CASE-BASED REVIEW

Diagnosis and Treatment of an Ovarian Endometrioma in a Young Woman with Dysmenorrhea

Case Study and Commentary, Cynthia M. Farquhar, MBChB, MD, MPH

Abstract

• **Objective:** To review the diagnosis and treatment of endometriosis in young women.
• **Methods:** Qualitative assessment of the literature.
• **Results:** Endometriosis is one of the most common conditions affecting young women and may result in considerable patient suffering. Primary symptoms include dysmenorrhea, dyspareunia, noncyclic pelvic pain, and subfertility. Diagnosis is reliably made only by laparoscopy, but extent of disease on laparoscopy often does not correlate with symptoms. Medical therapy emphasizes ovarian suppression, but large lesions respond poorly and recurrence is common following medication cessation. If endometriosis is diagnosed at the time of laparoscopy, laparoscopic surgery is the treatment of choice, particularly in reproductive-age women with endometriomata, in which excision should be performed. Recurrence of endometriosis following laparoscopic surgery is common. Further studies are needed to determine whether postoperative medical treatment is beneficial.
• **Conclusion:** Endometriosis may result in considerable patient suffering as well as a significant economic burden of care.

In asymptomatic women, the prevalence of endometriosis ranges from 2% to 22%, depending on the diagnostic criteria used and the populations studied [1–4]. The incidence of endometriosis ranges from 40% to 60% in women with dysmenorrhea and from 20% to 30% in women with subfertility [2,5,6]. The severity of symptoms and the probability of diagnosis increase with age [7]. Incidence peaks at about age 40 years [8]. Diagnosis is reliably made only by laparoscopy. However, symptoms and laparoscopic appearance do not always correlate [9].

The cause of endometriosis is unknown, but several factors are believed to play a role in mediating its development. Embryonic cells may give rise to deposits being present in distant sites such as the umbilicus, the pleural cavity, and even the brain, whereas retrograde menstruation may deposit endometrial cells in the pelvis and throughout the peritoneal cavity, which may explain diaphragmatic lesions [10,11]. However, retrograde menstruation occurs in almost all women in whom it is sought, yet not all women who have retrograde menstruation develop endometriosis. It is not clear why only a proportion of women develop endometriosis, and one popular explanation for the peritoneal deposits is the failure of immunologic mechanisms to destroy the endometrial cells that are passed through the fallopian tubes into the pelvis. The quantity and quality of endometrial cells, the extent of the inflammatory activity in the peritoneal fluid, angiogenesis, and the production of antibodies against endometrial cells have also been suggested to have a role in the development of endometriosis [12,13]. Risk factors generally relate to the exposure to menstruation; early menarche and late menopause increase the risk because the pelvis has had a greater exposure to
menstruation, whereas the use of oral contraceptives generally means lighter and shorter periods and, therefore, reduced risk of endometriosis [8].

Most primary care physicians will be involved in the care of young women with menstrual problems, and endometriosis is one of the most common and certainly more debilitating conditions that young women may have. For these patients, one must be concerned not only about the immediate issue of pain management but also about long-term outcomes. While management of an ovarian cyst is usually surgical, it is important to consider how surgery may impact on future fertility and on recurrence of pain and endometriosis. The challenge for the physician is to preserve fertility while ensuring optimal management of pain.

Clinical decision making is increasingly being made on the basis of well-designed clinical studies, preferably randomized controlled trials (RCTs) summarized in systematic reviews. Unfortunately, for many of the clinical questions in endometriosis, there is a lack of well-designed RCTs to guide appropriate interventions. Currently, clinical practice guidelines on diagnosis and management of endometriosis are available from the Royal College of Obstetricians and Gynaecologists [14], and guidelines on medical management of endometriosis are available from the American College of Obstetricians [15]. In addition, the European Society of Human Reproduction and Embryology has recently published draft endometriosis guidelines for comment (available at www.eshre.com/emc.asp?pageId=555).

### CASE STUDY

#### Initial Presentation

A 25-year-old insulin-dependent diabetic woman presents to a new gynecologist complaining that she has “had it” with her painful and disabling menstrual periods.

#### History

The patient reports that she typically has a 7-day period every 28 days. She usually experiences pain on the first 3 days and vomits 1 to 2 times with each period. The pain usually precedes the vomiting. During her period, the patient sometimes is unable to stand up. The Visual Analogue Scale for pain on average each period varies from 6 to 8. This pattern has been present for several years.

The patient reports that 3 months ago she went to the emergency department with severe abdominal pain and vomiting that began the first day of her period and persisted for 3 days. She was admitted for intravenous fluids, blood glucose monitoring, and pain relief and was discharged home 48 hours later, as the pain had settled and her vomiting had stopped. Upon discharge, she was instructed to schedule a visit with her endocrinologist for diabetes follow-up, but her diabetes was ruled out as the cause of her severe abdominal pain. She reports that her last 2 periods were also painful but did not require more than oral pain relief. She denies pain with micturition or defecation and does not have pain other than related to menstruation.

The patient requires insulin 4 times a day and has only been ketoacidotic on 1 occasion. She has occasional hypoglycemic attacks. She has never been pregnant and uses condoms for contraception. She uses no other medications. She is a self-employed house painter. She does not smoke. None of her family members has diabetes or endometriosis.

#### Physical Examination and Transvaginal Ultrasonography

The patient is afebrile, with normal blood pressure and pulse. Abdominal examination reveals no peritonism or guarding. On pelvic examination, the gynecologist detects a fullness on the right side of the pelvis. No nodules are detected in the posterior fornix. Transvaginal ultrasonography performed in the physician’s office reveals a 6-cm cyst on the right ovary, with internal echoes consistent with an endometrioma. The gynecologist recommends laparoscopic evaluation to confirm the diagnosis of endometriosis.

- What information is important to seek in the clinical examination of women with chronic dysmenorrhea or pelvic pain?
- What is the role of ultrasonography in assessing these patients?
- Which patients should undergo diagnostic laparoscopy?

### Approach to the Clinical Examination

Any woman who regularly experiences pain in the few days

<table>
<thead>
<tr>
<th>Table 1. Common Presenting Features of Endometriosis</th>
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<tbody>
<tr>
<td><strong>Symptom/Complaint</strong></td>
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<tr>
<td>Dysmenorrhea</td>
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<tr>
<td>Dyspareunia</td>
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<tr>
<td>Painful micturition</td>
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<tr>
<td>Painful defecation</td>
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<tr>
<td>Chronic lower abdominal pain</td>
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<tr>
<td>Chronic lower back pain</td>
</tr>
<tr>
<td>Adnexal masses</td>
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<tr>
<td>Infertility</td>
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is detected, ultrasonography can differentiate between an endometrioma and a dermoid cyst in the majority of cases, although differentiating between an endometrioma and a hemorrhagic cyst is not as accurate. Differential diagnoses include ovarian cyst torsion and appendicitis. In some women, no obvious pathology will be found and dysmenorrhea will be the only explanation.

Indications for Laparoscopy

Only laparoscopy can reliably rule out endometriosis. Laparoscopy is also accurate in detecting endometriosis, unless small deposits exist deep in the ovary or in the rectovaginal septum. However, given that 60% to 70% of women in their twenties experience dysmenorrhea, it is not practical or logical to consider performing laparoscopy on all young women who present with painful periods [19]. Furthermore, the severity of symptoms is generally a poor predictor of pathology [9]. However, a proportion of women will require further investigation to help guide management. For adolescents who present with dysmenorrhea, the recommended approach is to first prescribe nonsteroidal anti-inflammatory drugs and oral contraceptives [20,21]. Failure to obtain significant pain relief with these agents is usually an indication for further investigation, including transvaginal ultrasonography and laparoscopy [22]. Other indications for laparoscopy include severe pain over several months, pain requiring systemic therapy, pain resulting in days off work or school, and pain requiring admission to a hospital.

Staging of Endometriosis

The revised American Society of Reproductive Medicine staging instrument is commonly used to grade the severity of endometriosis (from stage I through stage IV) according to peritoneal and ovarian involvement and adhesion formation (Figure) [23]. Stage I disease is generally limited to peritoneal deposits, which are not infiltrating; stage II disease involves deeper lesions; stage III or stage IV disease is characterized by infiltrating lesions of the ovary and ligaments, with extensive adhesion formation. It is recommended that all diagnostic laparoscopies use the staging system, although in practice it is used most often as a research and audit tool. It is more likely to predict fertility than pain.

Management of Case Patient

Three weeks later, the patient is admitted to the hospital and undergoes a laparoscopic right ovarian cystectomy for an endometrioma. The cyst is adherent to the underlying ovarian fossa. Despite being a right ovarian endometrioma, there are dense adhesions to the sigmoid colon. The adhesions between the sigmoid and the ovary are carefully dissected, and the ovarian cyst wall is stripped out and sent for histologic examination. There is no indication of deep sigmoidal endometriosis following the adhesiolysis. At

Role of Transvaginal Ultrasonography

Transvaginal ultrasonography is a reliable technique, although failure to reveal cystic structures does not exclude the diagnosis of endometriosis. Transvaginal ultrasonography will not reliably detect lesions less than 2 cm and is unable to detect adhesions [17]. The sensitivity and specificity of ultrasonography for the detection of an endometrioma are 88.9% and 91.0%, respectively [18]. Once an ovarian cyst is detected, ultrasonography can differentiate between an

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the end of the procedure, a levonorgestrel intrauterine system (LNG-IUS) is inserted.

The patient has a good recovery from surgery. During her first 2 periods after surgery, she experiences occasional cramps. During her next period, at 3 months after surgery, there is no pain but the period lasts 10 days. A year after surgery the patient is well, with no pain and occasional spotting only.

• What are current options for treating endometriomata, and how do they compare in terms of long-term effectiveness for symptom relief?

Medical Treatment

In women with endometriomata, the role of medical therapy is generally limited to postoperative approaches, although medical therapy may be considered if there are contraindinations to surgery. Endometriomata are suppressed while on gonadotrophin-releasing hormone (Gn-RH) analogues; however, once the treatment ceases, the lesions return to their previous size.

In women with endometriosis, the main aim of medical treatment is to suppress menstruation and induce atrophy of the endometriotic implants. Treatment options for medical therapy include oral contraceptives, progestogens, androgenic agents, and Gn-RH analogues (Table 2). All of these treatments suppress ovarian activity, although the extent to which they achieve this varies among agents. Gn-RH analogues are often considered the gold standard medical treatment for endometriosis because, when compared with progestogens and androgenic agents, suppression of the ovary is greatest with the Gn-RH analogue [24]. However, in comparative clinical studies, all of these medical therapies are effective in relieving pain and inducing atrophy while on therapy, although few studies report the laparoscopic scores following treatment [25–27]. There is no evidence that one Gn-RH analogue is superior to another.

Each medical treatment has a different side effect profile. Progestogens are associated with irregular menstrual bleeding, weight gain, mood swings, and decreased libido. The side effects associated with the most commonly used androgenic agent, danazol, include skin changes, weight gain, and occasionally deepening of the voice. Gn-RH analogues dramatically lower estrogen levels by suppressing the hypothalamic-pituitary-ovarian axis; side effects include the development of menopausal symptoms and the loss of bone mineral density with long-term use (both reversible), which may be managed by using estrogen therapy in an add-back regimen. Gn-RH analogues are given by injection or nasal spray.

For women with all grades of endometriosis, recurrence of painful symptoms after 6 months of medical therapy (with ovulation suppression using Gn-RH analogues, danazol, or medroxyprogesterone acetate) may be as high as 50% in the 12 to 24 months following cessation of the treatment [28,29]. Symptom recurrence may in part be due to the fact that large lesions respond poorly to medical therapy. It is generally accepted that large cysts of endometriosis are not amenable to medical treatment, although temporary clinical relief will be achieved. Furthermore, hormonal suppression does not influence the extent of adhesions, which are often associated with large lesions. These high rates of recurrence
following medical therapy have led to a greater role for surgery in the management of endometriosis.

**Surgical Treatment**

Surgery for endometriosis can be performed laparoscopically or as an open procedure and involves excision and/or laser or diathermy ablation of the endometriotic tissue with or without adhesiolysis. Surgical excision of endometriotic tissue results in improved pain relief and improved quality of life 6 months later compared with diagnostic laparoscopy only [30]. Approximately 20% of women do not report an improvement after surgery for endometriosis [30]. A recent Cochrane review of RCTs comparing laparotomy and laparoscopy for benign ovarian cysts showed that although the duration of surgery was longer in the laparoscopy group compared with the laparotomy group, febrile mortality was decreased for those undergoing laparoscopy and the total number of complications was decreased after laparoscopic procedures [31]. In addition, laparoscopy was associated with reduced pain and length of hospital stay [31]. Another Cochrane review of 2 RCTs comparing excision or drainage and ablation for endometriomata 3 cm or larger reported that recurrence of endometrioma and symptoms was reduced and subsequent spontaneous pregnancy increased in the women who underwent excision [32–34]. The risks of excisional surgery are destruction of the underlying ovary and reduced ovarian reserve. There is no evidence that this occurs, whereas a recurrence of the endometrioma will inevitably mean further surgery [32]. Consequently, laparoscopic excisional surgery should be the favored surgical approach to treatment of endometriomata, although it is unclear if this advice applies to smaller cysts of endometriosis.

**Prevention of Recurrence**

Recurrence of endometriosis following laparoscopic surgery is common [35,36]. Even in the hands of the very experienced laparoscopic surgeon, the cumulative recurrence rate after 5 years is nearly 20% [37]. A recent study reported that 34% to 45% of women who underwent laparoscopic surgery and who received no other treatment experienced a return of dysmenorrhea within 1 year of surgery [38]. Disappointment with these results has led gynecologists to consider whether medical therapy following surgery may have advantages.

The decision about medical therapy following surgery will depend on the plans for fertility. A systematic review of RCTs of 3 to 6 months of postoperative medical therapy using Gn-RH analogues, danazol, progestogens, or oral contraceptives showed that none of these treatments was associated with improvements in pain reduction, recurrence of endometriosis, and fertility, but the number of studies was small [39]. Further studies may provide evidence that medical treatments following surgery for endometriosis are beneficial. If there are no immediate plans for conceiving, it is.

### Table 2. Medical Treatments for Endometriomata

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Recommended Duration of Treatment</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone acetate/progestogens</td>
<td>Ovarian suppression</td>
<td>Long term</td>
<td>Weight gain, bloating, acne, irregular bleeding</td>
<td>May be given orally or by depot injection</td>
</tr>
<tr>
<td>Danazol</td>
<td>Ovarian suppression</td>
<td>6–9 mo</td>
<td>Weight gain, bloating, acne, hirsutism, skin rashes</td>
<td>Adverse effects on lipid profiles</td>
</tr>
<tr>
<td>Gonadotrophin-releasing hormone (Gn-RH) analogues</td>
<td>Ovarian suppression by competitive inhibitor of Gn-RH</td>
<td>6 mo</td>
<td>Hot flashes, other symptoms of hypoestrogenism</td>
<td>Given by injection or nasal spray only</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Ovarian suppression</td>
<td>Long term</td>
<td>Nausea, headaches</td>
<td>Can be used to avoid menstruation by skipping the placebo pills</td>
</tr>
<tr>
<td>Levonorgestrel intrauterine system</td>
<td>Endometrial suppression and, in a proportion of patients, ovarian suppression</td>
<td>5 yr</td>
<td>Irregular bleeding</td>
<td>Also reduces menstrual blood loss</td>
</tr>
</tbody>
</table>

**NOTE.** In patients with endometriomata, the role of medical therapy is limited to postoperative management. The decision about medical therapy will depend on plans for fertility and ongoing symptoms. The side effect profile may influence the choice.

- What is the most effective approach to prevent recurrence of endometriosis following surgical treatment?
ENDOMETRIOSIS

reasonable to wait for the symptoms to recur following surgery. If dysmenorrhea continues following surgery, oral contraceptives could be prescribed, as these agents can be given long term. The Gn-RH analogues and danazol are limited to 6 months of treatment because of their side effects. Medroxyprogesterone acetate (30–50 mg/day) can be given for longer, although long-term use is associated with decreased bone mineral density and, therefore, annual bone mineral densities should be measured.

Another option for treatment in a woman not planning to conceive in the first year or so after surgery is the LNG-IUS. Although the intrauterine device was originally designed as a method of contraception, the addition of progesterone to the device means that it can now be used for managing menstrual disorders, particularly heavy menstrual bleeding [39]. The LNG-IUS releases 20 µg of levonorgestrel per day and has been shown to result in a profound reduction in menstrual blood loss in women with menorrhagia; 20% of the women using the LNG-IUS were amenorrheic after 1 year while still continuing to ovulate [40]. The LNG-IUS, which must be replaced every 5 years, has also been reported to improve dysmenorrhea. A major disadvantage of the device is frequent and variable intermenstrual bleeding and spotting during the first few months of use. Use of the LNG-IUS in women with endometriosis has been less well documented, but a recent RCT has suggested benefit in women with endometriosis [41]. In the study, 40 women were randomized to either LNG-IUS or no treatment following surgery for endometriosis. Moderate or severe dysmenorrhea recurred in 2 of 20 (10%) women in the postoperative LNG-IUS group compared with 9 of 20 (45%) women in the surgery-only group. LNG-IUS has also been used in women with rectovaginal endometriosis with good effect, although the study was small and not randomized [42].

In the future, aromatase inhibitors may play a therapeutic role in endometriosis, as they have been shown to inhibit estrogen production selectively in endometriotic lesions, without affecting ovarian function [43].

• What long-term outcomes are important for women diagnosed with endometriosis?

Unfortunately, few studies have addressed this question. Long-term outcomes for women with endometriosis are pain management and prevention of recurrence of endometriosis. Five years of follow-up after laparoscopic surgery suggest that 20% to 34% of women will have a recurrence of symptoms and disease [37,38]. In addition, preserving fertility and ovarian function must be considered. Few studies have reported quality of life measures, although an RCT found that the measures were improved following surgery [30]. For women who are not planning to start a family within a few months of surgery, treatment with the LNG-IUS or an oral contraceptive could be considered, although there is no evidence of benefit with such therapy, it would seem reasonable in order to protect fertility. Repeated surgeries may result in reduced fertility and ovarian function. Multiple surgeries also may result in chronic pain conditions, including the more intractable neuropathic pain. In addition, sexual function may be adversely affected by endometriosis, particularly if the uterosacral ligaments are involved. In some women, hysterectomy and possibly bilateral oophorectomy eventually may be the only option, especially if medical treatments are unsuccessful, if repeated surgeries do not provide relief, and if fertility is not desired.

• What is the prognosis for future fertility in a woman with an endometrioma?

Few studies have addressed fertility as an outcome. There has been concern that ovarian endometrioma capsule excision may lead to removal of normal ovarian tissue and that the capsule ablation procedure may lead to thermal damage to the underlying ovarian cortex and a risk of incomplete destruction of the endometriotic tissue [44]. Hence, both interventions may lead to ovarian cortical damage and reduced fertility. A systematic review with 2 RCTs suggests benefit with laparoscopic excision of endometriomata, as pregnancy rates are increased fivefold compared with ablation [46]. However, these 2 RCTs have only 88 patients in total and further studies would be welcome [47,48]. The other concern is the impact of endometriomata on artificial reproductive techniques. The draft guidelines from the European Society of Human Reproduction and Embryology recommend removal of an endometrioma if it is 4 cm or more in diameter, as there is a reduced risk of infection, improved access to follicles, and possibly improved ovarian response.

CONCLUSION
Endometriosis should be suspected in any woman of reproductive age who presents with chronic dysmenorrhea or pelvic pain. Correlation of the pain with the menstrual cycle is important for the diagnosis, but many alternative diagnoses should be ruled out in these patients. Only laparoscopy can reliably identify endometriosis. If endometriosis is diagnosed at the time of laparoscopy, laparoscopic surgery should be the treatment of first choice, especially in a reproductive-age woman with an endometrioma, in whom excision should be performed if possible. Laparoscopy is associated with reduced postoperative pain and shorter hospital stay. In
addition, adhesion formation is likely to be reduced and fertility preserved. Ideally, the cyst wall should be stripped out, instead of drainage and ablation, as the recurrences are fewer and pregnancy rates improved [32]. At present, there is no evidence of benefit of postoperative medical treatment, but the studies to date are small and there is insufficient follow-up to rule out a benefit. The presence of endometriomata at the time of artificial reproductive technique cycles does not preclude successful pregnancy outcomes.

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Financial disclosures: None.

References


