Endometriosis is a frequent clinical problem for women of reproductive age and can markedly influence both reproductive prognosis and quality. Treatment includes medication and surgical intervention. How ever, treatment is often disappo inting because recurrence after successful treatment is frequent that endometriosis can be considered a “malignancy” of a benign disease. Extrapelvic endometriosis is not rare and has been described in locations ranging from the lungs to the lower extremities and most or organs in between.

In this study, we tried to identify its risk factors and presented our experience in managing such disease.

Methods. We studied twenty-three women with pathologically confirmed wound endometriosis after surgery between January 1990 and June 1999 retrospectively.

Results. Patients were classified into three groups according to the types of operations in cluding obstetric surgery (n = 6186), gynecologic surgery (n = 3231) and laparoscopic procedures (n = 2184), which made a significant difference in the occurrence rate of endometriosis (p = 0.04): 2.7 per 1000 obstetric surgeries, 1.5 per 1000 cases of gynecologic surgery, and 0.5 per 1000 laparoscopic procedures. Obstetric surgery showed the relative risk of occurrence of wound endometriosis 7.71 (95%: 1.03–57.92) compared with laparoscopic procedures. The mean time for occurrence of wound endometriosis in patients with normal preoperative CA-125 (< 15 mIU/ml), 760 days, was significantly longer than that in patients with abnormal preoperative CA-125 (> 15 mIU/ml) of 496 days (p = 0.03). Preoperative CA-125 level, patient’s age, preoperative extent of endometriosis, or operative time made no significant contributions to the occurrence of wound endometriosis. Combination therapy of surgical excision and postoperative adjuvant therapy of GnRH-agonist or Danazol® showed the better prognosis, as it could decrease the recurrence rate of wound endometriosis (42.9% versus 11%, p = 0.01).

Conclusion. Obstetric surgery may be an important risk factor in contributing to wound endometriosis, and aggressive behavior of endometriosis itself might also be a possible risk factor because it shortens the time of occurrence of wound endometriosis after surgery. Therapy might be dependent on individuals. Surgical excision with postoperative adjuvant therapy of either GnRH-agonist or Danazol® might be valid, although its effectiveness needed proven in the future.
METHODS

We retrospectively studied 23 patients (mean ± SD age: 30.9 ± 4.6 years, range 23-43 years) at our institute and one associated teaching hospital between January 1990 and June 1999. Only endometriosis located below the previous operation scar and above fasia was included. When the initial operations were not performed in our institute or wound endometriosis was accompanied with intra-abdominal lesions such as endometriosis spots at the time of incision, they were excluded from this study. The follow-up period was calculated from the date of diagnosing wound endometriosis to the date of last follow-up (June 30, 2000). Of these 23 patients, wound endometriosis occurred after obstetric surgeries such as cesarean section or hysterotomy for terminating pregnancy (group A), after abdominal gynecologic surgeries such as exploratory laparotomy for to tal hysterectomy, to tal oophorectomy, partial oophorectomy, myomectomy, managing endometriosis, or other gynecologic surgery (group B), and laparoscopic procedures for diagnosis or surgery (group C). In the same period, three different major types of operations included obstetric surgeries (n = 6186), abdominal gynecologic surgeries (n = 3231), and laparoscopic procedures for diagnosis or surgery (n = 2184).

Statistical analysis of data was done using the statistical software, SAS, version 6.12 (SAS Institute, Cary, NC). The Z test for comparison of proportions with a Yates continuity correction was used to compare estimated in incidence of wound endometriosis among different groups. Continuous data among three groups were compared using Kruskal-Wallis test. Probability values below 5% were considered statistically significant.

RESULTS

In this report, the estimated incidence of wound endometriosis was 0.2%. The median follow-up time was 1411 days, ranging from 436 to 3487 days. The occurrence rates differed significantly among the three groups (p = 0.04): 2.7 per 1000 obstetric surgeries, 1.5 per 1000 cases of abdominal gynecologic surgeries, and 0.5 per 1000 laparoscopic procedures. Obstetric surgery showed the relative risk of occurrence of wound endometriosis, 7.71 (95% CI: 1.03-57.92), compared with laparoscopic procedures. There was no statistical difference compared with abdominal gynecologic surgery: the risk of 1.08 (95 CI: 0.67-4.88). Of 23 cases of wound endometriosis, unsuspected endometriosis was found in 78.3% (n = 18) before operation although the most common surgical reason was unexplained cyclic abdominal wall pain (n = 8). Many scar tissues were sent to pathology because no other identified mass, lesion, or diagnosis could be found during inspection. Eleven patients (48%) presented an abdominal scar mass with changeable size during menstruation, seven patients (30%) presented a cyclic abdominal pain, and one patient (5%) had both. Two patients (one in group A, and one in group C) complained of chronic and intermittent wound discharge. Only two patients were free of symptoms. One was in group A and the other was in group B.

The median time for occurrence of wound endometriosis in patients with normal preoperative CA-125 (< 15 mIU/ml- based on laboratory control in our hospital) was 760 days, which was significantly longer than 496 days in patients with abnormal preoperative CA-125 (> 15 mIU/ml) (p = 0.03). Preoperative CA125 level, patient’s age, preoperative extent of endometriosis during the first operation, or operation time (Table 1) made no significant contribution to the occurrence of wound endometriosis.

Wound endometriosis was managed in three approaches. Patients in group I received surgery and excision only, patients in group II received surgery and adjuvant therapy of gonadotropin-releasing hormone agonist (GnRH-agonist) and patients in group III received surgical excision and postoperative Danazol® treatment (Table 2). None of them was treated by bilateral oophorectomy. Combination therapy of surgical excision and postoperative Danazol® treatment showed the better progno sis because it might
decrease the recurrence of wound endometriosis after primary excision (42.9% versus 11%, p = 0.01).

**DISCUSSION**

Despite extensive research, the natural history of endometriosis is still poorly understood, and its biology remains enigmatic ranging from a stable state to an actively progressive disease. However, wound endometriosis is still an extremely rare phenomenon, although handfuls of cases of scar endometriosis are reported in the literature. The estimated incidence varies from 0.03 percentage to 10.0 percentage. Scar endometriosis occurs most commonly after uterine surgery. Our study found the highest incidence of wound endometriosis in patients with obstetric surgery. Obstetric surgery for mid-trimester termination would increase the incidence of wound endometriosis to 0.43% (2/468) when compared with 0.26% (15/5718) after cesarean section.

The definitive cause of scar endometriosis is unknown. Transplantation theory has been well accepted. Ridley and Edwards injected menstrual endometrium into a woman’s abdominal wall with resultant abdominal wall endometriosis. Surgical trauma might influence “tumor” implantation because promotion of tumor metastasis could be observed clinically and experimentally. With endometrial cells present at an early stage of wound healing, these newly implanted cells may benefit from the protective barrier and nutrition source provided by clot formation; growth may be promoted by local immune

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### Table 1. Characteristics of the patients with wound endometriosis

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 17)</th>
<th>Group B (n = 5)</th>
<th>Group C (n = 1)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated incidence (per 1000 operations)</td>
<td>2.7</td>
<td>1.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.04</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31 ± 5&lt;sup&gt;a&lt;/sup&gt; (23-43)</td>
<td>30 ± 3&lt;sup&gt;a&lt;/sup&gt; (24-32)</td>
<td>28 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.82</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>63 ± 14&lt;sup&gt;a&lt;/sup&gt; (41-85)</td>
<td>69 ± 22&lt;sup&gt;a&lt;/sup&gt; (45-102)</td>
<td>56&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.73</td>
</tr>
<tr>
<td>Interval between operation and wound endometriosis (days)</td>
<td>730 ± 360&lt;sup&gt;a&lt;/sup&gt; (310-1700)</td>
<td>890 ± 400&lt;sup&gt;a&lt;/sup&gt; (350-1420)</td>
<td>390&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.12</td>
</tr>
<tr>
<td>Preoperative CA-125 (mIU/ml)</td>
<td>40 ± 57&lt;sup&gt;a&lt;/sup&gt; (15-245)</td>
<td>41 ± 24&lt;sup&gt;a&lt;/sup&gt; (15-80)</td>
<td>&lt; 15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.44</td>
</tr>
</tbody>
</table>

All data presented as mean ± SD (range).

<sup>a</sup>p < 0.0001 by Z-test (group A as reference); <sup>b</sup>p < 0.001 by Z-test (group A as reference).

### Table 2. Management and outcomes of patients with recurrent wound endometriosis

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 14)</th>
<th>Group II (n = 6)</th>
<th>Group III (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent wound endometriosis</td>
<td>6 (42.9%)</td>
<td>1 (16.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Secondary management</td>
<td>Group I:2</td>
<td>Group II:3</td>
<td>Group III:1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Secondary recurrence</td>
<td>Group I:1 (50%)</td>
<td>Group II:1</td>
<td></td>
</tr>
<tr>
<td>Third management</td>
<td>Group II:1&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>16-month follow-up did not show evidence of recurrence;<br><sup>b</sup>This patient who received surgical excision for her wound endometriosis was initially treated with Danazol® but switched to receive GnRH-agonist due to possible side effects of Danazol® (an elevating liver enzyme: aspartate aminotransferase and alanine aminotransferase).
suppression and growth factor secretion. Sugarbaker et al. proposed a “tumor cell entrapment hypothesis”, in which a few endometrial cells (epithelial and/or stromal cells) can generate endometriosis in optimal conditions. This is the major mechanism for endometriosis recurrence or metastasis. This endometrial cell might be present in the peritoneal cavity before surgery and might arise from contamination from surgical manipulations, especially the obstetric surgery such as hysterectomy for terminating pregnancy or cesarean section. Of course, hematogenous spreading was supposed to be another possible mechanism. Yet, we did not favor this proposal based on clinical observation—failure of metastasis in blood reservoir organs (metastatic inefficiency) and experimental models—failure of cutaneous metastasis with direct intracardiac tumor injection.

There is still conflict, because surgeons have long been aware of the importance of sterile operative field to avoid wound infection or tumor recurrence at the site of a surgical wound. Nearly all obstetricians will clean the abdominal cavity and irrigate the abdominal wall before closing an abdominal wound. Why do obstetric surgeons still present the highest incidence of wound endometriosis? Some clinical observations may partly explain the possible causes. Obstetric surgery can expose a large amount of endometrial cells or tissue during the operation, and these cells can be entrapped in the raw surface of the abdominal wall. Further more, a large amount of amniotic fluid which might contain “some” active endometrial tissue might flood the abdominal wall. Finally, obstetric surgery causes significant blood loss than abdominal gynecologic surgery or laparoscopic surgery, and this would provide a relatively rich nutritional environment for the growth of endometrial tissue in the wound. Although surgeons clean wounds as usual, “escapeced” cells lodged in the wound cannot be avoided.

In our study, laparoscopic surgery would be a better choice for diagnosing and managing endometriosis. However, one must be careful about the possible tricks. First, among 2184 laparoscopic surgeries, up to 46.5% (n = 1015) of cases were diagnosed as endometriosis-related diseases such as endometriosis, ovarian chocolate cyst, and adenomyosis of the uterus, and the cure rate was 1.0 per 1000 laparoscopic procedures. Second, cyst, and adenomyosis of the uterus, and the occurrence of related diseases such as endometriosis, ovarian chocolate cyst, and adenomyosis of the uterus, and the cure rate was 1.0 per 1000 laparoscopic procedures. Second, one must be careful about the possible tricks. However, one must be careful about the possible tricks. However, some lesions under suspicion of wound endometriosis, even though not being recognized during surgery, would offer a chance to receive pathological evaluation, especially in patients with unexplained abdominal pain. Third, nearly eighty percent of patients with wound endometriosis in this study were not recognized before or after the operation. Pneumoperitoneum was the major factor that contributes tumor implantation clinically and experimentally. Pneumoperitoneum creates a pressure gradient with subsequent outflow of gas and floating tumor cells through the port wounds (chimney effect). This phenomenon does not occur in a standard wound. However, wound endometriosis after laparoscopic surgery is so rare. In fact, to date there is still no reported case addressing port site endometriosis, although it may indeed be present just as in our series (one case) with out being reported in the literature.

In this study, it was very interesting to find that preoperative abnormal serum CA125 was associated with early occurrence of wound endometriosis. Unfortunately, serum CA125 was neither sensitive nor specific for endometriosis. It could not explain the complete extent or severity of endometriosis, either. It did not provide any suggestion to use them for performing any invasive procedures with out further evidence of disease. Thus, some of the recurrences can rather be attributed to the highly aggressive behavior of the endometriosis itself than the complications of surgery. However, to answer this question, a new design should be ceased to combine and evaluate the detailed data in patients with and without wound endometriosis in each group. If cesarean sections took a longer period of time to develop wound endometriosis, the affected cases were diagnosed as endometriosis-related diseases such as endometriosis, ovarian巧克力 cyst, and adenomyosis of the uterus, and the cure rate was 1.0 per 1000 laparoscopic procedures. Second, one must be careful about the possible tricks. However, some lesions under suspicion of wound endometriosis, even though not being recognized during surgery, would offer a chance to receive pathological evaluation, especially in patients with unexplained abdominal pain. Third, nearly eighty percent of patients with wound endometriosis in this study were not recognized before or after the operation. Pneumoperitoneum was the major factor that contributes tumor implantation clinically and experimentally. Pneumoperitoneum creates a pressure gradient with subsequent outflow of gas and floating tumor cells through the port wounds (chimney effect). This phenomenon does not occur in a standard wound. However, wound endometriosis after laparoscopic surgery is so rare. In fact, to date there is still no reported case addressing port site endometriosis, although it may indeed be present just as in our series (one case) with out being reported in the literature.

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groups, some problems should be pointed out. At first, the wound of the exploratory laparotomy might be different from that of obstetrics surgery, the longitudinal incision versus the transverse incision. Although the detailed data were unavailable in this study, our review of all surgeries in near a half year of 1999 found that transverse incision was performed in about 80.4% of obstetric surgeries (251/312) and 78.4% of gynecological surgeries (98/125), respectively. The difference seemed unremarkable. Second, the underlying disease might be different. Endometriosis-related disease was found in 46.5% (1/1015) of laparoscopic surgeries and 35.2% (1137/3231) of gynecologic surgeries. In fact, the occurrence rate of scar endometriosis was 1.0 per 1000 laparoscopic procedures and 1.8 per 1000 gynecological procedures in cases with endometriosis-related disease. An estimated incidence of scar endometriosis after surgical management for endometriosis-related disease was 1.4 per 1000 operative procedures.

Diagnosis of wound endometriosis is sometimes very difficult because of the high possibility of underestimation in occurrence of wound endometriosis. To diagnose the wound endometriosis, both clinical history and physical examination might be important. If the symptoms are cyclic or associated with menstrual cycle, wound endometriosis should be considered. In this study, nearly all patients had some clinical presentations such as abdominal wall pain, wound discharge and changeable size of the wound; however, neither the doctor nor the patient paid much attention to it, which resulted in such a high proportion of missing diagnosis. In addition, the initial presentation might be valuable in aiding diagnosis. Ultrasound and computed tomography were reported usefully. There is also a rationale to use magnetic resonance imaging to aid in the diagnosis of wound endometriosis, although no data could be found in the literature. Fine-needle aspiration biopsy was reported to be effective for diagnosis. GnRH-agonist was also used to treat wound endometriosis successfully. We also had an excellent experience in managing various kinds of hormone-dependent tumors. However, the possibility of malignancy arising from the extra-ovarian endometriosis should always be kept in mind. Surgical approach was a good strategy to treat wound endometriosis initially, but frequent recurrence after primary excision was found in this study. Furthermore, it was interesting to find recurrence always at the same area. This implied that the initial incision might be incomplete (difficult evaluation of safe margin) or spreading endometriosis during manipulation.

Combination of surgical excision and postoperative adjuvant therapy either of Danazol® or of GnRH-agonist is recommended because it seemed to decrease the occurrence of wound endometriosis in this study. However, these patients were of ten at reproductive age. In addition, delay of diagnosis and possibly late recurrence of wound endometriosis were common. Finally, the three groups in this study might already be different from the beginning. The management strategy must be made individually, then.

Wound endometriosis is still a rare and troublesome event. Some limitations in this study could not be avoided, which is very common in a retrospective study. For example, some cases might miss in follow-up period or identifying wound endometriosis. In addition, the surgical procedures might lack the details such as the causes of operation with underlying endometriosis or not, the approach routes using longitudinal or transverse incision, the operative methods, and the length of incision. How ever, there were some interesting findings. Obstetric surgery may be an important risk factor in contributing to wound endometriosis, and the aggressive behavior of endometriosis itself might be a possible risk factor. The occurrence of wound endometriosis might already be different from the beginning.

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