognition of this benign entity is essential to avoid misdiagnosis and unnecessary aggressive management.

Keywords: Endometriosis, appendix, appendectomy, pelvic pain

ÖZET
Endometriozis, endometriyal bezlerin ve stromanın uterusun duvarı ve kavitesi dışında varlığı olarak tanımlanır. Apendiks endometriozisi ilk olarak 1860 yılında von Rokitansky tarafından tanımlanmıştır. Apendiks endometriozisi oldukça nadir görülen bir durumdur ve gastrointestinal sistem endometriozis olgularının çok küçük bir kısmını oluşturur. Endometriozisin patogenezine ilişkin üç ana teori vardır: implantasyon ve retrograd menstrüasyon, çölomik metaplazi ve hematolojik veya lenfatik metastaz. Bilinen bir tıbbi öyküsü olmayan, karın ağrısı ile başvuran 26 yaşında kadın hasta ve adet düzensizliği ile başvuran, herhangi bir bilinen tıbbi sorunu olmayan 50 yaşında kadın hasta sunulmuştur. Apendektomi örneklerinin histopatolojik incelemelerinde endometriozis odakları tespit edilmiştir. Apendiks endometriozisi, endometriozisli hastalarda nispeten nadir olmakla birlikte, genel popülasyonda daha da nadirdir. Sadece akut ve kronik apendisit semptomlarına neden olmakla kalmaz, aynı zamanda döngüsel ve kronik sağ alt kadran ağrısı, melena, alt bağırsak kanaması, çekum invajinasyonuna neden olduğu bilinmektedir. Apendisit ayırıcı tanısında düşünülmelidir. Bu benign durumun tanınması, yanlış tanı ve gereksiz agresif tedavilerin önlenmesi açısından önemlidir.

Anahtar Kelimeler: Endometriozis, apendiks, apendektomi, pelvik ağrı

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INTRODUCTION

Endometriosis is a disease characterized by the presence of endometrial glands and stroma outside the uterine cavity and muscular layer, and is estimated to affect approximately 4–50% of women of reproductive age. Up to 50% of affected patients experience pelvic pain and infertility. Clinical manifestations vary depending on the location of the lesions. In addition to pelvic involvement, gastrointestinal tract involvement represents an important clinical manifestation of the disease. Gastrointestinal endometriosis is reported to occur in 3–34% of patients with endometriosis and may cause a wide spectrum of symptoms (1). Appendiceal endometriosis (AE) was first described by von Rokitansky in 1860. The reported prevalence of AE in the literature ranges from 0.8% to 22%. While the prevalence of AE among patients with endometriosis is approximately 2.8%, it is considerably lower in the general population, estimated at around 0.4% (1). Cecal and appendiceal involvement is rare and may mimic malignancy by presenting with anemia. The incidence is highest in women of childbearing age. Clinical presentation varies according to lesion location and may include tenesmus, hematochezia, iron deficiency anemia, epigastric pain, and even pneumothorax. This

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broad clinical spectrum further complicates the diagnosis of endometriosis (2). From a clinical perspective, most cases of gastrointestinal endometriosis are asymptomatic. The disease predominantly involves the serosal layer and therefore often lacks overt clinical signs. Moreover, cecal pathologies usually present with delayed and nonspecific symptoms, further challenging timely diagnosis (2).

Appendicitis is one of the most common causes of abdominal pain, with a lifetime risk of 8.6% in males and 6.7% in females, and the majority of appendectomies are performed for this diagnosis. Luminal obstruction is the most common etiological factor of appendicitis, particularly in the pediatric population. Three main theories have been proposed to explain the pathogenesis of endometriosis: retrograde menstruation with implantation, coelomic metaplasia, and hematogenous or lymphatic dissemination (3).

Although endometriosis is more prevalent in women of reproductive age, its sequelae may also be observed in the postmenopausal period and may present solely with gastrointestinal manifestations (4). In this study, we report two cases of appendiceal endometriosis and review the relevant literature.

CASE REPORTS

Case-1:

A 26-year-old female patient with no known medical history was admitted to Konya Numune Hospital with right lower quadrant abdominal pain. Physical examination revealed right lower quadrant tenderness. Abdominal ultrasonography demonstrated a dirty mesentery, and the appendix could not be clearly visualized, and further clinical evaluation for acute appendicitis was recommended. Laboratory examination revealed significantly elevated inflammatory markers: C-reactive protein (CRP) was 81.36 mg/L (reference range: 0–5), white blood cell (WBC) count was 19.43 $\times 10^9$/L (reference range: 4.0–9.75), and neutrophil percentage was 88.5% (reference range: 42–73). Hemoglobin level was near the lower limit of normal (10.5 g/dL; reference range: 10.3–15.4), mean corpuscular volume (MCV) was low (74 fL; reference range: 75–98), and hematocrit was reduced (31.3%; reference range: 32.7–46.6). Based on the combined evaluation of clinical, laboratory, and imaging findings, an appendectomy was performed with a presumptive diagnosis of acute appendicitis. Intraoperatively, the appendix was found to be minimally enlarged and was resected.

Gross pathological examination showed a slightly enlarged appendix. Histopathological evaluation revealed neutrophil-rich inflammation involving the appendix wall and serosa. Additionally, endometrial glandular structures of varying sizes accompanied by a cellular stroma measuring approximately 0.6 cm in diameter were observed within the muscular layer of the appendix (Figure 1). Immunohistochemical analysis demonstrated CD10 positivity in the stromal component, supporting the diagnosis of endometrial stroma. Vimentin expression was also positive in the glandular structures, consistent with endometrial tissue. Considering the histopathological and immunohistochemical findings together, the final diagnosis was endometriosis externa associated with acute appendicitis.

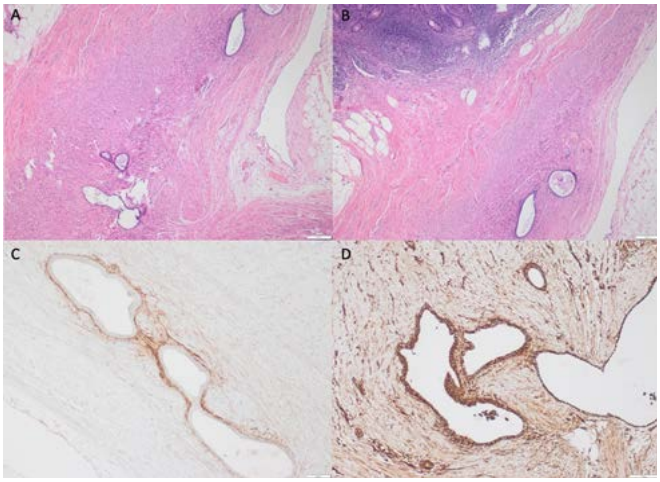

Figure 1. Histopathological appearance and immunohistochemical staining pattern of the primary lesion. A: In hematoxylin and eosin staining, sparse benign glandular structures within the muscular tissue of the appendix wall (x40). B: In hematoxylin staining, benign glandular structures within the muscular layer as well as the appendix mucosa (x40). C: Immunohistochemical CD10 staining showing (+) expression in the narrow stroma surrounding the glands (x100). D: Immunohistochemical Vimentin staining showing (+) expression in glandular epithelia (x100).

Case-2:

A 50-year-old female patient with no known comorbidities presented with a complaint of heavy menstrual bleeding. Transabdominal ultrasonography revealed multiple uterine fibroids, the largest measuring 7.5 cm in diameter. A total hysterectomy was planned. During surgery, a separate appendectomy was also performed due to suspicion of adhesion of the appendix to the surrounding tissues. No endometriotic foci were detected in the uterus, ovaries, or fallopian tubes.

Histopathological examination of the appendix revealed endometrial stromal and glandular structures measuring approximately 0.5 cm in diameter within the muscular layer at the tip of the appendix, similar to the findings observed in Case 1 (Figure 2). In this region, immunohistochemical staining demonstrated CD10 (+), Vimentin (+), and Estrogen Receptor (ER) (+) expression, consistent with endometrial tissue. Based on these findings, the final pathological diagnosis was endometriosis externa, and reactive lymphoid hyperplasia. Informed consent forms were obtained from both cases.

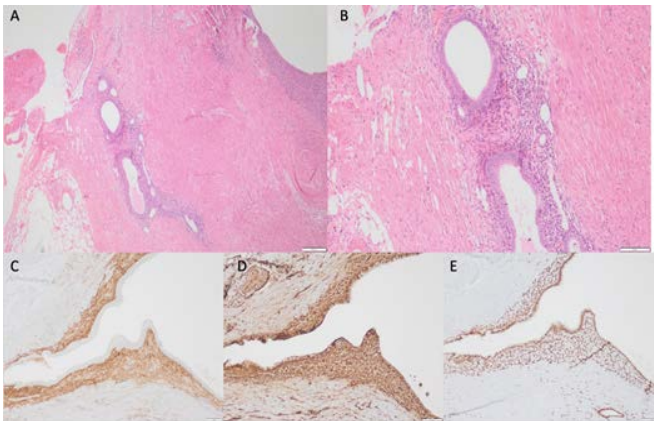

Figure 2. Histopathological appearance and immunohistochemical staining pattern of the second specimen. A: In hematoxylin and eosin staining, sparse benign glandular structures within the muscular tissue of the appendix wall and cellular stroma surrounding them (x40).
B: Benign glandular structures within the muscular layer on hematoxylin and eosin staining, stroma (x100). C: Immunohistochemical CD10 staining showing (+) expression in the narrow stroma surrounding the glands (x100). D: Immunohistochemical Vimentin staining showing positive expression in glandular epithelia (x100). E: Immunohistochemical Estrogen receptor staining showing positive expression in both stroma and glandular epithelia (x100).

DISCUSSION

Appendiceal endometriosis is known to cause both acute appendicitis–like symptoms and cyclic right lower quadrant pain. It may also present with lower gastrointestinal bleeding, cecal intussusception, and perforation. Since right lower quadrant pain is commonly observed in women with endometriosis, the detection of AE is particularly important in patients with chronic pelvic pain undergoing laparoscopy (1). Colonic neoplasms, whether malignant or benign, typically present as a mass lesion in the colon. However, several other conditions may also lead to a colonic mass, including infectious and inflammatory bowel diseases. Additional causes include endometriosis, schwannoma, diverticular disease resulting in mass-like inflammatory changes, and even foreign bodies (2).

Atypical endometriosis can occur at extrapelvic sites, with the gastrointestinal tract being one of the most frequently involved locations. Within the gastrointestinal system, endometriosis most commonly affects the rectosigmoid colon. In contrast, cecal and appendiceal involvement are exceedingly rare, accounting for only a small proportion (approximately 5%) of gastrointestinal endometriosis cases (2). Laparoscopy remains the gold standard for the diagnosis of endometriosis, although non-invasive imaging modalities such as ultrasonography and magnetic resonance imaging (MRI) are frequently used. Once the diagnosis is established, first-line treatment consists of non-steroidal anti-inflammatory drugs and hormonal therapies. Surgical intervention should be considered in patients with contraindications to medical therapy or in those who fail to respond adequately. Although malignancy must always be considered as the primary diagnosis, alternative etiologies, including endometriosis, should also be taken into account, particularly in patients without clear risk factors for colorectal cancer (2).

Malignancy is another important cause of appendicitis, with an incidence ranging from 5.9% to 12% in patients presenting with an appendiceal mass. The most common primary appendiceal malignancies are neuroendocrine tumors, which are typically located at the tip of the appendix (3). According to the study by Feldhaus et al., appendiceal endometriosis is detected in less than 1% of women undergoing appendectomy. Other studies have reported an AE prevalence of 0.4% in the general population. Therefore, AE should be included in the differential diagnosis of appendicitis in female patients (3). The number, ages, and clinical presentations of AE cases in the articles we used as references are detailed in the table (Table 1). In a 12-year study by Mabrouk et al., AE was detected in 2.6% of patients with endometriosis who underwent surgery. AE was associated with adenomyosis, endometrioma, bladder endometriosis, and ileocecal involvement (5). Similarly, Centini

Table 1. Number, ages, and clinical presentations of appendiceal endometriosis cases in the references

References	Appendicial Endometriosis (n)	Age/ Gender	Symptom
Gustofson et al. (1)	4/ 120	18–45 years	Right lower quadrant pain
Togra et al. (2)	1	50-year-old female	Symptomatic anemia
Hale et al. (3)	1	49-year-old female	Incidental finding on computed tomography
Sooklal et al. (4)	1	51-year-old female	Asymptomatic, a colonoscopy for colorectal cancer screening
Mabrouk et al. (5)	50 / 1935	Not specified	Not specified
Centini et al. (6)	13 / 460	Not specified	Not specified
Ross et al. (7)	23 / 300	22–52 years	Patients undergoing coincidental appendectomy at the time of a primary gynecologic procedure.
Gupta et al. (8)	1	36-year-old female	Acute abdominal pain
Uwaezuoke et al. (9)	1	29-year-old female	Right iliac fossa pain

et al. reported a significant association between appendiceal, ovarian, and bladder endometriosis, suggesting that disease spread may occur via the dissemination of endometrioma fluid (6).

Ross et al. demonstrated that appendectomies performed for gynecological indications are associated with higher rates of endometriosis and abnormal pathological findings. Endometriosis was identified in 7.7% of routine pathological examinations (7). The mechanism by which endometriosis develops within the muscularis propria of the appendix in patients without a prior history of endometriosis remains unclear. This observation challenges the theory of retrograde menstruation, as direct seeding cannot occur without serosal involvement. Since both the appendix and the cecum originate from mesodermal tissue, the transformation of the intestinal wall supports the theory of coelomic metaplasia (8). In our cases, neither patient had a known history of endometriosis, yet endometriotic foci were detected within the muscular layer of the appendix.

Although acute symptoms generally resolve after appendectomy, lower abdominal pain may recur. This recurrence is most likely attributable to concomitant pelvic (particularly ovarian) endometriosis. Previous studies have shown that 56% of appendiceal endometriosis cases involve the body of the appendix, while 44% involve the tip, with no reported involvement of the appendiceal base. In our patients, endometrial tissue was localized at the tip of the appendix with involvement of the muscularis propria, while the mucosa and serosa were not affected (9). With increasing awareness and accumulated data, more effective screening tools for appendiceal masses and pathologies may be developed. In conclusion, as demonstrated in our case report, AE should be considered as an important and rare cause of appendicitis. This report highlights the clinical significance of recognizing appendiceal endometriosis as an underlying etiology of appendiceal mass lesions.

DECLARATIONS

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