Endometriosis and the appendix: a case series and comprehensive review of the literature

Robert L. Gustofson, M.D., Nancy Kim, Shannon Liu, and Pamela Stratton, M.D.

Reproductive Biology and Medicine Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland

Objective: To report the prevalence of appendiceal disease in women with chronic pelvic pain undergoing laparoscopy for possible endometriosis, summarize the literature, and more accurately estimate the prevalence of endometriosis of the appendix.
Design: Prospective case series and literature review.
Setting: Academic research institute.
Patient(s): One hundred thirty-three patients with chronic pelvic pain and possible endometriosis undergoing laparoscopy.
Intervention(s): History, physical exam, and abdominopelvic laparoscopy. Endometriosis and adhesions were excised using selective Nd:YAG contact laser trabeculoplasty and pathologically evaluated. Only patients with visible abnormalities involving the appendix were treated via concurrent laparoscopic appendectomy.
Main Outcome Measure(s): Appendiceal abnormalities at laparoscopy.
Result(s): Of 133 patients, 13 had a previous appendectomy with unknown pathology. Of the remaining 120 patients, 109 reported right lower quadrant pain. Of this subgroup, six patients had appendiceal pathology: four with pathology-confirmed endometriosis, one with Crohn's disease suspected at laparoscopy, and one with chronic appendicitis. The prevalence of appendiceal endometriosis in patients with biopsy-proven endometriosis (n = 97) or with right lower quadrant pain (n = 109) was 4.1% and 3.7%, respectively. This rate was similar to the 2.8% prevalence confirmed by literature review in patients with endometriosis but was much higher than that reported in all patients (0.4%).
Conclusion(s): Appendiceal endometriosis, while relatively uncommon in patients with endometriosis, is rare in the general population. In patients with right lower quadrant or pelvic pain, the appendix should be inspected for endometriosis and evidence of nongynecologic disease. (Fertil Steril® 2006;86:298–303. ©2006 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, appendix, appendectomy, pelvic pain, right lower quadrant, laparoscopy

Endometriosis, defined as the presence of endometrial glands and stroma outside the uterine cavity and musculature (1), is estimated to affect 4%–50% of reproductive aged women and results in pelvic pain and infertility in up to 50% of these patients (2). The disease remains enigmatic, because there are conflicting reports correlating the amount of disease and significance of symptoms present (3, 4). Symptoms of the disease may often be manifested by the location of lesions, e.g., increased dyspareunia with vaginal or uterosacral endometriosis (4). In addition to pelvic locations, endometriosis of the gastrointestinal tract may cause a wide array of symptoms and is involved in 3%–34% of patients affected by endometriosis (5–8). The subset of patients with endometriosis of the appendix is particularly interesting because of its acute and chronic manifestations.

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Reprint requests: Pamela Stratton, M.D., RBMB/NICHD, National Institutes of Health, 10 Center Drive MSC 1109, Bldg 10, CRC, 1-3140, Bethesda, MD 20892 (FAX 301-402-0884; E-mail: strattop@cc1.nichd.nih.gov).

Appendiceal endometriosis was first described in 1860 by von Rokitansky (9). Since that time, Sampson (10) proposed his theory of retrograde menstruation as the primary etiologic factor producing endometriosis and reported endometriosis affecting the appendix. In 1951, Collins (11) reported a cumulative 150 cases in the literature of endometriosis of the appendix. He further described over 50,000 random pathologic assessments of the appendix and reported the prevalence of appendiceal endometriosis as 0.054% (12). Numerous studies since that time have reported the prevalence of appendiceal endometriosis from 0.8% to 22%, depending on the population evaluated (13, 14).

Appendiceal endometriosis not only may cause symptoms of acute and chronic appendicitis (15–18) but also is known to cause cyclic and chronic right lower quadrant pain (19), melena (11), lower intestinal hemorrhage (20), cecal intussusception (21–27), and intestinal perforation (28, 29) especially during pregnancy. Because right lower quadrant pain is a common complaint of women with endometriosis, our goal is to describe the prevalence of endometriosis of the appendix and other appendiceal abnormalities in a group with chronic pelvic pain undergoing laparoscopy. In addition, we have summarized the published literature to more definitively calculate the prevalence in women with endometriosis.

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MATERIAL AND METHODS

Data were collected prospectively in a study protocol that was reviewed and approved by the Institutional Review Board of the National Institute of Child Health and Human Development at the National Institutes of Health Clinical Center.

Population

The patient cohort comprised 133 patients, aged 18–45 years, who were self-referred to the National Institutes of Health for evaluation of chronic pelvic pain and endometriosis from January 1999 to December 2004. Study inclusion criteria were: [1] intact reproductive organs; [2] good general health; [3] chronic pelvic pain and medical history consistent with endometriosis; [4] no desire for pregnancy during 2-year study period; [5] use of abstinence, barrier method, or sterilization for birth control during study; and [6] body mass index <40 kg/m^2. Exclusion criteria included: [1] infectious, gastrointestinal, musculoskeletal, neurologic, or psychiatric causes of chronic pelvic pain as evaluated by history and physical exam, review of past medical records, and questionnaire; [2] hysterectomy or bilateral salpingo-oophorectomy; [3] pregnancy; [4] lactation; [5] use of hormonal contraception, selective estrogen receptor modulators, progestins, estrogens, steroids, or ovulation induction in the previous 3 months; [6] medical or surgical treatment for endometriosis in the previous 6 months; [7] untreated, abnormal PAP smear; [8] history of venous thrombosis; [9] history of stroke, complicated migraine, or transient ischemic attack; and [10] bipolar or untreated major depression.

Intervention

All patients underwent a complete diagnostic evaluation which included detailed history and physical examination indicating the location of pain on the American Society of Reproductive Medicine pelvic pain standardized form (30) and abdominopelvic laparoscopy. All operative laparoscopies were performed under general anesthesia by the same physician.

The diagnosis of endometriosis was confirmed by direct visual inspection of the abdomen and pelvis at the time of laparoscopy. All visible lesions and adhesions were excised by selective Nd:YAG contact laser trabeculoplasty and the diagnosis of endometriosis was confirmed by microscopic pathology. A detailed description and diagram of both endometriosis implants and adhesion formation was completed during laparoscopy by a research fellow.

If the appendix appeared abnormal because of endometriosis or other minor abnormalities of the appendix, appendectomy was performed. The mesoappendix was isolated and coagulated followed by removal of the appendix by Endo Gia Universal 12-mm stapler (USSC, Norwalk, CT). If appendiceal abnormalities that also involved adjacent bowel were observed, intraoperative general surgery consultation was obtained and they were managed according to recommendations.

Selection of Studies

We conducted a computerized Medline/PubMed search (January 1950 through May 2005) using the following key words: endometriosis and appendix or appendectomy or appendicitis. All pertinent English-language articles were retrieved. A manual search of the references was then conducted for additional articles. Articles selected included only studies that contained the number of patients with visual observation at surgery or histologic confirmation of endometriosis of the appendix, total number of patients assessed, and clinical reason that the patients were evaluated. Case reports or series with fewer than three patients were omitted; however, their references were evaluated for additional articles. Data were abstracted by a single author and compiled for analysis.

RESULTS

The patient cohort comprised 133 women with chronic pelvic pain and possible endometriosis who completed a study

TABLE 1

Patient demographics and chronic pelvic pain characteristics.

	Biopsy-proven endometriosis and chronic pelvic pain (n = 97)	Chronic pelvic pain only (n = 36)
Age (y, mean ± SD)	32 ± 7.5	31 ± 6.1
Prior appendectomy (n)	10	3
Presence of right lower quadrant pain and an appendix (n)	79	30
One or more prior laparoscopies/laparotomies (n)	68	21
Appendiceal endometriosis (n)	4	—
Nongynecologic appendiceal abnormality (n)	1	1

Gustofson. Endometriosis of the appendix. Fertil Steril 2006.

TABLE 2

Summary of patients with endometriosis and other abnormalities of the appendix.

Patient	Age (y)	Intraoperative findings
1	36	Appendix adherent to left ovary in an endometrioma
2	32	Appendix adherent to sidewall with endometriosis
3	43	Appendix adherent to right ovary in an endometrioma
4	40	Appendix adherent to right sidewall with endometriosis
5	24	Edematous terminal ileum and appendix, Crohn's disease diagnosed/ no appendectomy[a]
6	30	Chronic appendicitis without endometriosis, fecalith present

[a] All patients had biopsy-proven endometriosis in other pelvic locations except Patient #5.

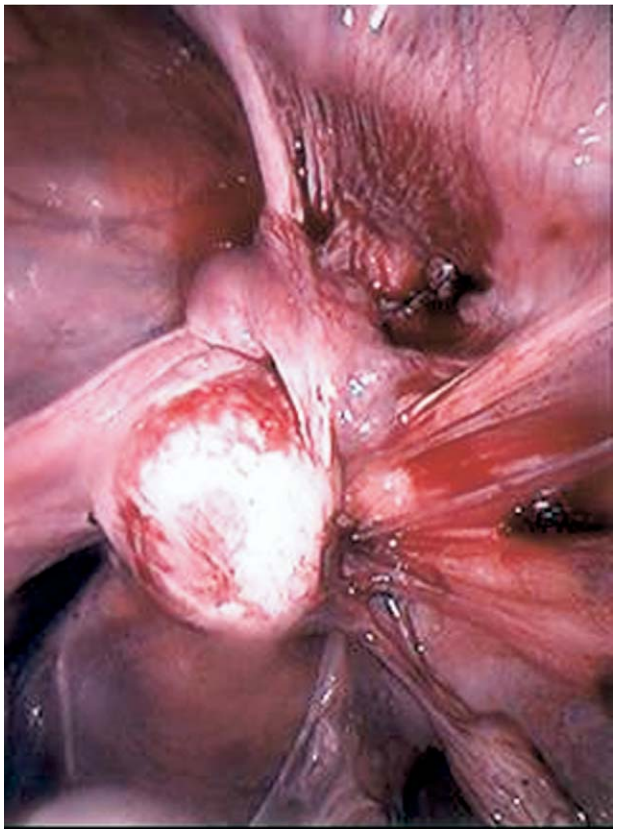
Gustofson. Endometriosis of the appendix. Fertil Steril 2006.

laparoscopy. Demographic and pelvic pain details are outlined in Table 1. Thirteen patients had a prior appendectomy with unknown pathology. Of the remaining 120 patients, 109 (87.6%) specifically reported having right lower quadrant pain. In this subgroup, four patients had endometriosis of the appendix and two had other nongynecologic pathology (Table 2). For example, patient 1 had adhesions of the appendix to the left ovary (Fig. 1), and the appendix of patient 4 was adherent to the right pelvic sidewall and right ovary (Fig. 2). Overall, 3.7% of patients (4 of 109) with an appendix, right lower quadrant pain, and possible endometriosis had endometriotic lesions of the appendix.

At laparoscopy, 97 of 133 patients (72.9%) had biopsy-proven endometriosis, 13 of 133 (9.7%) had evidence of endometriosis visible to the surgeon that was not confirmed on biopsy, 87 of 120 patients (72.5%) had both endometriosis and intact appendix, and 79 of these 87 (90.8%) also had right lower quadrant pain. All four patients with appendiceal endometriosis were in this subset of 79 women. Among those with biopsy-proven endometriosis and no prior appen-

FIGURE 1

Tethering of the appendix across the pelvis to the left ovary in patient 1.



Gustofson. Endometriosis of the appendix. Fertil Steril 2006.

FIGURE 2

The appendix is adherent to the right pelvic sidewall and appears to insert into the right ovary in patient 4.

Gustofson. Endometriosis of the appendix. Fertil Steril 2006.

TABLE 3

Literature evaluation of the prevalence of endometriosis of the appendix.

Author (ref.)	Year	Appendiceal endometriosis cases	Patients with endometriosis	Total patients	Prevalence (%) appendiceal endometriosis: Patients with endometriosis	Prevalence (%) appendiceal endometriosis: Patients with and without endometriosis
Unselected female patients undergoing appendectomy						
Smith GV (31)	1929	1	—	159	—	0.6
Masson JC (32)	1945	15	—	2,686	—	0.6
Thiersten ST & Allen E (7)	1946	2	—	866	—	0.2
Scott RB & TeLinde RW (33)	1950	7	—	516	—	1.4
Sutton CE & Hardy JA (34)	1952	15	—	6,911	—	0.2
Collins DC (12)	1955	27	—	50,000	—	0.1
Uohara JK & Kobara TY (14)	1975	12	—	1,496	—	0.8
Mittal VK *et al.* (17)	1981	16	—	50	—	32.0
Chiou YY *et al.* (35)	2003	9	—	2,442	—	0.4
Patients with endometriosis in any additional location						
Henrikson E (36)	1955	17	1,000	1,000	1.7	1.7
Kratzer GL & Salvati EP (5)	1955	1	255	255	0.4	0.4
Macafee CHG & Greer HLH (6)	1960	5	803	803	0.6	0.6
Burns FJ (37)	1967	10	360	360	2.8	2.8
Tedeschi LG & Masand GP (38)	1971	4	720	720	0.6	0.6
Weed JC & Holland JB (39)	1977	4	142	142	2.8	2.8
Prystowsky JB *et al.* (40)	1988	17	1,573	1,573	1.1	1.1
Harris RS *et al.* (19)	2001	12	337	337	3.6	3.6
Harper AJ & Soules MR (41)	2002	3	200	200	1.5	1.5
Douglas C & Rotimi O (42)	2004	2	379	379	0.5	0.5
Berker B *et al.* (13)	2005	51	231	231	22.1	22.1
Patients with and without endometriosis in any additional location						
Williams TJ & Pratt JH (8)	1977	19	485	968	3.9	2.0
Langman J *et al.* (43)	1981	6	276	3,578	2.2	0.2
Nielsen M *et al.* (44)	1983	22	800	10,000	2.8	0.2
Pittaway DE (45)	1983	13	104	500	12.5	2.6
AlSalilli M & Vilos GA (46)	1995	8	40	483	20.0	1.7
Lyons TL *et al.* (47)	2001	18	124	190	14.5	9.5
Onders RP & Mittendorf EA (48)	2003	2	3	61	66.7	3.3
Agarwala N & Liu CY (49)	2003	14	269	317	5.2	4.4
Gustofson RL *et al.*	2006	4	97	120	4.1	3.3
TOTAL		336	8,198	87,343	2.8	0.4

Gustofson. Endometriosis of the appendix. Fertil Steril 2006.

dectomy, having right lower quadrant pain increased the prevalence of appendiceal endometriosis to 5.1% (4 of 79) from 4.1% (4 of 87) (χ^2, P=.515). One patient required intraoperative general surgery consultation owing to inflammation of the bowel and appendix later diagnosed as Crohn's disease. The appendix exhibited an abnormality in 5.5% of patients (6 of 109) with both right lower quadrant pain and intact appendix, regardless of whether they had biopsy-proven endometriosis.

Review of the published literature was performed, and 29 studies met eligibility criteria, including the present study. All studies reported either the general female population or a subgroup with endometriosis and patients with endometriosis of the appendix (Table 3) (31–49). There were 332 patients with endometriosis of the appendix at surgery or pathologic examination out of 8,198 women with endometriosis, yielding a prevalence of 2.8%. When considering all patients, both with and without endometriosis, evaluated surgically or histologically, 336 women out of 87,343 patients had endometriosis of the appendix, resulting in a prevalence of 0.2%.

The prevalence odds ratio of concurrent appendiceal endometriosis was calculated when pelvic endometriosis was also present. All studies were included in the calculation except Agarwala and Liu (49), where it could not be determined which affected appendices were derived from patients with or without pelvic endometriosis. When pelvic endometriosis is present, the prevalence odds ratio of appendiceal endometriosis compared to the general population was 20.9 (95% confidence interval 16.6–26.4).

DISCUSSION

Endometriosis is a disease common to reproductive-aged women and occasionally affects the appendix. In this large case series of patients with chronic pelvic pain and possible endometriosis, the prevalence of endometriosis and all other abnormalities of the appendix ranged from 3.3% to 5.0% in those with an appendix. The reported prevalence of appendiceal endometriosis is congruent with the rate (2.8%) from a review of the literature; to the best of our knowledge, this report is the most comprehensive review of the published literature to date.

Our large series offers several caveats. First, it is important to recognize that women with endometriosis or pelvic pain may have appendiceal abnormalities. The four women with appendiceal endometriosis also had endometriosis in another pelvic location; however, it is possible that endometriosis would only occur on the appendix. Second, of these four patients, two had appendiceal-ovarian endometriosis complexes. Finding the appendix attached to an ovarian endometrioma illustrates that the appendix may touch the adnexa or other pelvic organs when a woman is upright or ambulating. This suggests not only that it may contribute to pelvic pain but also that it is part of endometriosis findings in general.

Two other patients had appendiceal or bowel disease that was independent of endometriosis. In one patient, inflammation of the bowel was seen at laparoscopy and the diagnosis of Crohn's disease was confirmed with follow-up colonoscopy. In the second patient, chronic appendicitis was seen secondary to a fecalith. These abnormalities undoubtedly caused the pelvic pain, because the right lower quadrant pain resolved with appendectomy or treatment for Crohn's disease. This underscores the importance of preoperative counseling and obtaining consent for appendectomy. Further, it emphasizes the fundamental need for systematic inspection of the appendix as part of laparoscopic treatment in those patients with chronic pelvic pain.

In our review of the literature, we calculated a low prevalence of appendiceal endometriosis in those with endometriosis (2.8%), and an even lower rate among the general population (0.4%). Although our study is limited because we performed laparoscopic appendectomy on all subjects and therefore it may not reveal the true prevalence, others who routinely performed appendectomy as part of endometriosis surgeries have found a widely varied prevalence of disease (1.5%–22%) (13, 41). The true prevalence when laparoscopic appendectomy is uniformly performed likely resides between these two reports because each study has some limitations: Harper and Soules (41) may have underreported owing to limited pathologic sectioning, and Berker et al. (13) may have overestimated owing to exclusion of patients with any possible nongynecologic causes, solely right lower quadrant pain, or signs of acute appendicitis. Because incidental appendectomy is not without risk (50), our strategy of only performing appendectomies on those with visibly abnormal appendices appears to be congruent with current practice patterns and with greater likelihood of pain resolution (46).

In the comprehensive review of the literature, three studies reported a prevalence of disease much higher than the other studies. Mittal et al. (17) reported a 32.0% prevalence of appendiceal endometriosis, likely owing to a small sample size of patients with endometriosis. Berker et al. (13) reported a large series of patients with a prevalence of 22.1% but excluded a group of patients that may have endometriosis and other diagnoses, resulting in a larger denominator of patients. Finally, the report by AlSalilli and Vilos (46), like that by Berker et al. (13), was based in referral centers and may have a significant bias of patients with gastrointestinal involvement.

Despite the low prevalence of appendiceal disease, patients undergoing surgery for right lower quadrant pelvic pain or endometriosis should be counseled regarding the possibility of appendectomy. Additionally, the appendix and other abdominopelvic locations must be inspected for disease and treated, if found. It is also important to consider nongynecologic diagnoses, because those rather than endometriosis may be the cause of chronic pelvic pain.

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