Catamenial pneumothorax revisited: Clinical approach and systematic review of the literature

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Background: Catamenial pneumothorax is a rare entity of spontaneous, recurring pneumothorax in women. It has been associated with thoracic endometriosis, yet varying clinical courses and the lack of consistent intraoperative findings have led to conflicting etiologic theories.

Methods: We discuss etiology, clinical course, and surgical treatment of 3 women with catamenial pneumothorax. In addition, the world literature since the first description is reviewed.

Results: Three women (31, 32, and 39 years old) had recurrent, menses-associated, right-sided spontaneous pneumothoraces. They had undergone video-assisted thoracoscopic surgery previously, with various unsuccessful procedures. Finally, with video-assisted thoracoscopic surgery multiple small perforations in the tendinous part of the right diaphragm with adjacent endometrial implants were detected. After plication of the involved area, 2 patients have been free of recurrence for 22 and 13 months, respectively. Laparoscopic evaluation in 1 woman with a further recurrence revealed asymptomatic pelvic endometriosis. This patient has been free of recurrence since initiation of luteinizing hormone–releasing hormone analog therapy for 17 months. In a review of 229 cases of catamenial pneumothorax in the literature, adequate information was given for 195 patients (85.2%). One hundred fifty-four (79%) were treated surgically, with detailed findings reported for 140 (91%). Thoracic endometriosis was diagnosed in 73 patients (52.1%), and 54 (38.8%) showed diaphragmatic lesions. Pleurodesis, with or without diaphragmatic repair or wedge resection, was performed in 81.7% of the cases.

Conclusions: Catamenial pneumothorax may be suspected in ovulating women with spontaneous pneumothorax, even in the absence of symptoms associated with pelvic endometriosis. During video-assisted thoracoscopic surgery, inspection of the diaphragmatic surface is paramount. Plication of the involved area alone can be successful. In complicated cases, hormonal suppression therapy is a helpful adjunct.

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Since the first description by Maurer and colleagues¹ in 1958, 229 cases of a unique entity of spontaneous recurring pneumothorax in women have been reported.¹⁻⁹¹ Although varying clinical courses form the basis for conflicting etiologic theories, all of the reported cases demonstrate a repetitive occurrence in synchrony with the menstrual cycle. Not all of a patient's menses coincide with a pneumothorax, but each episode of a catamenial pneumothorax (CPT) is associated with the menstrual flow.

Clinical Summaries

Patient 1

In February 2002, a healthy 31-year-old woman, gravida 0, had her first episode of a right sided spontaneous pneumothorax and was treated with a chest tube. Because of a persistent air leak, in situ talcum pleurodesis was attempted but failed. During video-assisted thoracoscopic surgery (VATS), no specific lesions were seen. After the operation, no air leakage was observed, and the patient had a regular recovery. After a recurrence in July 2002, we noted multiple perforations (1-3 mm) in the tendinous part of the diaphragm during videothoracoscopy (Figure 1). Through a minithoracotomy, we reinforced the area by plication of the perforated area. A persistent air leak forced us to reexplore again, where we found and resected a subpleural bulla in the horizontal fissure. After recovery, the patient has been symptom free for 22 months. In retrospect, she realized that both her pneumothoraces had coincided with the beginning of her menses.

Patient 2

In December 2001, a healthy 32-year-old woman, gravida 0, had two right-sided spontaneous pneumothoraces and was treated with a medical talcum pleurodesis. During VATS after a second recurrence in May 2002, no lesions were found. We performed an apical pleurectomy down to the seventh rib. After another recurrence that coincided with her menses in August 2002, we discovered during reexploration several perforations in the centrum tendineum of the diaphragm, associated with purple nodules. Through a minithoracotomy, we excised a perforation with the adjacent nodule, reinforced the perforated portion with a double running suture, and performed a talcage. Histologic examination confirmed an endometrial implant (Figure 2). After release, she had a recurrence in October 2002. To explore the extent of a possible abdominal endometriosis, we undertook a rethoracoscopy in combination with laparoscopy. The intrathoracic findings were inconclusive, although we did not mobilize the whole basal portion of the lung. Laparoscopic exploration confirmed the suspicion of disseminated pelvic endometriosis. After recovery, luteinizing hormone-releas-

Figure 1. A, Intraoperative view onto tendinous part of right diaphragm in patient 1. Multiple perforations, ranging from 1 to 3 mm, were found. B, After elevation of diaphragm, convex apical surface of liver can be observed.

Figure 2. Section of diaphragm in patient 2 shows focal full-thickness defect consisting of cellular stroma with numerous hemosiderin-laden macrophages and sparse chronic inflammatory infiltrate. Epithelial strands extend into depth of stroma. Immunohistochemical stains were positive for CD10 within the stroma, supporting diagnosis of endometriosis.

TABLE 1. Main intraoperative findings in women with CPT reported in the literature

Diaphragmatic lesions	38.8%
Diaphragmatic endometriosis plus perforation	12.3%
Diaphragmatic endometriosis (no perforation)	10.2%
Diaphragmatic perforation (no endometriosis)	16.3%
Endometriosis of the visceral pleura	29.6%
Bullae/blebs/scarring	23.1%
No lesion	8.5%

Adequate description was documented for 140 of 154 operative cases. In the group with diaphragmatic lesions, there were 2 cases in combination with bullae, 1 case in combination with parenchymal endometriosis and bulla, and 1 case in combination with endometriosis of the visceral pleura.

TABLE 2. Surgical procedures applied for CPT reported in the literature

Pleurodesis	33.1%
Diaphragmatic interventions	38.8%
Diaphragmatic excision plus suture	17.5%
Diaphragmatic excision plus suture plus pleurodesis	14.7%
Diaphragmatic plication, mesh, etc	6.6%
Wedge resection	10.3%
Wedge resection plus pleurodesis	9.8%
Exploration	4.4%
Anatomic pulmonary resection	3.4%

Conclusive information was documented for 140 of 154 surgically treated women.

ing hormone analog therapy was started, and the patient has been symptom free for 17 months.

Patient 3

In September 2002, a 39-year-old woman, gravida 2/para 2, was treated with apical wedge resection and pleural abrasion after the first recurrence of a right-sided pneumothorax. In February 2003, after another recurrence, multiple perforations of varying sizes were located in the centrum tendineum of the diaphragm, associated with purple deposits. After biopsy, the area was plicated with a running suture. In addition, another apical wedge resection and a talcage were performed. The histopathologic workup revealed a diaphragmatic endometriotic implant, with discrete emphysematous changes in the wedge. The patient has been symptom free for 13 months.

Review of the Literature

Demographics

To date, 229 cases of CPT have been reported.¹⁻⁹¹ At onset of symptoms, the mean age was 34.2 ± 6.9 years (15-47 years), with age 36.1 ± 6.4 years at time of intervention. On average 5.1 ± 6.0 recurrences occurred before definitive treatment (several reports list more than 30 documented or

presumed recurrences before treatment^{1,6,33}). For 195 patients (85.2%), detailed descriptions were supplied. One hundred fifty-four of these women (79%) were treated surgically, and 41 (21%) received nonsurgical treatment (hormone therapy 13.5%, exclusive tube thoracostomy 1%, tubal ligation 1%, therapy refused, observation, loss to follow up, 5.5%). In a recent study on thoracic endometriosis (TE) syndrome,⁹² 76% of the patients with CPT (n = 80) underwent surgical exploration.

Clinical Findings

In 210 patients (91.7%) a right pneumothorax was diagnosed; in 11 (4.8%) the left side was affected, and in 8 (3.5%) bilateral pneumothoraces occurred. Among reports of 154 women undergoing surgical exploration, adequate information was supplied for 140 (91%). In 73 patients (52.1%) TE was diagnosed. Fifty-four women (38.8%) showed diaphragmatic lesions. In 44 women (31.6%) either discrete lesions or no pathologic findings at all were reported (Table 1). In the previously mentioned study on TE syndrome,⁹² pleural endometriosis was found in 13% of the patients, diaphragmatic defects in 26%, and cysts or blebs in 23%; no lesions were reported in 25% of the women.

Surgical Data and Outcomes

Attempts to achieve pleurodesis, either alone or in combination with other procedures, were performed in 81 cases (57.7%). Diaphragmatic interventions were done in 54 patients (38.8%). In 19 women (13.7%) anatomic or nonanatomic pulmonary resections alone were performed, and 6 patients (4.4%) underwent exploration alone (Table 2).

For 79 women (51.3%) sufficient information on the postoperative outcome was given. Among 28 patients receiving pleurodesis (mechanical abrasion, pleurectomy, or talcum), the median recurrence-free interval was 61 months (10 days–264 months). Among 15 women undergoing diaphragmatic excision (with or without pleurodesis), the median recurrence-free interval was 23.6 months (2-36 months). In a recent report on use of a mesh to cover diaphragmatic defects, 3 patients were observed for 30 to 45 months without recurrence⁸⁵; 1 patient reported in another publication had a recurrence after 2 months.⁸⁶ Twenty-seven patients were treated primarily with hormones; in several other cases this therapy was combined with surgery. Thirty percent of the women took ovulatory suppressants before, during, or after a CPT.

Discussion

We report on 3 cases of CPT in young women with a history of recurring spontaneous pneumothorax associated with the menses. The key pathologic findings were multiple diaphragmatic perforations with endometrial implants. Various hypothesis⁷¹ have been raised to explain the more than 200

reported cases of this peculiar syndrome during the last 4 decades, yet a unifying concept is lacking.

During menses, the dissolving cervical mucous plug may allow the ascent of air through the fallopian tubes. Spontaneous postpartal pneumoperitoneum⁹³ and postcoital pneumothorax⁴² have been reported. Spontaneous pneumothorax in men with diaphragmatic fenestrations has hitherto not been described; however, pneumothorax after therapeutic pneumoperitoneum in men with diaphragmatic lesions has been observed.⁹⁴ The theory of transfallopian ascent of air is supported by the fact that plication of diaphragmatic perforations and tubal ligation have cured CPT.^{35,89} However, recurrent, menses-synchronous pneumothorax was observed in 8 hysterectomized women¹⁷ and in 1 patient after tubal occlusion.⁵³

Maurer and colleagues¹ were first to associate CPT with endometriosis because they found erosive epiphrenic endometrial implants in their patient. Endometriosis affects 15% of all menstruating women,⁹⁵ mostly with pelvic manifestation. However, extrapelvic involvement, including TE, has been encountered.⁴¹ A significant association between TE and pelvic spread has been reported⁹²: CPT represents the most common manifestation of TE syndrome (73%), yet pelvic endometriosis was documented in only 28% of all cases and in only 13% could endometriotic epiphrenic lesions be demonstrated.⁹² However, in that study only 50% of the women with CPT were investigated for pelvic endometriosis, and only 3 quarters of them underwent surgical exploration.⁹²

In the literature, 43 (18.8%) women with CPT had pelvic endometriosis diagnosed on a clinical or histologic basis. Among all the surgically explored cases, TE was confirmed in 73 patients (52.1%), with 32 (22.5%) showing exclusively diaphragmatic endometriosis. Shirashi⁵⁶ contrasted the frequency of 20% for diaphragmatic endometriosis associated with CPT in the English literature with that of 49% in Japanese reports.

Theories of both implantation and metaplasia are discussed to explain endometriosis.⁹⁶ This phenomenon may be due to retrograde regurgitation of endometrial tissue during menstruation and secondary implantation on the pelvic peritoneal surface.⁹⁷ Reflux of endometrial fragments is common during menstruation,⁹⁸ and proliferating endometrial cells, capable of tissue adhesion and invasion and of angiogenesis, have been isolated from the peritoneal fluid during menses.⁹⁶ In vitro cultivation of ovarian surface epithelium in the presence of 17 β -estradiol can induce endometrial transformation (coelomic tissue metaplasia).^{99,100}

For the development of CPT, the thoracic location of the endometriotic tissue is instrumental. Endometrial tissue may circulate with the clockwise current of peritoneal fluid in the abdominal cavity—down the left peritoneal gutter,

over the pelvic floor, and up the right gutter to the peritoneal surface of the right diaphragm—which would explain the preferred occurrence of CPT on the right side.⁹⁹ Although there are small peritoneal stomata that enable particles below 30 μ m to enter diaphragmatic lacunae,¹⁰¹ to allow ascent of a sufficient quantity of air to cause a pneumothorax, a substantial defect in the continuity of the hemidiaphragm must be present. Kirschner¹⁰² introduced the concept of the porous diaphragm syndrome in 1998, proposing preexisting diaphragmatic defects allowing gas and fluids to traverse this anatomic boundary. The predominance of the right side may be explained by a pistonlike effect of the solid liver bulk, transmitting intraperitoneal pressure spikes across a perforated hemidiaphragm.

Aside from implantation and metaplasia, metastatic spread of endometrial tissue can lead to pulmonary lesions. Endometrial cells have been shown to actively invade local tissue and to embolize peripheral blood vessels.^{103,104} Pulmonary deposits of intravenously injected endometrial tissue in rabbits proliferate and slough in synchrony with the menstrual cycle.¹⁰⁵ We¹⁰⁴ and others⁹² have reported on hemoptysis as a result of pulmonary endometriosis.

Rossi and Goplerud¹⁴ have suggested that the menses-synchronous increase in prostaglandin F₂ could induce CPT. At peak levels during sloughing of the endometrial mucosa, the potent bronchial and vascular constrictor prostaglandin F₂ may cause the rupture of preformed subpleural blebs in otherwise normal lungs. This hypothesis could explain that in 23.1% of all explored cases, bullae or blebs were the only lesions discovered, and in 8.5% no pathologic findings were demonstrated.

Lillington and associates¹⁰ (coined the term *catamenial pneumothorax*). They proposed a model in which the expansion of intraparenchymal subpleural endometriotic tissue during menses would cause a check-valve airway obstruction, eventually leading to alveolar rupture.

Concerning the etiology of CPT, we hypothesize that transgression or erosion of the diaphragm as an anatomic boundary by endometriotic tissue represents the central pathophysiologic mechanism of CPT. McKnight and co-workers²³ have demonstrated in a patient with CPT endometriotic foci on the abdominal surface of the diaphragm. Although the thoracic cavity was not investigated, this demonstrates that endometriotic tissue can accumulate on the peritoneal side of the diaphragm, potentially traversing it through microchannels, through hereditary perforations, or by tissue invasiveness.¹⁰⁶ The last can be stimulated through a heat-stable factor from the peritoneal fluid,¹⁰⁷ and together with an increased proteolytic capacity¹⁰⁸ endometriotic cells can demonstrate a higher maneuverability with an enhanced potential for local invasiveness.

Taken together, we propose that endometrial mucosa, dispersed into the parametrial space undergoes a phenotypic

modification toward endometriotic tissue. Accumulating in the right subdiaphragmatic space, the cells either traverse the diaphragm through an active proteolytic process or are washed into the thoracic cavity across preformed lesions. Passively, CPT may be caused by transfallopian ascent of air when the cervical mucous plug dissolves during menses. Actively, endometriotic cells entering the thoracic cavity may lyse the visceral pleura, causing minute subpleural perforations in synchrony with the menstrual cycle.

Some comments on diagnostic pitfalls and therapeutic strategies for CPT may be helpful. For any women with a spontaneous recurring pneumothorax, a gynecologic history and evaluation of her menstrual cycle should be taken. Medical pleurodesis with talcum in a young patient, without VATS exploration, should be avoided. Many women with CPT do not have it diagnosed, because the discrete lesions can easily be overlooked. Therefore modern VATS technology with high-performance magnifying and imaging hardware can be decisive in advancing the correct diagnosis. In a recent prospective study, Alifano and associates⁹⁰ systematically evaluated women of reproductive age with spontaneous pneumothorax for the possibility of CPT. In 8 of 32 patients, either thoracic endometriosis or perforations of the diaphragm were found.

In CPT we are confronted with the localized complication of a systemic diseases. When CPT is suspected, VATS exploration is the preferred approach. If possible, it should be timed around the beginning of the menstrual flow to allow maximum visibility of the potential endometriotic implants. Because previous interventions to achieve pleurodesis may have masked the specific lesions, the diaphragm needs to be explored thoroughly, including visceral and parietal pleurae. All accessible lesions should be excised, and plication is recommended to seal and strengthen this area. In addition, we favor mechanical pleurodesis. In case of recurrence, further gynecologic evaluation may be helpful, because most women with CPT do not have symptoms of a simultaneously existing pelvic endometriosis. Hormonal therapy is a secondary therapeutic option, especially when considering the systemic nature of the disease. Use of a gonadotropin-releasing hormone analog can cure CPT⁸⁰; however, before initiating pharmacologic disruption of ovarian steroid genesis in a young woman, all surgical treatment options should have been exhausted.

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