

Clinicopathological features of endometriosis in abdominal wall – clinical analysis of 151 cases

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Summary

Objective: To explore the clinicopathological features of abdominal wall endometriosis (AWE). **Materials and Methods:** A retrospective study was made of 151 AWE patients, who were treated at Obstetrics and Gynecology Hospital, Fudan University from 2003 to 2010. **Results:** Most patients (80.1%) presented with cyclic pain and/or cyclic abdominal masses. The latent period of AWE patients was 31.48 ± 28.27 months (three to 192 months), which was not correlated with factors related to previous cesarean section (CS) (such as age at CS, incision site, gestational week at CS, baby's birth weight, lactation period, postpartum menstruation recovery, choices of contraceptives, etc). The duration of disease was 33.07 ± 28.58 months (two to 168 months), which was negatively correlated with the latent period ($r = -0.267, p = 0.043$). The pre-operational ultrasonography detection rate was 97.4% (147/151 cases). The lesion size detected by preoperative ultrasonography was significantly smaller than that measured intraoperatively by palpation ($21.6 \pm 20.7\text{mm}$ vs. $30.21 \pm 30.9\text{mm}$ $p < 0.05$). Moreover, only 26.5% (40/151 cases), in AWE patients the infiltration depth was revealed by preoperative ultrasonography. All patients received surgical treatment. The symptoms were relieved in 93.4% (141/151 cases) patients after surgery. The recurrence rate was 7.3% (11/151 cases) while the average recurrent time was 19.8 ± 15.99 months. The recurrence rate was significantly lower in postoperative medication group than that in non-medication one ($p < 0.05$). In addition, the morphologic features of AWE lesions also contributed to recurrence. The duration of disease in large scar endometrioma (LSE) group (the diameter of lesions \geq three cm) was significantly longer than that in small scar endometrioma (SSE) group (the diameter of lesions $<$ three cm), while SSE group had higher recurrence rate ($p < 0.05$). **Conclusions:** The indications of previous CS, factors related to delivery and lactation, have little effect on the exact time of AWE onset. Although ultrasonography is beneficial to preoperative diagnosis of AWE, its accuracy in evaluating lesion size and infiltration depth is limited, which should be interpreted appropriately. The morphologic features of AWE lesions may be correlated with the severity of disease. Surgery is the first-line treatment of AWE and postoperative medication might reduce recurrence.

Key words: Abdominal wall endometriosis(AWE); Features; Recurrence.

Introduction

Endometriosis is common in pelvic organs, such as ovary, peritoneum, and it is rare in the abdominal wall, bladder, perineum. Abdominal wall endometriosis (AWE) is the functional endometrial gland transfer to the lower abdominal wall. Due to the low incidence of AWE, there are only case reports available, therefore we only have little knowledge about its clinical characteristics. Also it is often misdiagnosed as incisional hernia, granuloma, and abdominal wall tumor. In recent years, with the increase of cesarean section (CS) and intrauterine operation, there are increasing cases of AWE. People seek to illustrate early detection, diagnosis, and prevention and individualized treatment about AWE. This paper retrospectively analyzed the clinical data of 151 AWE cases to explore their clinical features and personalized treatment.

Materials and Methods

One hundred and sixty-six cases of AWE patients were admitted in Obstetrics and Gynecology Hospital, Fudan University, and 155 patients completed the regular follow-up research (follow-

up rate: 91%, Follow-up time: 16-97 months). The average age was 31.27 ± 3.88 years (24-47), gravidity was 31.27 ± 3.88 weeks, and parity was 1.91 ± 0.9 . Nine cases accepted previous AWE surgeries (6%).

Clinical features

All patients had a history of CS and among them, 121 (80.1%) cases had periodic abdominal pain, or cyclical lower abdominal mass, 17 (11.3%) cases had irregular abdominal pain, and 13 (8.6%) cases had no discomfort. Eight patients were diagnosed in routine examination, five patients were diagnosed during undergoing other gynecological operations; among these, nine (6%) patients were found with ovarian endometriosis and nine (6%) patients with adenomyosis (Table 1).

AWE Features

All patients underwent ultrasound examination, and ultrasound showed that 147 patients (97.4%) had low- or low-middle echo area in abdominal incision at the skin. The other four cases had no positive findings in ultrasound examination. Preoperative ultrasound examination inspected the number of lesions: 125 (85%) cases with single lesion, 19 (10.9%) cases with two separate lesions, and six (4.1%) cases with three or more lesions. The average lesion size was $21.6 \pm 20.7\text{mm}$ (10-60). Only 40 cases

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Table 1. — Previous cesarean section cases.

	Cases	Percentage
Cesarean section incision position		
Transverse incision	112	74.2
Vertical incision	39	25.8
Operation indications		
Social factor ^a	60	39.7
Fetal factor ^b	79	52.3
Maternal factor ^c	12	8.0
PROM		
Yes	113	74.8
No	38	25.2
Gestational weeks		
Preterm	16	10.6
Full term	124	82.1
Prolonged	11	7.3
Lactation		
No	26	17.2
Yes	125	82.8
Lactation duration		
≤ 6 months	62	49.6
6-12 months	56	44.8
> 12 months	7	5.6
Postpartum menstruation recurrence		
≤ 6 months	102	67.5
6-12 months	40	26.5
> 12 months	9	6.0
Contraception after CS		
IUD	70	46.3
Oral contraceptive	9	6.0
Condoms or without contraception	72	47.7

^a: selective cesarean operation regarding those who were not willing to undergo vaginal delivery, absolute no operation indications. ^b: placenta previa, cephalopelvic disproportion, fetal macrosomia, breech presentation, twins.

^c: gestational hypertension, high myopia.

recorded an invasion depth, in which five cases involved the fat layer involved, 15 cases involved the fascia, eight cases involved muscle, and 12 cases involved the extraperitoneum.

Treatment

Preoperative management: 34 patients firstly used medications for three to eight months before surgery, respectively, nine (6.0%) cases with GnRHa, nine (6.0%) cases with progesterone, 16 (10.6%) cases took traditional Chinese medicine, and the other 117 (77.5%) patients did not take any medications.

Surgery: 151 cases underwent surgeries, and excision range including the tissues around the lesion edge for one cm. Among them nine cases underwent hysterectomy and nine cases ovarian endometrioma decortication. The postoperative histopathological diagnosis indicated endometriosis in the incision sites. The largest lesion diameter in the operative exploration was 30.21 ± 30.9 mm (10-110). Each patient had an average of 1.17 ± 0.54 (1-4) lesions, which involved invasion to the fat in 42 (27.7%) cases, the fascia in 72 (47.7%) cases, the muscle in 25 (15.6%) cases, and the extraperitoneal in 12 (8.0%) cases. Abdominal wall lesions were located in two vertices: cesarean incision left and right of transverse incision, or the upper and lower ends of the vertical incision; 38 (25.2%) cases of lesions were located in the central of cesarean incision and the remaining five (3.3%) cases were not mentioned in the patient's medical records. A total

of 19 (12.6%) patients with resection of the lesion in the fascial defect were repaired with a patch.

After the operation, 57 patients were treated with drugs, respectively 30 (19.9%) cases with GnRHa, ten (6.6%) cases with gestrinone, 13 (8.6%) cases with oral contraceptive, and traditional Chinese medicine in four (2.7%) cases.

Follow-up

The authors conducted regular follow-ups, every three months during which they examined the change in clinical symptoms through gynecological examination and ultrasonography. The follow-up periods were 16-97 months. Postoperative cyclic abdominal wall pain that became milder was considered to be symptomatically relieved. After surgery symptoms were relieved for three months, but cyclic and recurrent abdominal wall pain that continued to the preoperative level, or pathologically diagnosed AWE after surgery again were defined as the recurrence.

Statistical method

All the data were analyzed by SPSS 13.0 analysis software. Count data was analyzed chi square test and measurement data was analyzed by analysis of variance. $P < 0.05$ was considered statistical significance.

Results

The incubation period and clinical course

The incubation period is time interval from after CS to present the related clinical symptoms and signs. The incubation period of 151 cases with AWE was 31.48 ± 28.27 months (3-192), and there is no significant correlation with the last cesarean birth related factors, such as age of CS, incision position, the baby during pregnancy, birth weight, the time of postpartum lactation, the time of postpartum menstrual recovery, and postpartum contraceptive or not.

Clinical course is the time interval from the appearance of clinical symptoms and signs to accept the operation. The clinical course of 151 cases with AWE was 33.07 ± 28.58 months (2-168). The clinical course of patients who used preoperative medication was 41.85 ± 36.9 months, which was longer than the patients who did not use preoperative medication (27.81 ± 22.1 months), but there were no statistical significance ($p = 0.06$). The length of clinical course was negatively correlated with the incubation period ($r = 0.267$, $p = 0.043$).

Preoperative and postoperative detection accuracy

The ultrasound in the detection rate of AWE was 97.4%, and the maximal diameter of the lesions detected by ultrasonic before operation was 21.6 ± 20.7 mm, which was significantly smaller than the largest lesion size (30.21 ± 30.9 mm) during the operating exploration. Preoperative ultrasonography revealed the depth of invasion in only 40/151 (26.5%) patients.

The relationship between morphological characteristics and disease severity of lesions

Taking three cm as the standard [1], the intraoperative lesions were divided into two groups: large scar en-

Table 2. — Comparison of LSE and SSE.

	LSE (101 cases)	SSE (50 cases)	<i>p</i>
Incubation period (months)	31.78	28.83	0.75
Clinical course (months)	37.53	23.68	0.02
Premedication (cases)	20 (19.8%)	14 (28%)	0.51
Depth of invasion (cases)			
Fat	21	21	
Fascia	52	20	
Muscle layer	18	7	
Peritoneal	10	2	0.36
Postoperative medication (cases)	38 (37.6%)	19 (38%)	0.94
Postoperative symptoms (cases)			
Relief	96	45	
Unrelief	5	5	0.59
Postoperative recurrence (cases)			
Yes	3	8	
No	98	42	0.004

ometrioma (LSE) and small scar endometrioma (SSE). One hundred and one cases were LSE, and 50 cases were SSE. As can be seen in Table 2, clinical course of LSE group was significantly longer than that of SSE group, and the recurrence rate in SSE group was higher than that of LSE group ($p < 0.05$).

Curative effect and related factors

After operation the symptoms of 141 cases were alleviated, but ten (6.6%) cases had no change. In 151 patients there were 11 cases of recurrence, and the recurrence rate was 7.3%. The average recurrence time was 19.8 ± 15.99 months. Premedication were not associated with local recurrence ($p > 0.05$). Recurrence rate of postoperative medication group was significantly lower than untreated group (3.5% vs. 9.6%, $p < 0.05$), but there was no significant difference between different types of medications ($p > 0.05$).

Discussion

The incidence of AWE

Although AWE is a common subtype of endometriosis out of the pelvis, it accounts for only 1.04% of endometriosis [2]. It is usually associated with cesarean operation incision, and it is reported that the occurrence rate of AWE after full term CS is 0.03-0.47% [3, 4], but in rare cases can also be found in umbilical and inguinal sites of endometriosis in patients without history of operation [5]. AWE might be related to operating procedure itself, since it is usually secondary to CS. The present study firstly analyzed the relationship between previous CS and this current episode of disease, including childbirth and puerperium situation.

Occurrence of operation and AWE

Most scholars believe that free endometrial debris will invade into incision during operation, which leads to AWE.

This reason may highly related to the operating skill and operating procedure of the surgeon [6, 7]. The present authors analyzed the indication of cesarean birth operation of the AWE patients, including fetal, social, and maternal factors. Compared with the emergent cesarean cases, cases due to social factors usually have more adequate preoperative preparation, less operating risk and difficulty, less bleeding, shortened operation time, and less chance of endometrial implanting during the operation. Among these 151 cases of AWE, the indication of social factors accounted for 39.7%, emergency cases accounted for 60.3%, while epidemiological investigation of 933 cases of CS in the corresponding period showed that social factors accounted for 35.9% [8]. There was no significant difference between the two studies. Therefore cesarean operation indication is not associated with the occurrence of AWE. These suggest that although the operative procedure could facilitate the endometrium implant into the operation incision, but the implanting risk for every cesarean birth is equal. Thus, the occurrence of ectopic endometrium growth may not specially correlated to operation itself, but may be related to genetics, local environment of wound, endocrine metabolism, and other factors [4].

Delivery and occurrence of AWE

Ectopic endometrium implanting to the incision is as the relationship between seed and soil, which might be affected by the local environment of wound and endocrine level. The incubation period of AWE after CS to the clinical findings to some extent reflects this impact. Postpartum estrogen levels decline and is not conducive to the growth of the endometrium. Some scholars believe that because lactation can maintain low levels of estrogen, hence breastfeeding can prevent the occurrence of postpartum advocate AWE in a certain extent [6]. In this study, 82.8% of the patients had postpartum breastfeeding, of which 49.6% patients' lactation time was less than half a year, 44.8% patients' lactation time was half a year to one year, and 5.6% patients' lactation time was more than one year. Postpartum breastfeeding, breastfeeding duration, and menstrual recovery time were independent from the incubation period ($p > 0.05$). The present authors analyzed all of the possible reasons: one might be due to AWE as a special site of endometriosis, in which the ectopic endometrium is surrounded by fiber tissue hyperplasia, and the blood circulation is poor and thus less affected by the hormone levels. On the other hand, it may be related to local abnormal expression of estrogen and progesterone receptors in AWE, which have autocrine positive feedback mechanism, leading to high estrogen producing levels in the ectopic endometrium [9].

Clinical manifestations and diagnosis of AWE

The typical clinical manifestation of AWE is cyclical lower abdominal mass and lower abdominal pain associ-

ated with the menstrual cycle. In this study 80.1% patients were in the presence of periodic abdominal pain and cyclical lower abdominal mass, consistent with those reported in the literature. In addition, 8.6% of asymptomatic patients were found during physical examination or operation by other reasons, which suggests the actual incidence of AWE in population, is currently much higher than estimated. Because the patients' symptoms are not typical and lesions need to grow to a certain size to cause clinical symptom, the diagnosis AWE can be delayed.

Reports varied about the onset latency and the average incubation period was 22-72 months [5, 7, 10]. The AWE latency of this group was 31.48 ± 28.27 months (3-192), and there was no correlation between the factors of previous CS (including CS age, incision position (transverse incision/vertical incision), neonatal gestational weeks, infant birth weight, postpartum lactation time, postpartum menstrual recovery time, whether postpartum contraception was used, and AWE. There was only negative correlation ($r = 0.267$, $p = 0.043$) between the clinical AWE symptoms and the operation time as disease course, indicating that the more later finding of AWE, the more serious the symptoms were and the need for surgical treatment.

Diagnosis of AWE

The mass in abdominal incision site is tenacious and the surrounding tissue boundary is less clear, with or without tenderness. Ultrasound is not very specific for the diagnosis of AWE; the image displays as: heterogeneity hypoechoic, cystic, and containing viscous liquid [11]. However, the ultrasound examination is helpful for the preoperative diagnosis if combined with the patients' clinical symptoms and signs, and the present data showed that the preoperative diagnosis rate of AWE was 97.4%. CT and MRI can be used for preoperative evaluation, but also have no specified characteristics [12].

Although ultrasonography is helpful in preoperative diagnosis of AWE, the estimation accuracy of lesion range is limited. In this study, only 26.5% patients (40/151 cases) with preoperative ultrasonography suggested that the lesion invasion depth and preoperative ultrasound measurements of lesion size were significantly smaller than the laparotomy lesion sizes (21.6 vs. 30.21 cm, $p < 0.05$). These might be related to the following reasons: ultrasound has no specificity for the diagnosis of AWE; the boundary between AWE and surrounding tissue is less clear; the capacity of ultrasound that clearly distinguishes the fat, fascia, muscle, and peritoneal is limited; therefore the capacity of the lesion invasive depth diagnosis is also limited. Therefore, the advantages and disadvantages of ultrasound applied in the diagnosis of AWE should be well-understood, resulting in earlier diagnosis of AWE, full evaluation during perioperative period, and better individual treatment options.

The morphological characteristics of lesions

In order to understand the clinical characteristics of different size lesion, the present authors classified the lesion size by three cm, and the patients were divided into two groups: LSE group (largest lesion diameter line \geq three cm) and SSE group (largest lesion diameter line $<$ three cm), and they found that by comparison, in LSE group, the patients had longer disease course than those in SSE group (37.53 vs. 23.68 months, $p < 0.05$), but in LSE group, the recurrence rate was much lower ($p < 0.05$). This indicates that it takes longer for the patients to undergo surgery from clinical symptom emerging in LSE group.

Ultrasound imaging of LSE often showed less cystic structure or fistula and unclear boundary with rich peripheral vascular. Unlike clear ultrasonography of SSE [13], LSE tends to be diagnosed as granuloma or sarcoma, which may prolong the diagnosis time. The present data showed that there were no difference between LSE and SSE groups in the invasion depth and the medication usage during perioperative time, but 70% postoperative recurrence cases (8/11 cases) were SSE group, and its recurrence rate was significantly higher than LSE group. The recurrence may have no correlation with the disease course, but associated with lesion pathophysiological characteristics, such as the abnormal expression of progesterone/estrogen receptors, genetic polymorphism, epigenetics, and immune factors [14]. LSE and SSE groups may represent two different subtypes, which deserve further research.

The treatment of AWE

The preferred method in the treatment of AWE is operation, because the surrounding tissue becomes fibrosis, and drugs are unable to reach the ectopic lesions to completely eradicate them. The surgical resection of the lesion is usually required to achieve radical resection. It signifies that the lesion and its surrounding tissues should be removed and the incisional margin should be negative of endometriosis. Resection should be at least 0.5 to two cm distant from the lesion. For larger abdominal wall defects, patch or skin flap transplantation could be used. In this study, 151 patients were treated surgically, and the extent of resection was one cm around the margin of the lesions. Postoperative symptom relief rate reached up to 93.4%. Therefore, thorough surgical treatment may be the key to obtain a high remission rate. Medical treatment of AWE remains controversial. Although drugs can temporarily alleviate the symptoms, the relief is often short-term and recurrence occurs shortly after drug withdrawal. Therefore drugs are usually used as adjuvant therapy, and treatment must follow the principle of individuality. Commonly used medications are GnRHa, gestrinone, and oral contraceptives. The present data showed that postoperative medication could improve the prognosis, reduce the recurrence, and preoperative medication were no apparently beneficial to relieve symptoms and reduce relapse. Postoperative

medication can inhibit ovarian function while reducing the level of estrogen, causing atrophy of ectopic endometrium, thereby inhibiting its growth and prevent relapse. Although this study showed that premedication did not improve the prognosis, but some scholars believe that, for larger lesions, which is difficult are excise, GnRHa should be used for three to six months before surgical treatment. The mass size might be decreased and the operation difficulty may be decreased, in could achieve complete lesion excision. Therefore, how to use medical treatment by individual and reasonable principles is worth discussing further. The principle should consider the patients' age, course of disease, the size of the lesions, their own economic conditions, and other factors. Combined medical treatment individually and postoperatively may reduce the risk of recurrence.

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