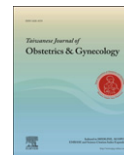


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Original Article

Long-term follow-up of patients surgically treated for ruptured ovarian endometriotic cysts

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Abstract

Objective: Approximately 4% of women are admitted to hospitals because of ovarian cyst rupture, hemorrhage, or torsion. Endometriotic cyst rupture is a rare surgical emergency associated with severe peritonitis and pelvic adhesion, and we aimed to determine its prognosis and long-term outcome.

Materials and Methods: We reviewed and analyzed the medical records of 11 patients (mean age, 31.8 ± 7.2 years) with ruptured endometrioma and a history of dysmenorrhea (4.9 ± 2.3 of maximum 10) who were surgically treated, and then regularly followed-up for more than 3 years (range, 35–261 months).

Results: Previous ultrasound examinations revealed pelvic cysts in seven patients. Three patients had a history of endometrioma surgery. In the emergency room, eight patients complained of uterine motion tenderness. Sonography revealed residual ovarian tumors (size range, 4.2–10.4 cm), with or without fluid accumulation in the cul-de-sac. Surgical enucleation by laparoscopy or laparotomy revealed high revised American Fertility Society endometriosis scores (78 ± 20.1) as well as high adhesion scores (48.7 ± 11.3). In the postoperative period, four patients had recurrent ovarian tumors that were related to elevated serum cancer antigen 125 levels and high postoperative pain scores. In contrast, three patients who became pregnant during the postoperative period had low serum cancer antigen 125 levels and pain scores.

Conclusion: Endometrioma rupture should be considered in females presenting with sudden lower abdominal pain, associated with a history of dysmenorrhea and preexisting pelvic cysts. Emergency surgical intervention may lead to a better prognosis, particularly in patients without a history of previous endometrioma surgery.

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Keywords: Endometrioma rupture; Outcome; Surgery

Introduction

Approximately 4% of women are admitted to hospitals because of ovarian cyst rupture, hemorrhage, or torsion [1]. Ovarian cysts can be either physiologic (e.g. follicle and corpus luteum) or pathologic (e.g. endometrioma, mucinous,

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or serous cystadenoma) events. Patients with ruptured follicles can present with mittelschmerz during ovulation. A ruptured corpus luteum often occurs on Days 20–26 of the ovarian cycle, and unilateral lower abdominal pain often occurs during the first trimester of pregnancy in these patients.

Several sporadic case reports of endometriotic cyst rupture, some of them during pregnancy, have been published. Endometriotic cyst rupture may result in the shedding of endometriotic fluid into the pelvic cavity, which may induce further inflammatory reaction and adhesion. The prognosis and long-term outcome are still not well established [2–4]. We

summarize our experience regarding treatment as well as more than 3 years of follow-up in 13 cases of endometrioma rupture.

Materials and methods

Patients

Follow-up sessions were conducted for 11 patients who underwent emergency surgical management for endometrioma rupture at the Chang-Gung Memorial Hospital between January 1988 and December 2006. All patients suffered from pelvic cysts with a sudden onset of abdominal pain. Emergency laparotomy or laparoscopy was performed in all patients. Surgical pathology demonstrated these cysts to be endometriomas.

Demographic data

Data on age, body mass index, obstetric observations, previously known ovarian cysts, dysmenorrhea, pain score, and any history of pelvic surgery or infertility were recorded.

Preoperative symptoms or signs

All patients underwent a sonographic evaluation with or without a computed tomography examination of the pelvic organs. Additionally, patients with a sexual exposure also underwent a pelvic examination. Laboratory investigation included complete blood count, hemoglobin, and serum cancer antigen 125 (CA-125). Laparoscopy or laparotomy was selected based on the patient's vital stability.

Operation findings

Latency from the pain attack to surgery, operative method, operative time, rupture site, revised American Fertility Society (rAFS) score, adhesion score, and length of hospital stay were recorded.

Clinical outcomes

We recorded the months of follow-up as well as the use of postoperative medications, including the gonadotropin-releasing hormone analog, danazol, oral contraceptive pills, or Chinese herbal therapy. Outcomes were evaluated by the pain score, sonographic findings, serum CA-125 levels, further surgery (e.g. cyst aspiration), or pregnancy.

Results

The demographic data are listed in Table 1. The mean age was 31.8 ± 7.2 years and the mean body mass index was 19.4 ± 2.0 . Most patients (8 of 11 cases, 72.7%) were nulligravid. All our patients had a history of dysmenorrhea with pain scores ranging from 3 to 8 points (with 0–10 points of visual score). Follow-up sessions were conducted for seven patients in our clinic because of chronic pelvic pain and dysmenorrhea. Ovarian tumors were detected in all patients. Three patients (Cases 3, 4, and 8) had a history of ovarian endometrioma and underwent laparoscopic enucleation or sonar-guided transvaginal aspiration of the ovarian tumor; one patient sought examination and treatment for infertility.

During the preoperative evaluations (Table 2), all patients experienced a sudden onset of abdominal pain accompanied with nausea, vomiting, and/or diarrhea. The pain attacks occurred from Day 10 to Day 20 of the menstrual cycle; 8 of the 11 patients accepted a pelvic examination, which revealed significant uterine tenderness. Onsite ultrasonography detected at least one ovarian cyst (diameter range, 4.2–10.4 cm) in all patients, and fluid accumulation in the cul-de-sac in three cases. Fever (body temperature higher than 37.5°C) was noted in two patients. Laboratory data indicated leukocytosis (white blood cell count higher than $10,000/\mu\text{L}$) in five cases and low hemoglobin (less than 10 g/dL) in two cases. Serum tumor marker, CA-125, levels were elevated (higher than 35 IU/mL) in four of the six cases tested, an extremely high level (higher than 2000 IU/mL) was noted in one case, and moderately high

Table 1
Demographic data

Case	Age	BMI	Obstetric data	Pain score (0–10)	Known ovarian tumor		Previous pelvic surgery	Infertility (y)
					Location	Size (cm)		
1	23	18.3	Nulligravid	3	No record		None	Nil
2	27	16.9	Para 2	3	No record		None	Nil
3	34	21.5	Nulligravid	8	Right	10.0	Endometrioma enucleation twice	Nil
					Left	3.2		
4	36	19.2	Para 1	8	Right	4.3	Endometrioma enucleation	Nil
					Left	3.6		
5	24	23.3	Nulligravid	5	Right	6.0	None	Nil
6	31	19.7	Abortion 1	3	Right	7.2	None	Nil
7	49	17.6	Nulligravid	3	No record		None	Nil
8	35	19.9	Nulligravid	8	Right	9.5	Endometrioma enucleation	2
					Left	4.7	Transvaginal aspiration	
9	29	18.8	Nulligravid	3	Left	7.8	None	Nil
10	34	17.1	Nulligravid	3	No record		None	Nil
11	28	20.8	Nulligravid	7	Right	6.6	None	Nil

BMI = body mass index.

Table 2
Preoperative symptoms or signs

Case	Cycle day of attack/ vital signs	Pelvic examination	Sonography done in emergency department			Serum CA-125 (IU/mL)
			Location of main cyst	Tumor size (cm)	Other findings	
1	Day 15/fever	No sexual experience	Right	6.5	Nil	Not checked
2	Day 13/fever	Lifting pain	Right	6.3	Nil	2,844.3
3	Day 10	Lifting pain	Left	10.4	Nil	Not checked
4	Day 16/tachycardia	Lifting pain	Right	4.8	Nil	11.4
5	Day 11	No sexual experience	Right	4.6	Nil	Not checked
6	Day 14	Lifting pain	Right	5.9	Nil	12.3
7	Day 16	Lifting pain	Right	4.2	Fluid in cul-de-sac	85.2
8	Day 17	Lifting pain	Left	6.6	Fluid in cul-de-sac	256.9
9	Day 16/tachycardia	No sexual experience	Left	7.2	Fluid in cul-de-sac	Not checked
10	Day 15	Lifting pain	Left	5.4	Nil	Not checked
11	Day 20	Lifting pain	Right	6.2	Nil	36.0

CA-125 = cancer antigen 125.

levels were noted in two cases (Cases 7 and 8). Abdominopelvic computed tomography was performed in two patients to rule out pelvic malignancy. Emergency surgery was performed immediately following the preoperative surveys.

Eight patients accepted surgery within 24 hours of their pain attack and one patient was operated after 48 hours because of her delayed visit (Table 3). Six patients had laparoscopic surgery and five underwent a laparotomy. Seven cases had right-sided- and four cases had left-sided ruptured endometriomas. The rAFS scores (78 ± 20.1 ; range, 48–102) and adhesion scores (48.7 ± 11.3 ; range, 28–64) revealed that all patients had severe endometriosis and pelvic adhesions. The length of hospital stay was related to the operative method (laparoscopy 3–5 days; laparotomy 4–8 days).

The mean follow-up period was more than 3 years (mean, 85.6 ± 65.3 months; range, 35–261 months; Table 4). Eight patients were administered medications postoperatively. One patient received Chinese herbal medicine for 2 years. During the follow-up period, 3 of the 11 cases (27.3%) reported a recurrent pain of a higher score and 5 of the 11 cases (45.5%) had an elevated serum CA-125 level, of which 4 (80.0%) had recurrent tumors, as revealed by sonography. Three patients later successfully conceived and delivered.

However, the infertility patient did not conceive until recently and received further cyst aspiration for her recurrent ovarian endometrioma.

Discussion

Endometriosis is a common gynecologic diagnosis with prevalence in the general population of around 10% [5]. Patient surveys performed in the United Kingdom and the United States found that women with endometriosis suffered from a variety of complaints, including pelvic pain (70–71%), dysmenorrhea (71–76%), dyspareunia (44%), and infertility (15–20%). When the ectopic endometrial tissue implants inside the ovary, it forms an ovarian cyst or ovarian endometrioma. Spontaneous rupture of an endometriotic cyst is very rare. Only a few cases have been reported till date, most of which were associated with early pregnancy. The etiology of endometrioma rupture is presumably the increasing size of the ovarian tumor as well as the rising pressure and tension inside the cyst, which reflect the degree of rapid growth and proliferation of endometrial tissue in the tumor [6]. During pregnancy, endometriomas may undergo decidualization and become soft and fragile [7], in response to pressure from the

Table 3
Operation findings

Case	Latency from attack to surgery	Operation						Hospitalization (d)
		Methods	Operation time (min)	Blood loss (mL)	Rupture side	rAFS score	Adhesion score	
1	<6 h	Laparotomy	180	1200	Right	58	28	8
2	<6 h	Laparoscopy	125	50	Right	90	64	5
3	24–48 h	Laparotomy	160	700	Left	102	56	4
4	<6 h	Laparoscopy	115	50	Right	102	56	3
5	6–24 h	Laparoscopy	135	50	Right	86	60	3
6	<6 h	Laparoscopy	103	250	Right	56	44	3
7	<6 h	Laparotomy	110	50	Right	62	46	7
8	<6 h	Laparotomy	95	1100	Left	102	56	4
9	24–48 h	Laparotomy	90	200	Left	82	52	5
10	<6 h	Laparoscopy	65	50	Left	48	38	3
11	>48 h	Laparoscopy	100	50	Right	70	36	4

rAFS = revised American Fertility Society.

Table 4
Clinical outcomes

Case	Follow up (mo)	Postoperative medications	Pain score (0–10)	Serum CA-125 (IU/mL)	Sonography		Further procedures
					Location	Tumor size (cm)	
1	261	Danazol (6 mo)	4	23.6	Nil	Nil	Pregnancy
2	122	Chinese herb (24 mo)	1	24.1	Nil	Nil	Sterilization
3	108	Danazol (5 mo)	8	50.8	Right	4.3	Nil
4	91	Nil	6	108.4	Left	3.6	Cyst aspiration
5	85	Leuprorelin (3 mo)	8	51.7	Right	5.5	Cyst aspiration
6	61	Nil	5	14.9	Nil	Nil	Pregnancy
7	53	Nil	2	4.3	Nil	Nil	Intrauterine device use
8	51	Danazol (3 mo)	4	53.7	Right	3.5	Cyst aspiration
9	39	Danazol (3 mo)	3	36.1	Nil	Nil	Nil
10	36	Havina (4 mo)	2	11.6	Nil	Nil	Pregnancy
11	35	Leuprorelin (3 mo)	4	17.9	Nil	Nil	Nil

CA-125 = cancer antigen 125.

cyst and the adjacent enlarging uterus. According to the location of the endometriotic lesion, a ruptured endometrioma, colonic perforation, hemoperitoneum, and even fetal death because of a tear in the uterine vessels have been reported [8]. A ruptured endometrioma during the menstrual cycle has also been reported [4]. To our knowledge, this is the first case series to report rupture during a nonpregnant period and in the periovulatory stages. In patients with recurrent endometriomas, the rapid enlargement of an ovarian endometrioma is classified as advanced stage and aggressive. According to the AFS classification, an endometriotic cyst is classified as moderate to severe in cases of adhesion formation and additional disruption of the pelvic anatomy. An increase in the shearing force and tension between previous adhesions and a rapidly enlarging ovarian endometrioma result in an altered anatomical position and further rupture events [9].

Most patients who have suffered from an ovarian cyst rupture can identify the onset time because of maximal pain at symptom onset [1]. In contrast to a ruptured corpus luteum that often occurs from Day 20 to Day 26 of the menstrual cycle, in our study, the ruptured ovarian endometriomas occurred between Day 10 and Day 20, thus indicating a hormonal role in influencing and regulating the size of ovarian tumors as well as in cyst wall weakening. The acute event is frequently induced following acute inflammatory reactions, such as fever, and presents with nausea, vomiting, rebound tenderness, and muscle guarding because of endometriotic fluid being associated with peritoneal irritation. The clinician should differentiate ruptured endometrioma from other gynecologic problems, such as pelvic inflammatory diseases, tubo-ovarian abscess rupture, or corpus luteum rupture. Other nongynecologic causes, such as a ruptured appendicitis, diverticulitis, bowel obstruction, or hollow organ perforation, also need to be excluded.

If a pelvic examination is performed, lifting pain assists in distinguishing a cystic rupture from physical ascites, and the severity depends on the volume of fluid released into the peritoneal cavity [1]. Sonography aids the diagnosis and helps to distinguish ovarian tumors based on size, wall thickness, single or multiple cysts, and solid components.

The sonographic features of endometrioma vary, but most cysts reveal low-level internal echoes with hyperechoic wall foci. A ruptured ovarian endometrioma is diagnosed by the presence of free fluid, with or without an ovarian tumor. If fluid is noted, a culdocentesis may be useful. In our review, sonography revealed only three cases with fluid in the cul-de-sac, although all cases presented with a residual ovarian tumor. The residual size of the ovarian tumors ranged from 4.2 cm to 10.4 cm. On tracing their histories, it was revealed that all patients who were previously evaluated in our clinics had a known ovarian tumor. Thus, endometrioma rupture should be included in the differential diagnosis of young females with acute abdominal pain and previous known ovarian cysts.

The level of CA-125, a tumor-associated antigen, assists in the preoperative distinction of benign versus malignant ovarian tumors. Malignancy cannot be ruled out when the level is greater than 300 IU/mL [3], so a detailed history and survey are justified. Case 2 had an extremely high serum CA-125 level (2,844.3 IU/mL) on the day of evaluation, which decreased to 24.1 IU/mL after laparoscopic enucleation of the ovarian tumor. This is in concurrence with an earlier report of a 24-year-old woman with a ruptured endometrioma with an extremely elevated serum CA-125 concentration mimicking ovarian malignancy and a rapidly decreasing serum CA-125 level after surgery [10]. Kurata et al [4] presented a case of bilateral ovarian endometrioma rupture with an elevated CA-125 level in the serum (9,537 IU/mL) as well as in the peritoneal fluid (16,000 IU/mL). They suggested the possibility of ascites-serum exchange involving the transfer of endometriotic cyst fluid throughout the peritoneal surface into the systemic circulation, resulting in an extremely high serum CA-125 level corresponding to the high level in the peritoneal fluid. This hypothesis can help explain why serum CA-125 levels in endometriosis can occasionally be as high as those observed during malignancy.

It has been suggested that serum CA-125 levels are significantly higher in patients with more extensive adhesions to the peritoneum, omentum, ovary, fallopian tube, colon, and cul-de-sac or in those with a ruptured endometrioma [11].

Serum CA-125 levels have been used to identify the severity and recurrence of endometriosis. When compared with laparoscopy, it is an inexpensive and less invasive test. Although the sensitivity of CA-125 levels is limited (all stages: sensitivity 28% and specificity 90%; moderate-to-severe endometriosis: sensitivity 47% and specificity 89%) in women with surgically confirmed endometriosis as assessed in a meta-analysis, their role in reflecting peritoneal conditions should not be ignored [12]. Of the five cases with increased CA-125 levels during the follow-up period, three self-reported a high pain score (above 5 points) and four revealed recurrent endometriomas.

Ruptured ovarian tumors are usually treated with analgesia and observation, unless ovarian torsion, unstable hemodynamic status, or persistent symptoms are observed. Clinical conditions should be closely monitored during conservative treatment. If the presentation worsens or does not improve, more aggressive intervention is suggested. In our patients, there was a slight improvement in postoperative pain scores (4.3 ± 2.3 vs. 4.9 ± 2.3). In addition to the clinical vital signs, patient age, tumor size, malignant potential, and a surgeon's experience, can all play a role in determining the operative method.

Of the 11 cases, 8 patients accepted emergency surgery within 24 hours, whereas 3 did so after 24 hours (24–48 hours, 2 patients; >48 hours, 1 patient). We could not evaluate the outcome in terms of latency between attack and surgery because of the limited number of cases (Table 3). If patients insist on conservative management, they should be informed of the effects of prolonged endometriotic fluid retention in the peritoneal cavity after rupture. Ishikawa [9] demonstrated that natural killer cell activity was suppressed by the supernatant of endometriotic tissue cultures and was significantly lower in experimental endometriosis than in a sham (abdominal fat tissue; $p < 0.001$). Nevertheless, natural killer cell activity recovered after the endometrial implants were excised. Badawy et al [6] observed a higher concentration of transforming growth factor- $\beta 1$ (TGF- $\beta 1$; range, 451–1,462 pg/mL) and an increased proliferation rate of cultured human endometrioma cells in chocolate-cyst fluid. The angiogenic activity of TGF- β stimulates vascularity and induces inflammatory-type reactions in the surrounding tissues, such as the ovary or other abdominopelvic structures, which may contribute to further adhesion formation. These two studies support the findings that endometriotic fluid from a ruptured endometrioma has increased levels of growth factors, such as TGFs, that inhibit natural killer cell activity. Endometriotic fluid has also been shown to induce adhesions, a rapid progression of endometriosis, or even endometrioma.

Endometrioma recurrence affects 8–32% of women, and pain recurs in 10–40% of cases. This unfavorable outcome is associated with prior surgery, the presence of adhesions, and the use of ovulatory drugs. However, pregnancy is protective against recurrent symptoms, such as dysmenorrhea, dyspareunia, chronic pelvic pain, and even recurrent endometrioma [13]. Follow-up sessions were carried out for more than 3 years for all patients. Four patients (Cases 3–5 and 8), who had a history of dysmenorrhea, higher pain scores, and known

ovarian cysts, developed recurrent ovarian tumors. They also had bilateral ovarian tumors and had previously undergone surgery for endometrioma at least once. During the operation findings, their AFS and adhesion scores were higher (rAFS score, 98 ± 8 vs. 66.6 ± 15.0 ; adhesion score, 57 ± 2 vs. 44 ± 11.7) as compared with the other seven cases, which had a favorable outcome. Those three cases became pregnant after their respective operations, so they did not complain of recurrent dysmenorrhea. Furthermore, there was no recurrence of ovarian tumors during the follow-up period (35–261 months). Because of the limited case numbers, it is not clear whether postoperative medication is useful in preventing recurrence.

Endometrioma rupture should be included in the differential diagnosis of young women with known ovarian cysts and previous surgery for endometrioma. These patients also need to be informed of the prognostic factors and recurrent symptoms. A long-term follow-up and a comprehensive review of their clinical symptoms are necessary for early detection of recurrence.

Conclusions

A ruptured ovarian endometrioma is highly suspected in the following cases: free fluid present in the cul-de-sac with or without an ovarian tumor, sudden onset of abdominal pain, a surgical history of endometrioma, or clinically suspected endometriosis (e.g. dysmenorrhea and known ovarian tumors). Endometrioma rupture should be considered in females presenting with sudden lower abdominal pain associated with a history of dysmenorrhea and preexisting ultrasound-detected pelvic cysts. Emergency surgical intervention may result in a better prognosis. However, patients with a history of previous endometrioma surgery, further presenting with recurrent endometrioma rupture, may have poorer outcomes.

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