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Diameter of dominant leiomyoma is a possible determinant to predict coexistent endometriosis

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ABSTRACT

Objective: To identify the frequency and assess risk factors for unexpected discovery of peritoneal endometriotic implants in patients who underwent myomectomy or hysterectomy for symptomatic uterine leiomyomas.

Study design: We retrospectively collected medical records of 829 patients with symptomatic leiomyomas in The University of Tokyo Hospital. All the patients underwent abdominal or laparoscopic surgeries between January 2001 and December 2010 and the presence or absence of endometriosis during surgery was analyzed. Possible determinant to predict coexistent endometriosis was statistically investigated.

Results: In total, 105 leiomyoma cases (12.7% in 829 patients) were diagnosed with endometriosis. Patients with small dominant leiomyomas were significantly complicated by peritoneal endometriotic implants (small leiomyomas were classified as <8 cm). The patients with both diagnoses were more likely to be infertile and at age 39 years or younger than those with leiomyoma alone.

Conclusions: Women undergoing myomectomy or hysterectomy with both endometriosis and leiomyomas have several different clinical features compared with women with only leiomyomas. The size of largest leiomyoma may provide an important clue for coexistent endometriosis. Women with substantial infertility despite a smaller leiomyomas burden may be more likely to have a surgical indication for concomitant endometriosis.

1. Introduction

Endometriosis is one of the most common gynecologic diseases, and is known to affect 2–10% of reproductive-age women [1,2]. While many patients are asymptomatic [3], endometriosis is frequently associated with infertility and pain symptoms including chronic pelvic pain, dysmenorrhea, dyspareunia, and dyschezia [3–7]. Pelvic examination, ultrasound, magnetic resonance imaging (MRI), and laboratory tests are utilized as non-invasive diagnostic tools with a high degree of reliability [3,6–9], but direct visualization of endometriotic implants is the mainstay for the definite diagnosis of endometriosis [3,6,7]. Current treatment strategies include surgery, ovarian suppression therapy, or both.

Uterine leiomyoma is also one of the most common gynecologic diseases, and is known to affect 20–50% of reproductive-age women [10–12]. Menstrual disorders (menorrhagia and dysmenorrhea), mass effects (pelvic pressure and urinary frequency), and infertility are representative symptoms associated with uterine leiomyoma [13]. Transvaginal ultrasound is commonly utilized to detect uterine leiomyoma with a high degree of sensitivity [14]. Surgery is the mainstay for the treatment of symptomatic leiomyomas, and approximately 175,000 hysterectomies and 20,000 myomectomies are performed for the management of leiomyomas in the United States each year [10,11].

Recently the presence of uterine leiomyoma has been identified as an independent risk factor for the presence of endometriosis [1,4,15]. Both uterine leiomyoma and endometriosis are estrogen-dependent diseases [16,17]. One possible mechanism of their association would be the obstruction theory: obstruction of menstrual flow caused by leiomyomas may promote reflux of menstrual flow, finally resulting in the implantation and/or transplantation of endometrial tissue according to the Sampson's theory [17]. Although endometriosis can be diagnosed during operations for leiomyomas, the rate of endometriosis in patients with leiomyomas has been poorly studied because there have been no large well-defined studies with adequate adjustment for confounding factors.

The aim of this retrospective study was to clarify the frequency of discovering endometriosis during surgery for symptomatic leiomyomas and to identify the risk factors for coexistence of these enigmatic diseases. We found that the diameter of the dominant

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Table 1
Analysis of dominant leiomyoma and location for the rate of coexistent endometriosis.

Dominant leiomyoma	Total leiomyoma	Intramural leiomyoma	Submucous leiomyoma	Subserous leiomyoma
<8 cm	17.2% (76/443)	18.4% (47/256)	15.7% (13/83)	15.4% (16/104)
≥8 cm	7.5% (29/386)	8.9% (21/237)	7.7% (1/13)	5.1% (7/136)
Total	12.7% (105/829)	13.8% (68/493)	14.6% (14/96)	9.6% (23/240)

We stratified 829 cases by the characteristics of the dominant leiomyoma, including its size and type. Smaller leiomyomas were significantly associated with coexistent endometriosis in any types of leiomyomas, and we found that the threshold of the size was 8 cm.

leiomyoma is a possible factor for the prediction of coexisting endometriosis.

2. Materials and methods

Subjects who underwent surgery for symptomatic leiomyomas between January 2001 and December 2010 were included in this study and the medical records of 1133 patients were reviewed retrospectively. All the patients were confirmed to have pathologically proven leiomyomas. This study protocol was reviewed and approved by the Human Ethical Committee of The University of Tokyo Hospital.

Inclusion criteria included being of premenopausal age and having regular menstrual cycles. Exclusion criteria included pregnancy, ovarian tumor, congenital uterine abnormality, and uterine malignant tumor. Patients with a past history of endometriosis and/or adenomyosis were excluded from this study. Demographic data such as age, presenting symptoms, fertility history, and physical data were collected from medical records. Number and location of leiomyomas were judged by MRI and ultrasound before surgery, and the size of leiomyomas was measured using preoperative MRI and/or ultrasound. The surgical interventions included in this study were abdominal myomectomy, abdominal hysterectomy, laparoscopic myomectomy, laparoscopic hysterectomy, and laparoscopically assisted myomectomy, defined as a laparoscopic surgery using a small laparotomy incision [18]. Endometriosis was diagnosed by visualization of clinically evident lesions such as peritoneal implants, peritoneal windows, endometriomas, and deep infiltrating nodules of endometriosis [19], and by biopsy results when applicable. The revised American Society for Reproductive Medicine (ASRM) classification of endometriosis was used to assess the stage of the condition [19].

Statistical analyses were performed using JMP version 5.1 for Windows. Categorical variables were compared by chi-square test for correlations between parameters and the frequency of finding endometriosis. In order to eliminate confounding factors, we divided the patients into two groups by existence or non-existence of each factor and used multivariate logistic regression analysis. Odds ratios along with 95% confidence intervals were estimated to indicate the strength of these correlations. P value less than 0.05 was considered statistically significant.

3. Results

Of 829 patients diagnosed with leiomyomas, 105 patients were confirmed to possess both leiomyoma and endometriosis, and 724 patients were without endometriotic lesions. Of the 105 patients, 80 subjects were diagnosed with stages I–II (mild) endometriosis. The frequency of discovering endometriotic implants was not different between abdominal surgeries and laparoscopic surgeries (12.2% in 188 cases vs. 12.8% in 641 cases; $P = 0.878$).

The relationship between the characteristics of largest leiomyomas and the frequency of discovering endometriotic implants is shown in Table 1. The majority of endometriosis (76/105 cases, 72.4%) was detected in patients with a dominant leiomyoma <8 cm, and a statistically significant difference in concomitant diagnosis of leiomyoma and endometriosis was demonstrated between the two groups according to the diameter of largest leiomyoma (Table 1). Other characteristics exhibited no significant differences, but patients with subserous leiomyomas were less likely to be diagnosed with endometriosis than those with intramural or submucous leiomyomas (9.6% vs. 13.9%; $P = 0.089$).

We then compared the patients with concomitant leiomyomas and endometriosis to those with leiomyomas alone, in consideration of presenting symptoms and clinical data using multivariate logistic regression analysis (Table 2). Of 13 factors, three factors were identified as independent and significant factors for coexistence of endometriosis: patients who underwent surgery at age 39 years or younger (OR = 1.58, 95% CI: 1.03–2.44), infertile patients (OR = 4.07, 95% CI: 2.61–6.33), and patients with large leiomyomas (OR = 0.39, 95% CI: 0.25–0.62).

4. Comment

Uterine leiomyoma is a benign gynecological disease, and the diagnosis of uterine leiomyoma can be made by transvaginal ultrasound. In general, asymptomatic leiomyomas can be followed without intervention [20,21], since relief of symptoms is the major goal in the management of uterine leiomyoma [22]. Considering the fact that uterine leiomyoma is a significant risk factor for the presence of endometriosis [1,4], it would be beneficial for women with leiomyoma to undergo investigation for possible factors to predict coexistent endometriosis. Appropriate diagnosis of endometriosis is crucial for the patients with unexplained infertility, and up to 50% of women with endometriosis are estimated to be infertile [6].

In our study, the frequency of discovering endometriotic implants during laparoscopic and abdominal surgery was 12.7%, and this figure was consistent with a previous multi-center study [15]. However, we have to take notice that there is a limitation of that study because endometriosis was not histologically proven in all the cases. In contrast to our data, a recent study has shown that 86% of patients with symptomatic leiomyomas had a concomitant diagnosis of endometriosis during laparoscopic surgery [1]. The authors suggested that exploratory laparotomy would often underestimate the prevalence of endometriosis because the vast majority of their patients were diagnosed with stages I–II endometriosis. We performed a systematic inspection of the pelvic and abdominal cavity for recognizing and diagnosing endometriosis, and the majority of our patients were also diagnosed with stages I–II endometriosis. The frequency of discovering endometriotic implants was not different between abdominal and laparoscopic surgeries (12.2% vs. 12.8%). Although our study included a mixture of laparotomy and laparoscopy similar to the Italian group [15], we can conclude that the frequency of discovering endometriotic implants during operation for symptomatic leiomyomas would be around 12%, at least in our population.

We aimed to extract characteristics of leiomyomas to identify possible determinants of coexistent endometriosis. Although we were unable to point out significant differences in any types or locations of leiomyomas (Table 1), we hypothesized that patients