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Thoracic endometriosis syndrome: Comparison between catamenial pneumothorax or endometriosis-related pneumothorax and catamenial hemoptysis



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ABSTRACT

Objectives: To evaluate the clinical features of thoracic endometriosis syndrome (TES) represented by catamenial pneumothorax (CP), endometriosis-related pneumothorax (ERP), and catamenial hemoptysis (CH). **Study design:** In this retrospective study, we enrolled 25 patients with TES, 18 of whom had CP/ERP and 7 had CH, to investigate the clinical presentation, effectiveness of treatment, and recurrence rates in these disorders.

Results: The age at onset was significantly lower in patients with CH than in patients with CP/ERP ($P < 0.05$). In 94.4% of patients with CP/ERP, pneumothorax was observed on either the right side or bilaterally, however there was no tendency toward laterality of CH among our cases. In our study, patients with CP/ERP predominantly underwent surgical management and the recurrence rate during treatment was higher in patients with CP/ERP than in those with CH. We found that the recurrence frequency of CP/ERP was lowest under the combination therapy with thoracic surgery and postoperative hormonal therapy.

Conclusion: Our findings suggest that CP/ERP and CH are different pathological conditions and CP/ERP is more difficult to manage than CH.

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Introduction

Thoracic endometriosis syndrome (TES) is one of extra-genital endometriosis, which is characterized by the presence of endometrium-like tissues in the thoracic cavity. Manifestations of TES include: catamenial pneumothorax (CP), catamenial hemothorax, catamenial hemoptysis (CH), and lung nodules [1]. According to a meta-analysis of published cases between 2001 and 2007, the clinical presentation of TES includes pneumothorax (72%), hemoptysis (14%), hemothorax (12%) and lung mass (2%) [2]. Recently, endometriosis-related pneumothorax has been reported to develop as either catamenial pneumothorax or non-catamenial pneumothorax [3–5]. Non-catamenial endometriosis-related pneumothorax is also included in TES. TES has been recognized as a rare condition, and the etiology and pathology are still not well known. The three hypotheses that may explain the pathogenesis of thoracic endometriosis include coelomic metaplasia, lymphatic or

hematogenous embolization, and retrograde menstruation through a defect in the diaphragm [1,6]. None of these can explain all of the clinical presentations of TES. The management of this condition is highly variable because of the lack of recommendations. Although combined surgical and hormonal treatment have been proposed, there is no consensus [7]. A recent study reported that patients with CP had more hospitalizations and more frequent surgeries than those with non-catamenial pneumothoraces according to a large nationwide database of hospitalized patients [8]. Furthermore, the recurrence rates of CP/ERP, even after surgery or hormonal therapy were high at 32% and 27%, respectively [3]. Therefore, we sought to perform a retrospective analysis of cases of TES in our facility to investigate the clinical presentations, effectiveness of treatment, and recurrence rates.

Materials and methods

Cases

We identified 25 patients treated for thoracic endometriosis between January 2000 and December 2016 at Tokyo University

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Hospital. We retrospectively analyzed the clinical features and management (including age, BMI, parity, symptomatology, laterality, method of diagnosis, complications, surgical management, hormonal therapy, and recurrence) by reviewing the medical records. These factors were compared between patients with catamenial pneumothorax, or endometriosis-related pneumothorax (CP/ERP), and patients with catamenial hemoptysis (CH). For recurrent cases of CP/ERP, the cumulative recurrence frequency was calculated by dividing the number of recurrences by the observational period, and this was analyzed based on the method of treatment. The observational period was defined as the time from the diagnosis of TES to either loss to follow-up or December 2016. This study was approved by the Institutional Review Board of Tokyo University Hospital and informed consent was waived owing to the retrospective nature of this study.

Definition of thoracic endometriosis syndrome

In this study, the inclusion criteria for TES were: (1) pathological diagnosis (presence of endometrial glands and stroma, or isolated endometrial stroma staining positively with estrogen/progesterone receptors and/or CD10), (2) intraoperative findings (presence of endometriotic lesions on visceral and parietal pleura or on diaphragm), (3) chest computed tomography (CT) imaging (the presence of pleuro-diaphragmatic nodules, ground glass opacity, and air filled cavities), (4) Clinical symptoms and chest X-ray examination (recurrent episodes of pneumothorax, hemoptysis, hemothorax or chest pain related to menstruation).

Statistical analysis

The statistical analyses were performed using JMP pro version 13 (SAS Institute Inc, Cary, NC, USA). The continuous data are presented as means and standard deviations (SD) and were analyzed using *t*-tests. The categorical data were analyzed using chi-square test and Fisher's exact tests and are presented as numbers and percentages. A *P* value < 0.05 was considered statistically significant.

Results

Characteristics of patients

As shown in Table 1, the characteristics of patients with TES were compared between patients with CP/ERP and those with CH. Of the 25 patients with TES, 18 presented with CP/ERP (72.0%), and 7 with CH (28.0%). The mean age at diagnosis of TES was 34.8 ± 7.3 years, and the mean age of diagnosis was significantly lower in the CH group (29.6 ± 4.6 years) than in the CP/ERP group (36.8 ± 7.3 years). The mean body mass index (BMI) of patients with TES was 19.5 ± 1.9 kg/m², and there was no significant

difference between the two groups. We found that only 13 of our 25 patients had medical histories that provided smoking status, of which 8 patients were in the CP/ERP group, and 5 patients were in the CH group. Of these, there was one cigarette smoker in the CP/ERP group and one cigarette smoker in the CH group. Seven of 25 (28.0%) cases involved coexisting pelvic endometriosis, and we found no significant difference between the cases of CP/ERP and CH.

Symptom and diagnosis

As shown in Table 2, all of the CP/ERP cases involved dyspnea, and all the CH cases involved bloody sputum. As for laterality, 16 cases (89%) in the CP/ERP group were right-sided, one case was left-sided (5.6%), and one case was bilateral (5.6%). In the CH group, three cases were right-sided, three cases left-sided, and one case with unknown laterality. There was a significant difference in the frequency of right-sided versus left-sided disease between CP/ERP and CH (*P* < 0.05). The symptoms occurred during menstruation in all the 7 CH patients, but only in 14 of 16 CP/ERP patients. Additionally, in two of the cases, the symptoms occurred during the non-menstrual period (in these two cases, endometriosis was confirmed in the thoracic cavity by operative pathology). All of the patients in the CH group were diagnosed based on their symptoms, and in the CP/ERP group, 7 of 18 were diagnosed by symptoms and chest X-ray examination, 6 by pathology of surgical specimens, 3 by operative findings, and 2 by CT imaging.

Treatment and recurrence

The details of recurrence and treatment of the two groups is shown in Table 3. During or after treatment, ten of 18 cases in CP/ERP group recurred, and no cases in the CH group recurred (*P* < 0.05). In 15 of the 18 patients with CP/ERP, thoracic surgery was performed, as shown in Table 3, while there were no cases of CH in which thoracic surgery was performed (*P* < 0.05). Of the 15 cases of CP/ERP, after thoracic surgery recurrence occurred in seven cases (46.7%), and a second surgery was performed in three cases due to recurrence. The details of thoracic surgery are listed in Table 4. Postoperative recurrence occurred even during postoperative hormonal therapy in the CP/ERP group only. No recurrence was observed during hormonal therapy (HT) in the CH group.

We analyzed the recurrence frequency of CP/ERP according to the treatment provided. The observational periods, after the diagnosis of TES, were divided into four periods defined as: "No surgery/Before surgery," "After Surgery," with HT, and without HT. Next, we determined the cumulative treatment period and the total recurrence count. The recurrence frequency was calculated as the total recurrence count divided by each cumulative treatment period. As shown in Table 5, in the "No Surgery/Before Surgery" period, one recurrence occurred during the period without HT, and

Table 1
Demographic and clinical characteristics of patients with thoracic endometriosis.

(Number of Cases)	In total (25)	CP/ERP (18)	CH (7)	P-value	
Age at diagnosis (y.o.)	34.8 ± 7.3 (18–47)	36.8 ± 7.3 (18–47)	29.6 ± 4.6 (22–35)	<i>P</i> < 0.05	
BMI (kg/m ²)	19.5 ± 1.9 (15.4–22.9)	19.7 ± 1.9 (15.4–22.9)	19.2 ± 1.9 (16.5–21.5)	n.s.	
Smoking history	2/13 (15%)	1/8 (13%)	1/5 (20%)	n.s.	
Parity	0	14/25 (56%)	9/18 (50%)	5/7 (71%)	n.s.
	> = 1	11/25 (44%)	9/18 (50%)	2/7 (29%)	–
Infertility	6/25 (24%)	6/25 (24%)	5/18 (28%)	1/7 (14%)	n.s.
Pelvic endometriosis (duplicate included)	7/25 (28%)	7/25 (28%)	6/18 (33%)	1/7 (14%)	n.s.
	Ovarian Endometrioma	4/25 (16%)	3/18 (17%)	1/7 (14%)	n.s.
	Adenomyosis	5/25 (20%)	4/18 (22%)	1/7 (14%)	n.s.
	Intestinal Endometriosis	1/25 (4%)	0/18 (0%)	1/7 (14%)	n.s.
History of gynecologic surgery	8/25 (32%)	8/25 (32%)	6/18 (33%)	2/7 (29%)	n.s.

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