

A Case Report of Recurrent Spontaneous Pneumothorax Secondary to Thoracic Endometriosis Syndrome

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Abstract Endometriosis is a benign condition in which ectopic endometrial glands and stroma are present outside of the uterine cavity. It commonly affects the pelvic organs but can also spread throughout the entirety of the body, including the thoracic cavity. The ectopic presence of endometrial glands and stroma in lung or pleura can produce a range of clinical and radiological manifestations – catamenial pneumothorax, catamenial hemothorax, catamenial hemoptysis, and pulmonary nodules – collectively referred to as “thoracic endometrial syndrome.” Thoracic endometriosis constitutes an uncommon cause of spontaneous pneumothorax in nonsmoking women of childbearing age. Symptoms are often non-specific and the diagnosis is often delayed. A thorough menstrual history and its temporal relationship to pneumothorax onset should be assessed in every woman presenting with recurrent pneumothorax. Thoracic endometriosis syndrome is very manageable with the advancements of VATS and hormonal therapy, but we as clinicians should have this on our differential diagnosis when a young, reproductive-aged female presents with a spontaneous pneumothorax to expedite appropriate care. Here we present a case of a 44 year old female with recurrent spontaneous pneumothorax that was attributed to thoracic endometriosis that will hopefully educate providers to have a high clinical suspicion in patients to obtain an accurate diagnosis and initiate proper treatment.

Keywords: *thoracic endometriosis syndrome, recurrent spontaneous pneumothorax, catamenial pneumothorax*

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1. Introduction

Endometriosis is a benign condition in which ectopic endometrial glands and stroma are present outside the confines of the uterine cavity. Endometriosis most commonly affects the pelvic organs (e.g., ovaries, fallopian tubes, and various uterine ligaments), but can also spread throughout the entirety of the body, with the most common extra-pelvic location within the abdominal wall [1,2]. The ectopic presence of endometrial glands and stroma in lung or pleura can produce a range of clinical and radiological manifestations – catamenial pneumothorax, catamenial hemothorax, catamenial hemoptysis, and pulmonary nodules – collectively referred to as “thoracic endometrial syndrome,” or TES [1,2,4,5,6]. Thoracic endometriosis constitutes an uncommon cause of spontaneous pneumothorax in nonsmoking women of childbearing age with an approximate incidence of 7.3% among cases of ectopic endometriosis [2]. What follows is a case presentation of a recurrent spontaneous pneumothorax attributed to thoracic endometriosis and further discussion of thoracic endometriosis syndrome (TES).

2. Case Presentation

A 44-year-old African American female presented to the emergency department for shortness of breath and right-sided chest discomfort. The patient’s surgical history was significant for a partial hysterectomy for endometriosis prior this year and a right video-assisted thoracoscopic surgery (VATS) bullectomy with mechanical pleurodesis for a spontaneous right-sided pneumothorax attributed to bullous disease about seven months prior. The patient states her dyspnea began about 4 days prior to presentation, but progressively worsened and became associated with right-sided chest discomfort.

The patient was afebrile with heart rate of 71 bpm, blood pressure of 125/77, respiratory rate of 23, and oxygen saturation of 99% on a non-rebreather mask. She had diminished breath sounds on the right, but had no tracheal deviation, audible wheezes, or accessory muscle use during respirations.

The patient’s laboratory workup was unremarkable. Imaging was obtained, first a chest x-ray (CXR) followed by a chest computed tomography angiography (CTA) of the chest. The CXR was remarkable for a small right-sided

pneumothorax, with air at the apex and right lung base (Figure 1). The chest CTA was significant for a large right-sided pneumothorax (Figure 2).



Figure 1. Chest x-ray findings of right-sided pneumothorax



Figure 2. CTA chest showing large right-sided pneumothorax

A tube thoracostomy was performed in the emergency department with a 28 French chest tube with immediate improvement in her respiratory status. The following day, the patient was taken to the operating room for a flexible

bronchoscopy and re-do right VATS with mechanical pleurodesis. Intra-operatively, dark coffee colored discolorations were found to be present on the visceral pleura and on the pleural surface of the diaphragm.

On the lung, these areas were most noted on the right lower lobe. Due to these lesions, a right lower lobe wedge resection with biopsy was performed as well as a diaphragmatic pleural biopsy. A repeat mechanical pleurodesis and a partial pleurectomy in the thoracic cavity was performed, and a 28Fr chest tube left in place.

Final pathology of the right diaphragmatic lesion showed fibrovascular tissue with endometrial type stroma and chronic hemorrhage, consistent with endometriosis. Pathology of the RLL wedge resection showed lung tissue with benign intraparenchymal lymph node - negative for features of endometriosis.

The patient's course was complicated by a prolonged air leak requiring discharge with a Heimlich valve, which has subsequently been removed on outpatient follow-up without complication. She was also instructed to follow up with her OB/GYN for further management of thoracic endometriosis syndrome.

3. Discussion

Thoracic endometriosis syndrome is a rare condition and the diagnosis is often delayed or missed by clinicians, which can lead to recurrent hospitalizations and other complications. Although thoracic disease can occur in isolation, it can be associated with extensive endometriosis of the reproductive, genitourinary, and gastrointestinal systems; and among patients diagnosed with TES, 50-84% have associated endometriosis [4,7,8].

The most common presentation (approx. 70% of cases) of thoracic cavity specific endometriosis is catamenial (a term that refers to a temporal relationship with menses) pneumothorax, but it only makes up approximately 2.5% to 5% of cases of all women with spontaneous pneumothorax [1,2,4,7,8,9,10]. A small portion (10% or less) of the subset have a pneumothorax that has no temporal relationship with menses (non-catamenial pneumothorax), and are typically identified during surgery for a recurrent pneumothorax, as in our case [3].

Thoracic endometriosis should be suspected in young, reproductive-aged women (peak between 30 to 35 years old) with catamenial pneumothorax or hemothorax, especially those who have a history of prior uterine surgical interventions or pelvic endometriosis, as it is present in 65-84% of that patient population [7,8]. Symptoms of a catamenial pneumothorax begin within 72 hours after the onset of menstruation, with the most common complaints being chest or scapular pain and dyspnea [4-10]. The right hemithorax is involved the vast majority (as high as 95%) of the cases [2,4,5,6,7,8,9].

The etiology of thoracic endometriosis is not fully understood, but there have been several theories that have been discussed. First is the retrograde menstruation theory (or Sampson's theory), which suggests that endometrial cells travel into the peritoneal cavity via retrograde through the fallopian tubes and implant on the peritoneal surfaces. The circulation of the peritoneal fluid, which moves in a clockwise fashion from the pelvis to the right

paracolic gutter then onward to the right hemi-diaphragm where flow is eventually obstructed by the falciform and phrenocolic ligaments [4,5,6,7,10]. The endometrial tissue is then suspected to implant on the diaphragm as well as traverse into the thoracic cavity via congenital or acquired fenestrations in the diaphragm [4-10]. This theory supports the fact that the endometriosis is nine times more likely to occur on the right hemi-diaphragm than the left, but it also has flaws in that diaphragmatic defects are rare and pneumothorax can recur after diaphragmatic repair and/or hysterectomy [4,6].

A second theory, called coelomic metaplasia, advocates that peritoneal and pleural epithelium transform into endometrial tissue under the influence of physiological stimuli, such as estrogen [4,5,8,9,10]. This theory can explain the presence of endometrial tissue in patients without a uterus including me on prolonged estrogen therapy, but it fails to explain the right-sided thorax predominance seen in most TES cases [4,5,6].

An additional theory is benign metastasis of ectopic endometrial implants via lymphatic and/or vascular microembolization. This "metastatic theory" can explain the presence of both intrapulmonary and other extra-uterine sites of implantation (e.g., thorax, brain, and joints), but it comes up short on why thoracic endometriosis is found overwhelmingly on the right side [4,5,6,7,8,10].

The final proposed theory is the prostaglandin theory. Prostaglandin F_{2α}, which is detectable in the plasma of women during menstruation, is a potent constrictor of the bronchioles and vasculature. As the prostaglandin increases so should the constricted vessels and bronchioles, which can lead to ischemic changes and potentially alveolar rupture of previously formed subpleural blebs and bullae resulting in a pattern of catamenial pneumothorax [4,5,6,9,10].

Given the various different theories about the etiology of catamenial pneumothorax and the inconclusive nature of each, it is likely a multifactorial process that accounts for its development as none of these theories alone provide complete justification for the varied clinical presentations encountered in this disease process.

A diagnosis of TES in women is generally made based upon a thorough history and physical, recurrence of pneumothorax and its relation with the onset of menses, or a history of endometriosis. In most cases it is diagnosed retrospectively by intra-operative anatomic findings or histological diagnosis, as in our case [9,10].

The workup upon presentation is generally performed with diagnostic imaging. Despite low specificity, the most sensitive images for detecting a pneumothorax is a chest X-ray and CT scan, whereas an MRI is preferable for identification of diaphragmatic endometriosis with a sensitivity around 80% [1,2,4,5]. As previously discussed, the pneumothorax will most commonly be on the right side. Occasionally, even pneumomediastinum or pneumoperitoneum can be seen [1,2,4]. Furthermore, chest CTs are most likely to show abnormalities when patients are symptomatic (i.e., usually during menses) due to higher resolution [7].

Imaging can aid in the diagnosis, but the gold standard for a definitive diagnosis of thoracic endometriosis is video-assisted thoracoscopic surgery, or VATS, followed by tissue biopsy [4,7,9]. The most common findings during VATS are diaphragmatic lesions (38.8%), endometriosis

of the visceral pleura (29.6%), and discrete lesions such as bullae, blebs, or scarring (23.1%) [4]. Diaphragmatic endometrial implants tend to be black, blue, or reddish-purple in appearance, but there is a significant variety in morphological appearance [4].

There are some serum laboratory tests that may be elevated in patients with thoracic endometriosis, specifically CA-125 and CA 19-9, but are poorly sensitive and non-specific diagnostically [12]. Pleural fluid cytology is seldom helpful as well in diagnosis, but there have been reports of diagnostic fluid cytology and some clinicians send pleural fluid to evaluate for endometrial cells during initial chest tube placement if the patient fits the typical epidemiology of TES [7,11].

Spontaneous pneumothorax due to thoracic endometriosis syndrome is initially treated by managing the symptomatic presentation with stabilization of the patient (i.e., chest tube for pneumothorax) followed by secondary prevention of recurrence (e.g., blebectomy, pleurodesis, and hormonal therapy) [10]. As mentioned, VATS is the gold standard for diagnosis and treatment of TES, especially for catamenial pneumothorax. The purpose of thoracoscopy is to perform gross inspection of the pleura and diaphragm to directly visualize endometrial implants and diaphragmatic perforations, biopsy suspicious lesions, and usually perform therapeutic pleurodesis [5,9,10].

VATS allows for multiple treatment modalities depending on characteristics of lesions as well as location. For superficial endometriosis implants, lesions can be fulgurated using bipolar diathermy, CO₂ laser, Nd-YAG laser, argon laser, or plasma energy, while deeper lesions should be excised with sharp dissection [4]. Infiltrative parenchymal endometriosis nodules or large lesions are more appropriately with parenchymal-sparing procedures such as a wedge resection, sub-segmentectomy, or lobectomy [4].

Once the diagnosis is confirmed, adjunctive hormonal suppressive therapy is usually administered postoperatively for 6-12 months [10]. As with pelvic endometriosis, the backbone of therapy for TES is medical management to suppress ovarian steroid hormone production; it can also be used postoperatively to help minimize the risk of recurrence [4,5,9]. Generally, gonadotropin-releasing hormone (GnRH) analogs are first-line drugs because they are effective in suppressing the hypothalamic-pituitary-ovarian axis and thus the growth of endometrial cells [4,10]. However, side effects of osteoporosis and menopausal-like symptoms must be kept in mind when administering GnRH, and alternative medications such as oral contraceptives, progestins, danazol, and aromatase inhibitors can be considered [3,4,5,7]. Although GnRH analogs are commonly used, there has been no specific medication that has been shown to be superior, thus the decision of which drug to be used is influenced by cost, side effects, duration of treatment, and the patient's wishes in terms of fertility [6]. If results following hormonal therapy are positive and without concerning side effects, continuing hormonal therapy is an option with the hope that longer suppression of ovulation may result in thoracic endometriosis regression [3].

An additional treatment modality to consider, particularly in elderly patients and those who no longer wish to preserve fertility, is a bilateral salpingo-oophorectomy with or without hysterectomy. However,

this does not address existing endometrial implants that may become active following exogenous estrogen administration [4,7].

Despite combining the therapeutic arms of surgery and hormonal suppression, pneumothorax recurs in 8-40% of patients compared to less than 5% of patients surgically treated with primary spontaneous pneumothorax [3]. In one retrospective case series of 114 women followed for three years who had surgery for recurrent pneumothorax, the highest recurrence rates were observed in those with endometriosis-related catamenial and non-catamenial pneumothorax, when compared with non-endometriosis-related pneumothorax (32% and 27% vs. 5%) [3]. One way to potentially decrease the recurrence rate is to perform a pleurodesis during VATS as the rate falls by 20-25% compared with those who did not undergo a pleurodesis at the time of surgery [4]. Pleurodesis has also been shown to be superior to hormonal therapy alone at preventing recurrences [7].

Some patients may continue to experience monthly chest pain despite therapy. Persistent symptoms in this setting are presumably due to proliferation and shedding of visceral pleural endometrial implants accompanied by local inflammation from continued ovarian hormone stimulation [7,8].

4. Conclusion

It is plausible that many reproductive-aged females presenting with recurrent pneumothorax are misdiagnosed as spontaneous pneumothorax when in fact it may be attributable to thoracic endometriosis syndrome. Symptoms of TES are non-specific, so a high degree of clinical suspicion is necessary. A thorough menstrual history and its temporal relationship to pneumothorax onset should be assessed in every woman presenting with recurrent pneumothorax. In addition, intraoperative visualization of the diaphragmatic surface should be routinely performed in a patient with a high clinical suspicion, as patients diagnosed with catamenial pneumothorax have good outcomes with surgical and hormonal intervention.

Diagnosis is often delayed until several episodes have occurred because of failure to associate the patient's symptoms with menses. The mean time of diagnosis of thoracic endometriosis syndrome is around 8 months [7].

With the advancements of VATS and hormonal therapy, thoracic endometriosis syndrome is very manageable but we as clinicians need to get in the habit of having this on our list of differentials when a young, reproductive-aged

female presents with a spontaneous pneumothorax in order to begin the diagnostic then therapeutic process of this condition.

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