Catamenial Pneumothorax*

A Prospective Study

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Objectives: To evaluate the incidence of catamenial pneumothorax (CP) among women who have been referred for the surgical treatment of spontaneous pneumothorax (SP) and to study its pathogenic mechanisms.

Design: A prospective study of women of reproductive age who have been referred to our center for the surgical treatment of SP. Patients with pneumothorax secondary to a known lung disease were excluded.

Setting: A university hospital.

Methods: At the preoperative evaluation, special attention was given to the investigation of a possible temporal relationship between pneumothorax and menses. Video-assisted thoracoscopy constituted the operative technique of choice. The lung was inspected to identify blebs or bullae and the origin of possible air leaks. Signs of thoracic endometriosis were also carefully searched for. The diaphragm was systematically inspected to search for holes and/or endometrial implants. When limited diaphragmatic abnormalities were found, a partial diaphragmatic resection was carried out using an endoscopic stapler. In case of lesions that were not accessible by a purely endoscopic approach, a utility minithoracotomy was used.

Results: In an 18-month period, 32 women with SP were referred for surgery. In eight cases, the catamenial character of the pneumothorax was recognized by clinical history. In all these patients, the following diaphragmatic abnormalities were found at surgery: holes (one patient); endometrial implants (three patients); and both (four patients). Visceral pleural endometriosis was found in one patient. During pathologic examination, diaphragmatic endometriosis was confirmed in seven of the eight cases. In one patient, it was associated with pulmonary and pleural endometriosis. In only one patient (with multiple diaphragmatic holes and a pulmonary nodular brown lesion), endometriosis could not be confirmed at histology, but signs of parenchymal focal hemorrhages were found.

Conclusions: Our experience shows that (1) CP is more frequent than expected and (2) diaphragmatic abnormalities seem to play a fundamental role in its pathogenesis.

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Key words: catamenial pneumothorax; porous diaphragm; thoracic endometriosis; thoracoscopy

Abbreviations: CP = catamenial pneumothorax; SP = spontaneous pneumothorax

Catamenial pneumothorax (CP) is currently considered to be a very unusual clinical condition. The temporal relationship with menstruation defines the “catamenial” character of a recurrent pneumothorax. A retrospective review1 of the literature found only 80 reported cases. Several case reports have been published,2–5 thus proving an improved recognition of the disease and an increased interest in the medical community. Despite this, the exact incidence, the pathogenic mechanisms, as well as the optimal management of CP remain unclear. So, we undertook a prospective study of spontaneous pneumothorax (SP) in all women of reproductive age who had been referred to our center for surgical treatment.

Patients and Methods

All women of reproductive age who had been referred to our center over an 18-month period (ie, July 2000 to December 2001)
for surgical treatment of an SP were included in the study. Patients presenting with pneumothorax secondary to a known underlying lung disease were excluded. Indications for referral to our center were as follows: recurrent pneumothorax; persistent (i.e., > 5 days) air leak and/or pneumothorax despite adequate chest drainage; and failure of previous surgery.

In the study period, 138 patients with SP were referred to us for surgery. In 17 of these patients, pneumothorax was secondary to a known lung disease (mainly COPD). Among the remaining 121 patients, there were 32 women (26.5%). These last patients constituted the population of the study. Their mean age was 24.7 years (age range, 17 to 45 years).

A CP was defined as a spontaneous and recurrent pneumothorax occurring within 72 h from the onset of menstruation. At the preoperative evaluation, special attention was given to investigating the possible temporal relationship between the occurrence of pneumothorax and menses. In all the patients, the preoperative assessment included a chest radiograph, routine blood tests, ECG, and blood gas analysis.

Video-assisted thoracoscopy constituted the operative technique of choice. General anesthesia with double-lumen bronchial intubation was employed to allow single-lung ventilation. Patients were positioned in the standard posterolateral decubitus position. Three ports (5, 10.5, and 11.5 mm) were employed. They were inserted into the fourth intercostal space (anterior axillary line), the seventh intercostal space (middle axillary line), and the sixth intercostal space (in the auscultatory triangle), respectively. The lung was carefully inspected to identify blebs or bullae, and the origin of possible air leaks was assessed by inflating the lung after filling the cavity with saline solution. Signs of thoracic endometriosis were also carefully searched for. Visceral and parietal pleura were examined to detect nodular brown lesions, whereas the diaphragm was systematically inspected to search for holes and/or endometrial implants. Endoscopic stapling devices were used to resect blebs or bullae. Nodular brown lesions of visceral pleura also were resected by using these devices. In this instance, a limited pulmonary wedge resection including the diseased area was carried out. Lesions in the parietal pleura were removed by a limited parietal pleuromyotomy. When diaphragmatic abnormalities were found (i.e., holes or brown implants), a partial diaphragmatic resection (including the diseased portions) was carried out by using an endoscopic stapler, provided that the anticipated size of the diaphragmatic resection was limited (i.e., main axis < 3 cm). The diaphragm was lifted anteriorly while stapling across it in order to ensure that the underlying liver was not involved in the staple line.3

A utility minithoracotomy was carried out if diaphragmatic lesions could not be treated by a purely endoscopic approach (e.g., when they were close to the phrenic nerve or its main division branches, or when their number, size, or location would not allow a partial resection) but necessitated a limited open approach under video assistance. Obviously, in the case of a previous thoracotomy a repeat thoracotomy was performed.

In all cases, pleural abrasion of the whole parietal pleura was performed to achieve pleurodesis. The thoracic cavity was drained by two large-bore silicone tubes. Chest drainage was discontinued on the fifth postoperative day, provided that no air leak had been observed in the previous 24 h. All the patients with a CP received an ovarian suppression treatment in the 6 months after undergoing surgery under the care of the referring physicians (Table 1).

Informed consent was obtained from all subjects participating in the study, and the procedures used in the research were in accordance with the recommendations found in the Helsinki Declaration of 1975. Although special attention was given to recognize the catamenial character of the pneumothorax, patient management could not be considered different from standard care, so no sanction of the institutional review board was considered to be necessary.

Results

In 8 of the 32 women (25%), the catamenial character of pneumothorax was recognized on the basis of clinical history. Their mean age was 32.5 years (age range, 19 to 45 years). Two women had a history of secondary infertility (defined as a failure to conceive following 1 year of unprotected sexual intercourse after having had a child), whereas in no case was pelvic endometriosis known preoperatively (Table 1). In all eight women, the pneumothorax was recurrent (range, 1 to 4 previous episodes) and right-sided. In only one case was pneumothorax associated with a serohemorrhagic pleural effusion.

All eight patients underwent surgery, as follows: video-assisted thoracoscopy, five patients; video-assisted thoracoscopy with utility minithoracotomy, two patients; and standard posterolateral thoracotomy (in a patients referred for surgery after the failure of treatment by thoracotomy, which had been performed elsewhere), one patient. In all cases, the

### Table 1—Clinical Characteristics of Subjects*

<table>
<thead>
<tr>
<th>Patient No./ Age, yr/Age of Menarche, yr</th>
<th>Dysmenorrhea</th>
<th>Dyspareunia</th>
<th>Infertility</th>
<th>Gravity and Parity</th>
<th>Previous Treatments</th>
<th>Postoperative Treatment</th>
<th>Pelvic Endometriosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/28/13</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>G0P0</td>
<td>No</td>
<td>Triptorelin</td>
<td>No</td>
</tr>
<tr>
<td>2/30/14</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>G1P0 (1 VIP)</td>
<td>Pill</td>
<td>Chlormadinone acetate</td>
<td>Yes†</td>
</tr>
<tr>
<td>3/45/15</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>G4P4</td>
<td>No</td>
<td>Triptorelin</td>
<td>No</td>
</tr>
<tr>
<td>4/41/13</td>
<td>No</td>
<td>No</td>
<td>Secondary</td>
<td>G1P1</td>
<td>No</td>
<td>Cyproterone acetate</td>
<td>No</td>
</tr>
<tr>
<td>5/19/12</td>
<td>No</td>
<td>No</td>
<td>NE</td>
<td>G0P0</td>
<td>Pill</td>
<td>Chlormadinone acetate</td>
<td>No</td>
</tr>
<tr>
<td>6/25/13</td>
<td>Yes</td>
<td>Yes</td>
<td>NE</td>
<td>G0P0</td>
<td>Pill</td>
<td>Cyproterone acetate</td>
<td>No</td>
</tr>
<tr>
<td>7/33/14</td>
<td>Yes</td>
<td>No</td>
<td>Secondary</td>
<td>G1P1</td>
<td>No</td>
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<td>Yes†</td>
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<tr>
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<td>No</td>
<td>No</td>
<td>G3P2 (1 VIP)</td>
<td>Pill</td>
<td>Chlormadinone acetate</td>
<td>No</td>
</tr>
</tbody>
</table>

*NE = not evaluable; VIP = voluntary interruption of pregnancy.
†Values given after G and P indicate the number of pregnancies and deliveries, respectively.
‡Found at postoperative evaluation.
following diaphragmatic abnormalities were identified: multiple infracentimetric holes (one case); multiple nodular brown lesions (three cases); and associated holes and nodular lesions (four cases). One simple suture of the diaphragmatic perforations and seven partial resections of the diaphragm were performed.

Nodular brown lesions of lung parenchyma were seen in two patients. In one patient, both mediastinal and parietal pleura were involved. The excision of all these lesions also was carried out. An associated mild apical bullous dystrophy (with no air leak) was resected in four patients.

At pathologic examination, diaphragmatic endometriosis was confirmed in seven of eight patients (Fig 1, 2). In one patient, it was associated with pulmonary and pleural endometriosis. Endometriosis could not be confirmed at histology in only one patient (with multiple diaphragmatic holes and a pulmonary nodular brown lesion), but signs of parenchymal focal hemorrhages were found. Pathologic examination of resected apices (n = 4) found bullous dystrophy without signs of pulmonary or visceral pleural endometriosis.

One patient presented with a prolonged postoperative air leak. In the other patients, the postoperative course was uneventful. Postoperatively, all eight patients underwent gynecologic examination and pelvic echography. Pelvic endometriosis was found in two patients.

At the completion of the study (March 2002), follow-up was available for all patients (follow-up range, 2 to 15 months; mean follow-up, 6.6 months). One recurrence was observed. It occurred 12 days postoperatively and resolved spontaneously. In this patient, there was no further recurrence in the following 7 months. No patients developed postoperative symptoms that were possibly related to a late diaphragmatic hernia.

**Discussion**

CP involves women of reproductive age and occurs within 72 h from the onset of menstruation. The right side is involved in the great majority of cases (95%), in a recurrent manner. Several hypotheses about its pathogenesis have been raised including the following: (1) spontaneous rupture of blebs; (2) alveolar rupture caused by prostaglandin-induced bronchiolar constriction; (3) sloughing of endometrial implants of visceral pleura with subsequent air leak; and (4) in the absence of the cervical mucous plug, passage of air from the genital tract through congenital or acquired (ie, due to sloughing of diaphragmatic endometriotic foci) diaphragmatic defects.

Thus, it is classically known that CP would be a typical presentation of thoracic endometriosis. On the other hand, CP could occur also in the presence of diaphragmatic defects without signs of diaphragmatic or thoracic endometriosis (ie, porous diaphragmatic syndrome).

The exact pathogenesis of thoracic endometriosis remains unknown. The theory of coelomic metaplasia (ie, the metaplastic transformation of cells lining the pleural cavity) has been favored for many years; however, it cannot explain the possible intrapulmonary localization of the disease or its right-side predominance. Another theory has suggested pathogenesis in the transplantation of endometrium to ectopic sites after lymphatic or vascular embolization.
tion or retrograde menstruation.\textsuperscript{1,8} This last mechanism could explain the known right-sided predominance of the disease, which was confirmed in our experience. It is well-known that there exists a preferential flow of peritoneal fluids (including air) and endometrial tissue from the pelvis along the right paracolic gutter up to the subphrenic space.\textsuperscript{7} Furthermore, the anatomy of the two upper abdominal quadrants is different. A large, solid, and relatively fixed liver overlain by the right diaphragm causes a “piston” action, whereas the soft and compressible visceras of the left upper quadrant cannot exert such activity.\textsuperscript{7}

Among our patients, pelvic endometriosis was found in only two cases. This finding is in agreement with those of others,\textsuperscript{1} as less than one third of CPs have been reported to be associated with pelvic endometriosis, and previous pelvic surgery or uterus manipulation are found, surprisingly, in only 11% of cases. In our patients, pelvic endometriosis was searched for by gynecologic examination and ultrasonography. Although it is well-known that these methods lack diagnostic accuracy, routine laparoscopy was considered not to be appropriate by our gynecologists in women who were otherwise asymptomatic. On the other hand, an invasive pelvic examination was proposed to patients with symptoms of pelvic disease.

CP is considered to be a rare entity. In the large study by Nakamura et al,\textsuperscript{9} dealing with 664 cases of SP in women, 6 cases were considered to be catamenial. In that study, the authors performed a retrospective review of the clinical files of patients with SP who had been admitted to the hospital over an 8-year period. Unfortunately, the characteristics of patients with CP as well as the methods of diagnosis and treatment were not reported, thus precluding the possibility of comparison with our data. In the retrospective study by Shearin et al,\textsuperscript{10,11} 11 cases of CP were found among 196 cases of SP in women (5.6%). Although not specifically stated, the catamenial character of the pneumothorax probably was recognized because of the temporal relationship with menses. The management of CP was largely variable, as follows: two patients were treated with rest; thoracocentesis was employed in one patient; the remaining eight patients were operated on by thoracotomy (the type of thoracotomy was not specified). Endometriosis was never found at histology, and diaphragmatic defects were seen in only one case.

In our study, CP seems to be much more frequent, accounting for 25% of all SPs in women who were referred for surgery. There are probably at least two reasons for these discrepancies. First, our series deals only with patients who were referred for surgery. Second, due to the prospective character of the study, the catamenial type of SP was probably more accurately searched for at medical visits and lesions were more carefully detected during surgery. We employed video-assisted thoracoscopy in all but one case. It is noteworthy that video-assisted thoracoscopy gives an increased magnification and exposure that is sometimes better than thoracotomy. This could provide a further explanation of the finding of high incidence of thoracic endometriosis in our series.

It should be considered that a misdiagnosis is also possible at thoracotomy, especially if an axillary incision is employed (as was usually the case for women with SP up to the last decade), or during videothoracoscopy if the patients are positioned for an axillary thoracotomy (i.e., with the arm elevated). Misdiagnosis may be due to the difficulties of correctly exploring the diaphragm in this position. In this series, we employed video-assisted thoracoscopy with the patients positioned for a standard posterolateral thoracotomy. Under these conditions, a complete exploration of the chest cavity is possible, and in most instances resection of endometrial implants and/or repair of diaphragmatic holes may be performed easily. Although simple thoracoscopic pleurodesis seems to provide satisfactory results,\textsuperscript{1} in our opinion the resection of endometrial implants (whenever found) should be carried out to take away endometriosis sources, thus probably limiting further endometrial spreading. If diaphragmatic lesions are found, a limited diaphragmatic resection is often possible by using endoscopic staplers, without need of an open approach.\textsuperscript{3} Resection of the diseased diaphragm allows its closure, thus treating a pathogenic mechanism of the CP. If the number, and/or size, and/or location of diaphragmatic abnormalities contraindicate an endoscopic diaphragmatic resection, an open approach under video assistance is necessary. This approach allows either resection and repair by suture or a simple repair by suture according to the standard surgical technique. We think that endoscopic diaphragmatic stapling may be considered safe (in terms of the possibility of late hernias) only if employed in small resections and/or to close small defects, whereas its use should be discouraged in the remaining cases. In our opinion, pleurectomy plays a major role in determining the outcome, due to the impossibility of dealing with microscopic diaphragmatic disease, the behavior of which is unpredictable. We favor careful pleural abrasion and think that treatment with pleurectomy or talc pleurodesis should be considered in case of treatment failure.
In our series, a diaphragmatic abnormality was found in all cases. In all but one patient, diaphragmatic endometriosis was found, whereas in the remaining patient diaphragmatic holes without endometriosis were found. On the other hand, pulmonary endometriosis was suspected in two patients but was proven histologically in only one patient. It is noteworthy that apical bullous dystrophy was a frequent feature in our series; however, it was not responsible for the air leak during surgical exploration. Thus, our experience allows us to think that diaphragmatic abnormalities play a fundamental role in the pathogenesis of CP, whereas other nondiaphragmatic causes would probably play a minor role.

Although it has been pointed out that surgery provides significantly better results compared to medical treatment alone, the pharmacologic inhibition of sex hormones is still considered to be of fundamental importance in the treatment of endometriosis. Although it is not known whether there is a real need for a medical treatment of isolated thoracic endometriosis after the complete resection of lesions, we think that the association of medical treatment with video-assisted thoracic surgery should probably be considered as the optimal treatment modality for these patients. Further studies including a larger number of patients with a longer follow-up time are mandatory to confirm the high incidence of CP among female patients who are referred for surgery and to evaluate the management modalities that have been proposed in the present study.

References