Clinical-Pathological Findings of Catamenial Pneumothorax: Comparison between Recurrent Cases and Non-Recurrent Cases

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Purpose: Catamenial pneumothorax (CP) is classified as thoracic endometriosis syndrome. There are few reports of CP, and the clinical manifestations of this disease are unclear. The aim of the present study is to clarify the features of CP.

Methods: The clinical and pathological files of the 92 female patients pathologically diagnosed with thoracic endometriosis are included in this study. The clinical data and pathological findings of the recurrent and non-recurrent groups are compared.

Results: Thirty-six patients (39.1%) experienced recurrence, 37 (40.2%) patients did not, and 19 (20.4) patients could not be evaluated. The ratio of the endometrial gland in the diaphragm is significantly higher in the recurrent cases in comparison to non-recurrent cases (66.7% vs. 37.8%, \( P = 0.01 \)).

Conclusions: The recurrence rate of CP is high. Further study of the optimal management strategies is needed, especially for CP cases with the endometrial gland in the diaphragm.

Keywords: catamenial pneumothorax, spontaneous pneumothorax, thoracic endometriosis, ectopic endometriosis

Introduction

Catamenial pneumothorax (CP) is one of the causes for the spontaneous pneumothorax (SP) in females.1) CP is classified as thoracic endometriosis syndrome, with catamenial hemothorax, catamenial hemoptysis, and lung nodule.1) Mostly, CP is a SP due to thoracic endometriosis.2) There are few reports of CP, and the clinical manifestations are unclear. The aim of the present study is to elucidate the clinical-pathological findings of CP by investigating a large population of CP patients.

Materials and Methods

Patients

The clinical and pathological files of all patients who underwent surgery for SP in this hospital between January 2005 and December 2010 were retrospectively reviewed. The patients pathologically diagnosed with thoracic endometriosis were included in this study. Thoracic endometriosis was diagnosed, when endometrial stroma was present, regardless of the presence of the endometrial gland. Endometrial stroma was immunohistochemically confirmed by strong nuclear staining for either estrogen or progesterone receptor. The patients were referred to a board certified doctor specialized in gynaecology and obstetrics.
in gynecology to investigate pelvic endometriosis by physical examination and transvaginal ultrasonography. The level of serum cancer antigen (CA) 125 was measured before surgery. CA125 levels were considered normal at 35.0 U/mL (hospital laboratory reference value). This study was approved by the institutional review board of Nissan Tamagawa Hospital.

**Treatment**

All patients suspected to have CP underwent an examination by thoracoscopy under local anesthesia before surgery. Thoracoscopy was performed in the operating room. Under O₂ administration by a face mask, the patient was placed in a dorsal position, and subcutaneous anesthesia with 15–20 ml of 1% lidocaine was performed. Disposable flexible plastic trocar tubes were then inserted through the middle clavicular line of the sixth intercostal space. We next introduced a flexible thoracoscope into the thoracic cavity and inspected the lung and the diaphragm to identify blebs or bullae, as well as signs of thoracic endometriosis. After the examination, the trocar was removed, and the procedure was finished by inserting a 18 Fr drainage tube from the incision into the chest cavity. All of the operations were performed under video-assisted thoracoscopy. The lung was inspected to identify blebs or bullae, and possible air leaks were detected by inflating the lung with saline solution. Signs of thoracic endometriosis were observed by careful examination of the visceral and parietal pleura, and the diaphragm was systemically inspected for holes and/or endometrial implants. Blebs, bullae, and brown nodules of the visceral pleura were resected by endoscopic stapling. Lesions in the parietal pleura were removed by limited parietal pleurectomy. The diaphragm was partially resected using an endoscopic stapler, and repaired by hand sutures when diaphragmatic endometriosis was suspected. In addition, a cellulose mesh (Surgicel Johnson and Johnson, Inc., New Brunswick, New Jersey, USA) was inserted to cover the tendinous part of the diaphragm. No hormonal therapy was routinely administered after surgery. Hormone therapy was only administered, when requested by the patient and in recurrent cases.

**Comparison between recurrent cases and non-recurrent cases**

The patients who had developed SP after the operation were included in the recurrent group, and the patients who had not developed SP for one year or more after operation were included in the non-recurrent group. The study compared age at operation, smoking history, the number of SP prior to surgery, the period from the first occurrence of SP to surgery, presence of pelvic endometriosis, the level of serum CA125, thoracoscopic findings and pathological findings of each group.

**Statistical Analysis**

Quantitative data were presented as the mean ± SD. The differences between days with and without SP were analyzed with the chi-square test for categorical variables, and student t-test for quantitative variables. A P value <0.05 was considered to be significant. A statistical software package (Statview, version 5.0; SAS Institute; Cary, North Carolina, USA) was used for this statistical analysis.

**Result**

A total of 670 female patients with SP underwent surgery during the 6-year study period. Ninety-two of those patients (13.7%) were pathologically diagnosed with thoracic endometriosis. Fifty-five patients (59.8%) were detected to have endometrial tissue only in the diaphragm, 22 (23.9%) in the diaphragm and the lung parenchyma, 10 (10.9%) in the diaphragm and the parietal pleura, and 5 (5.4%) in the diaphragm, the lung parenchyma, and the parietal pleura. The endometrial gland was observed only in the diaphragm of 47 patients (51.1%). Their median age at the time of surgery was 39 years of age (24–50). SP was right-sided in 91 (98.9%) of 92 patients, whereas a single woman had left-sided SP. The number of SP prior to surgery was 3.6 ± 2.0 (1–10), and the period from the first occurrence of SP to surgery was 15.5 ± 16.0 months (0–72). A total of 6 (6.5%) had a history of tobacco consumption. Fifty-four patients (58.7%) were diagnosed with pelvic endometriosis, 34 (37.0%) were diagnosed without pelvic endometriosis, and 4 (4.3%) were not checked by gynecologist. The mean serum CA125 level was 36.7 ± 42.3 (6–291) IU/mL.

An examination of thoracoscopy revealed holes in the diaphragm in 76 patients (82.6%) and nodules on the diaphragm in 34 patients (37.0%).

The observation period for the 73 patients (79.3%) who were followed after surgery was 44.1 ± 19.2 months (14–84). Nineteen patients (20.7%) were not followed after the surgery. There were 37 patients (40.2%) who did not develop SP after the operation. Thirty-six patients (39.1%) developed SP. Nine of those patients developed...
SP immediately after the operation, and did not show recurrence for one year or more afterward. Eight patients underwent further surgery, 5 patients were successfully treated with hormone therapy using a GnRH agonist for six months, and 14 patients were recommended to undergo further surgery. Six of the 8 patients who underwent further surgery (75%) were free from recurrence for 1 year or more after the second procedure.

There was no statistical difference in the mean age, smoking habit, the number of SP prior to the operation, the period from the first pneumothorax to surgery, presence of pelvic endometriosis, the level of serum CA125, and the thoracoscopic findings between the recurrent and non-recurrent cases (Table 1). An endometrial gland was seen on the diaphragm in 24 (66.7%) of 36 recurrent cases, and 14 (37.8%) of 37 non-recurrent cases, and this difference was statistically significant ($P = 0.01$). There was no significant difference among the two groups in the pathological findings such as endometrial tissue in the lung parenchyma and parietal pleura (Table 2).

### Discussion

The current study examined more CP patients than any previous study. CP accounted for 92 (13.7%) of 670 women who underwent surgery for SP. Nakamura, et al. reported that CP patients were diagnosed among less than 1% of female SP patients in 1984. The current study demonstrated that a considerable number of female SP patients were CP patients. This was consistent with other recent studies, reported that 24.6%–29.0% of female SP patients were CP patients. This increase was due to the fact that physicians were paying more attention to this disease. The median age of the CP patients was 39 years, which was consistent with other studies (31.9–35.0 years). Many patients appear to develop CP in their thirties, which is older than the usual age when patients develop pelvic endometriosis (in their twenties). Twenty-seven of 28 cases with CP were rightsided. This result was consistent with previous reports.

In our study, fifty-four patients (58.7%) were diagnosed with pelvic endometriosis. This ratio varied according to the reports (25%–84%). Majority of thoracic endometriosis were believed to be from pelvic endometriosis. The variations in these results might be due to the different methods used to detect pelvic endometriosis. It is thought that the rate of detection of pelvic endometriosis increases with the use of a laparoscope. The mean value of serum CA125 was 36.7 ± 42.3 (6–291) U/mL. Bagan, et al. reported that the mean value of serum CA125 of the patients with thoracic endometriosis was 76.1U/mL. The difference may be explained by the fact that the current study measure serum CA125 not only during the menstrual period but also during the intermenstrual period.

### Table 1 Comparison of clinical data in the recurrent and non-recurrent groups

<table>
<thead>
<tr>
<th>Valuables</th>
<th>The group of recurrence; n = 36</th>
<th>The group of non-recurrence; n = 37</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, year</td>
<td>38</td>
<td>39</td>
<td>–</td>
</tr>
<tr>
<td>Smoking history</td>
<td>2 (5.6%)</td>
<td>1 (2.7%)</td>
<td>0.56</td>
</tr>
<tr>
<td>The number of the pneumothorax until the operation</td>
<td>3.8 ± 1.7</td>
<td>3.3 ± 2.3</td>
<td>0.82</td>
</tr>
<tr>
<td>The period from the first pneumothorax to operation, month</td>
<td>14.2 ± 13.9</td>
<td>15.0 ± 15.8</td>
<td>0.31</td>
</tr>
<tr>
<td>Presence of pelvic endometriosis</td>
<td>23 (63.9%)</td>
<td>22 (64.7%)</td>
<td>0.94</td>
</tr>
<tr>
<td>The value of serum CA125, U/mL</td>
<td>38.0 ± 36.5</td>
<td>30.0 ± 27.0</td>
<td>0.30</td>
</tr>
</tbody>
</table>

CA 125: cancer antigen 125

### Table 2 Comparison of pathological findings in the recurrent and non-recurrent groups

<table>
<thead>
<tr>
<th>Valuables</th>
<th>The group of recurrence; n = 36</th>
<th>The group of non-recurrence; n = 37</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of endometrial gland</td>
<td>24 (66.7%)</td>
<td>14 (37.8%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Presence of endometrial tissue in the lung parenchyma</td>
<td>7 (19.4%)</td>
<td>13 (35.1%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Presence of endometrial tissue in the parietal pleura</td>
<td>6 (16.7%)</td>
<td>7 (18.9%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>
period, while they checked only the menstrual period.

The recurrence rate of CP in the present study is 39.1%. The reported recurrence rate of CP is 30%–32%. The high recurrence ratio of the present study may be due to the limited use of adhesion treatment. The majority of CP recurrences are believed to be due to microscopic thoracic endometrial tissue overlooked during the operation, and the re-dissemination of endometrial tissue from pelvic endometriosis. To avoid recurrence, there are two main options; adhesion treatment, and further surgery. Adhesion treatment may achieve short-term success, but this treatment makes further surgery difficult. Our study demonstrated that 75% of the patients who underwent further surgery were free from recurrence. We therefore believe that further surgery is an important choice for recurrent cases, and adhesion treatment should be avoided if possible.

Another possible reason for the high recurrence rate is that we do not routinely prescribe postoperative hormone therapy, because hormone therapy for CP is believed to be of limited efficacy. The recurrence rate is reported to exceed 50%, regardless of the use of these drugs. Among the medical options, GnRH agonists have been found to be the most effective for preventing CP recurrence. The administration of a GnRH agonist is limited to six months because of the side effects. We have the impression that preoperative hormone therapy is also not very effective. Thus, we do not routinely administer postoperative hormone therapy.

Our study demonstrated that the rate of an endometrial gland being present in the diaphragm was significantly higher in the recurrent group, although no other clinical data or pathological findings showed any significant difference between the two groups. This may be due to the fact that the presence of the endometrial gland is found when there is a large amount of endometrium. Therefore, there might be a greater dissemination of microscopic endometrial tissue that remained in thoracic space. The pathological findings of endometrial tissues are influenced by the time during the menstrual cycle when they are obtained. We performed the operation during the intermenstrual period to avoid any genital bleeding in the operation room. As a result, all the patients underwent surgery in either the late follicular phase or early luteal phase. During these periods, the endometrium becomes thicker with an increase in the number of gland. The difference in the menstrual cycle when the endometrial tissues were obtained is considered to not have substantially influenced the results of our study.

The present study has important strengths that differentiate it from previous studies. The most important of these is that it was the largest study that has been conducted so far. Because the Pneumothorax Research Center specialized in the treatment of pneumothorax, we were able to recruit a large patient population. The main limitation of this study was that, because we analyzed the clinical records retrospectively, there was a lack of details on the clinical histories and conditions of the patients.

Conclusion

The present study clarifies the features of CP. The recurrence rate of CP is high. The optimal management of CP needs further evaluation especially for the cases with endometrial gland involvement.

Disclosure Statement

We have no financial or other interest in the manufacture or distribution of the device.

References

2) Channabasavaiah AD, Joseph JV. Thoracic endometriosis: revisiting the association between clinical presentation and thoracic pathology based on thoracoscopic findings in 110 patients. Medicine (Baltimore) 2010; 89: 183-8.