

Thoracic Endometriosis Syndrome: A Review of Diagnosis and Management

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ABSTRACT

Background: Endometriosis is characterized by the presence of endometrial-like glands and stroma outside the uterine cavity and is believed to affect 6%–10% of reproductive-age women. Endometriosis within the lung parenchyma or on the diaphragm and pleural surfaces produces a range of clinical and radiological manifestations. This includes catamenial pneumothorax, hemothorax, hemoptysis, and pulmonary nodules, resulting in an entity known as thoracic endometriosis syndrome (TES).

Database: Computerized searches of MEDLINE and PubMed were conducted using the key words “thoracic endometriosis,” “catamenial pneumothorax,” “catamenial hemothorax,” and “catamenial hemoptysis.” References from identified sources were manually searched to allow for a thorough review.

Conclusion: TES can produce incapacitating symptoms for some patients. Symptoms of TES are nonspecific, so a high degree of clinical suspicion is warranted. Medical management represents the first-line treatment approach.

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When this fails or is contraindicated, definitive surgical treatment for cases of suspected TES uses a combined video laparoscopy performed by a gynecologic surgeon and video-assisted thoracoscopic surgery performed by a thoracic surgeon. Postoperative hormonal suppression may further reduce disease recurrence.

Key Words: Thoracic endometriosis, Catamenial pneumothorax, Catamenial hemothorax, Catamenial hemoptysis, Diaphragmatic endometriosis.

INTRODUCTION

Endometriosis is a common, benign condition characterized by the presence of endometrial-like glands and stroma outside the uterine cavity. It is estimated that endometriosis affects approximately 6%–10% of reproductive-aged women; however, we believe that the incidence of endometriosis is much higher.¹ Among this population, 12% are estimated to experience endometriosis of nonreproductive organs, referred to as extragenital endometriosis.^{2–7} The most common site of endometriosis outside of the abdominopelvic cavity is within the thoracic cavity^{8–10} (**Figure 1**). Endometriosis within the lung parenchyma or on the diaphragm and pleural surfaces produces a range of clinical and radiological manifestations, including catamenial pneumothorax, catamenial hemothorax, catamenial hemoptysis, and pulmonary nodules. Collectively, this is known as thoracic endometriosis syndrome (TES).^{8–10} Recently, Bobbio et al. proposed expanding this classic definition of TES to include endometriosis-related diaphragmatic hernia, catamenial chest pain, and endometriosis-related pleural effusion.¹¹

TES is currently considered to be a manifestation of endometriosis progression. This is evidenced through epidemiological observations demonstrating an older age at onset and coexisting pelvic endometriosis in women with thoracic endometriosis. When compared with a mean age at presentation of 25 to 30 y in patients with only pelvic endometriosis, the age at presentation of patients with thoracic endometriosis is increased to a mean of 35 y.^{8,12} Furthermore, patients typically experience symptoms of



Figure 1. Pleural endometriosis.

pelvic endometriosis approximately 5–7 y before developing symptoms of thoracic endometriosis.⁸ Although thoracic disease can occur in isolation, it is usually associated with extensive endometriosis of the reproductive, genitourinary, and gastrointestinal systems.^{7,8,12} Among patients diagnosed with TES, 50%–84% have concomitant pelvic endometriosis.¹² Thus, the purpose of this review are to describe the pathophysiology, clinical presentation, and diagnosis of TES and to discuss surgical techniques for video laparoscopic and video thoracoscopic management with or without robotic assistance.

Pathophysiology of Thoracic Endometriosis

Although the pathogenesis of thoracic endometriosis is not yet fully understood, several theories have been presented. As none of the theories alone can account for all clinical manifestations of the syndrome, the etiology of TES is likely multifactorial.

Retrograde Menstruation Theory

The most prominent theory, known as Sampson's theory of retrograde menstruation, proposes that endometrial cells undergo retrograde movement through the fallopian tubes into the peritoneal cavity, where they can implant on peritoneal surfaces.¹³ It is worth acknowledging that centuries before Sampson, other investigators, like Schron, had proposed the theory of retrograde menstruation.¹⁴ Circulation of peritoneal fluid containing effluxed endometrial cells follows a distinct pattern of movement within the peritoneal cavity. It flows from the pelvis through the right paracolic gutter to the right hemidiaphragm, while deviating away from the left hemidiaphragm due to obstruction of flow by the falciform and phrenicocolic ligaments.¹⁵ Upon reaching the right subdiaphragmatic area, endometrial cells are thought to implant on the diaphragmatic surface or undergo transperitoneal-

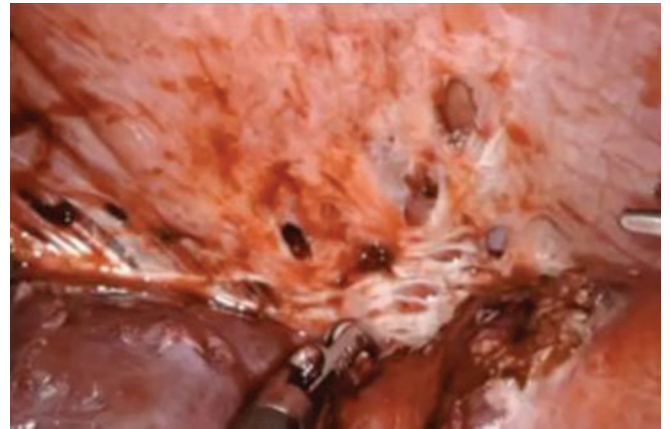


Figure 2. Acquired diaphragmatic fenestrations secondary to endometriosis.

transdiaphragmatic migration to the pleural cavity via congenital or acquired fenestrations within the diaphragm¹⁶ (**Figure 2**). This theory is supported by the observation that endometriosis is nine times more likely to occur on the right hemidiaphragm than on the left.^{8,12,17}

Coelomic Metaplasia Theory

The coelomic metaplasia theory hypothesizes that endometriosis arises by metaplasia of mesothelial cells lining the pleura and peritoneal surfaces into endometrial glands and stroma.^{18,19} Transformation of these cells may be influenced by physiologic stimuli such as estrogen.²⁰ Support for this theory is observed in endometriosis patients with Mayer-Rokitansky-Küster-Hauser syndrome, who lack a functional endometrium. Rare cases of endometriosis may even occur in men receiving high-dose estrogen.^{21,22} Although the coelomic metaplasia theory provides an explanation for pleural cases of thoracic endometriosis, it fails to explain bronchopulmonary lesions or the right-sided predominance seen in most cases of TES.

Lymphatic and Hematogenous Dissemination Theory

The theory of benign metastasis proposes that ectopic endometrial implants are the result of lymphatic or hematogenous dissemination of endometrial cells, suggesting a possible explanation for bronchopulmonary endometrial lesions.^{23,24} Upon review of autopsy data of humans with thoracic endometriosis, researchers observed that patients with bronchopulmonary endometriosis typically had bilateral lesions, whereas diaphragmatic and pleural disease was overwhelmingly right-sided.¹⁹ Perhaps the most com-

elling evidence for the theory of benign metastasis is derived from reports of endometriotic lesions occurring in distant sites of the body such as the brain or bone.²⁵

Prostaglandin Theory

A final theory for the pathogenesis of TES involves prostaglandin F2 α , a potent constrictor of the bronchioles and vasculature that is detectable in the plasma of women during menstruation.^{12,26–28} With this theory, it is hypothesized that circulating prostaglandin F2 α increases with menstruation, leading to the constriction of bronchioles and blood vessels. This can lead to alveolar rupture of previously formed subpleural blebs and bullae, resulting in a pattern of catamenial pneumothorax.^{18,27,29,30} This explanation is of particular importance in 23.1% of explored cases of TES in which blebs and bullae were the only lesions identified and 8.5% of cases in which pathologic findings were absent.^{12,31}

Clinical Presentation and Diagnosis of TES

Signs and Symptoms

The clinical presentation of TES can be variable, with many patients being asymptomatic. Symptomatic patients often experience a constellation of temporal symptoms and radiologic findings with menstruation, including catamenial pneumothorax (80%), catamenial hemothorax (14%), catamenial hemoptysis (5%), and, rarely, pulmonary nodules.⁸ However, symptoms have been reported before menstruation, during the periovulatory period, and following intercourse.^{27,32,33}

Symptoms of thoracic endometriosis are largely related to the anatomic location of the lesions. Pleural TES typically presents with symptoms of catamenial pneumothorax and chest or shoulder pain. Catamenial pneumothorax is defined as recurrent pneumothorax occurring within 72 h of the onset of menstruation.¹⁸ The symptoms experienced by patients are comparable to those of spontaneous pneumothorax and include pleuritic chest pain, cough, and shortness of breath. Furthermore, diaphragmatic irritation may produce referred pain to the periscapular region or radiation to the neck (most often right-sided). The right hemithorax is involved in up to 92% of cases, with 5% of cases involving the left hemithorax and 3% experiencing bilateral involvement.¹² Catamenial hemothorax is a less common manifestation of pleural TES. Similar to catamenial pneumothorax, it presents with nonspecific symptoms of cough, shortness of breath, and pleuritic chest pain. It is predominantly right-sided, although rare cases

of left-sided hemothorax have been reported.³⁰ Less common bronchopulmonary TES presents as mild to moderate catamenial hemoptysis or as rare lung nodules identified on imaging. Massive, life-threatening hemoptysis is rare. Pulmonary nodules can be an incidental finding at the time of imaging or can occur in symptomatic patients. They can vary in size from 0.5 to 3 cm.^{8,34} Outside of the well-established clinical manifestations of TES, cases of isolated diaphragmatic endometriosis are typically asymptomatic but can result in irritation of the phrenic nerve. This can produce a syndrome of only catamenial pain, presenting as cyclic neck, shoulder, right upper quadrant, or epigastric pain.^{2,9,10,31,35–37}

Because the clinical manifestations of TES can be variable and a temporal association with menstruation is not always recognized, a high level of clinical suspicion is essential to ensure a timely diagnosis.³⁸ Although the differential diagnosis of TES is broad, features that distinguish TES from other diseases with a similar presentation include the temporal relationship with menses, predominant right-sided symptoms, young age, presence of recurrent disease, and a history of infertility.

Diagnosis

Various diagnostic tests can be useful in guiding the differential diagnosis of TES. Useful modalities include chest radiographs (CXR), computed tomography (CT), magnetic resonance imaging (MRI), and bronchoscopy.

Despite low specificity, the most sensitive tests for detection of pneumothorax and hemothorax are CXR and CT, whereas MRI is preferable for the detection of diaphragmatic endometriosis with a reported sensitivity of 78%–83%.^{39–42} Pneumothoraces on CXR or CT can be of any size, are typically right-sided (88%–100%), and may result in a shifting of the mediastinum.⁴³ Other signs of thoracic endometriosis that may be present on CXR or CT include pneumomediastinum, pneumoperitoneum, ground glass opacities, bronchial wall thickening, thin-walled cavities within the lung parenchyma, or bullous formation.⁴⁴

Bronchoscopy, thoracoscopic biopsies, and cytological washings are often limited due to the propensity of endometrial implants to lie peripherally rather than along the mucosa of large bronchi.^{35,45–48} In cases of bronchopulmonary endometriosis, brush cytology has been reported to be superior in detecting ectopic endometrial cells compared with bronchoscopy-directed biopsies.⁴⁹

The gold standard for a definitive diagnosis of diaphragmatic endometriosis is video laparoscopy (VL), and video-

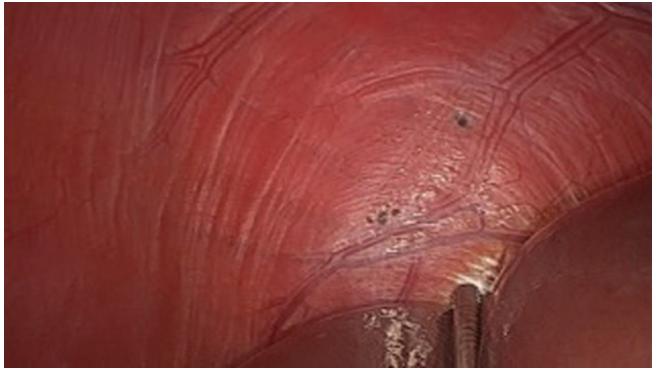


Figure 3. Retraction of the liver edge allows for a more thorough evaluation of the diaphragm.

assisted thoracoscopic surgery (VATS) for the diagnosis of thoracic endometriosis.³¹ In the largest review of patients with catamenial pneumothorax, 52.1% were diagnosed with thoracic endometriosis based on VATS findings.¹² The most commonly reported intraoperative findings included diaphragmatic lesions (38.8%); endometriosis of the visceral pleura (29.6%); discrete lesions such as bullae, blebs, or scarring (23.1%); and no findings (8.5%).¹²

Overall, diagnostic imaging and tissue sampling have inconsistent results. The diagnosis of thoracic endometriosis by endoscopic visualization can be delayed due to a traditional focus on pelvic disease, the variable appearance of endometriotic lesions, and unseen posterior diaphragmatic disease hidden behind the liver.^{10,37} The performance of diagnostic imaging and sampling may be improved if performed at the time of menses and compared with imaging performed at midcycle, as previously documented findings may disappear, thus increasing suspicion for TES.⁵⁰ Routine evaluation of the abdominal side of the diaphragm should be performed in all patients undergoing VL for suspected pelvic endometriosis. Improved endoscopic evaluation for suspected thoracic endometriosis can be achieved by utilizing the combined thoracoscopic and laparoscopic (combined VATS/VL) approach as described by Nezhat et al. in 2009.⁵¹ Additionally, techniques for optimal diaphragmatic evaluation have been described such as placing the patient in steep reverse Trendelenburg position and using an atraumatic liver retractor or grasping forceps to push the liver caudally (**Figure 3**). Use of a 30-degree endoscope or the adjustable viewing-angle endoscope can further aid visualization. In some cases, cutting the falciform ligament is necessary to allow for complete evaluation of the right hemidiaphragm.^{10,37}

Medical Management

As with pelvic disease, the first-line therapy for TES is medical management with the goal of suppressing ovarian steroid hormone production. Medical therapy can also be used postoperatively to reduce the risk of disease recurrence. Typically, gonadotropin-releasing hormone (GnRH) analogs are used first-line, as they are highly effective in suppressing the hypothalamic-pituitary-ovarian axis and the growth of endometrial-like cells, but they can be associated with the development of menopausal-like symptoms and osteoporosis.^{8,12,48,52,53} Alternatives to GnRH analogs include oral contraceptives, progestins, danazol, aromatase inhibitors, and most recently, GnRH antagonists. No difference in efficacy has been demonstrated between these medications.^{53,54} Factors such as drug cost, patient preference, and side effect profile should dictate which medication is selected. Discontinuation of hormonal suppressive therapy is associated with a high rate of recurrence.⁴⁷ Surgery should be considered in patients with refractory or recurrent disease.

Surgical Management: A Multidisciplinary Approach

As previously mentioned, thoracic endometriosis and pelvic endometriosis are often concomitant. When a patient presents with symptoms concerning for TES, a multidisciplinary surgical approach to treat both thoracic and pelvic disease in a single procedure provides the most effective outcome. This approach combines VL performed by a gynecologic surgeon and VATS performed by a thoracic surgeon who are familiar with endometriosis.

Treatment of Thoracic Lesions

VATS is the gold standard diagnosis and treatment for TES, most notably for catamenial pneumothorax.^{12,16,45,51,53} The VATS procedure allows for multiple treatment modalities depending upon the location and characteristics of identified lesions. In cases of superficial endometriotic implants, the surgeon can fulgurate lesions using bipolar diathermy, CO₂ laser, Nd-YAG laser, argon laser, or plasma energy, while deeper endometriotic implants should be excised using sharp dissection.^{45,51,55-57} In the case of infiltrative parenchymal endometriotic nodules or large lesions, the most appropriate operative course is parenchymal-sparing procedures such as wedge resection with a stapling device, subsegmentectomy, or in some cases, lobectomy.^{18,51,58,59}

An alternative intervention for TES is pleurodesis. This can be accomplished chemically with talc or tetracycline, or



Figure 4. Red lesions involving the left hemidiaphragm.

mechanically with pleural abrasion and partial pleurectomy.^{51,60,61} Use of pleurodesis was only demonstrated to allow a median recurrence-free interval of 61 mo in 28 patients. It was reported to decrease the recurrence rate of pneumothorax after VATS by 20%–25% compared with those who did not have pleurodesis performed at the time of surgery.^{51,62,63}

Treatment of Diaphragmatic Lesions

Video laparoscopic diagnosis and treatment of diaphragmatic endometriosis begins with an approach that will maximize visualization. Placement of a 10-mm port at the umbilicus and two or three additional ports in the left or right upper quadrant, depending on implant location, allows for inspection of the abdominopelvic cavity, posterior right hemidiaphragm, and the entire left hemidiaphragm.^{10,37,51} Optimal visualization of the diaphragm is obtained by positioning the patient in steep reverse Trendelenburg while gently pushing the liver caudally.^{10,37,51}

Endometriotic implants on the diaphragm are most commonly black, blue, or reddish-purple in appearance (**Figure 4**). However, there is significant variety in the morphological appearance of endometriotic lesions with clear vesicular lesions, fibrotic white lesions, and liver adhesions reported.^{10,37}

For endoscopic treatment of diaphragmatic endometriosis, hydrodissection followed by excision or CO₂ laser vaporization for superficial lesions has been recommended.^{10,37} Compared with electrocautery, the CO₂ laser is more precise with significantly less depth of penetration and less thermal spread. It can also reach areas, such as behind the liver, that are often difficult to access. Alternatives when a CO₂ laser is not available are plasma jet energy and ultrasonic energy. These are preferred to the use of cold scissors due to the potential for bleeding

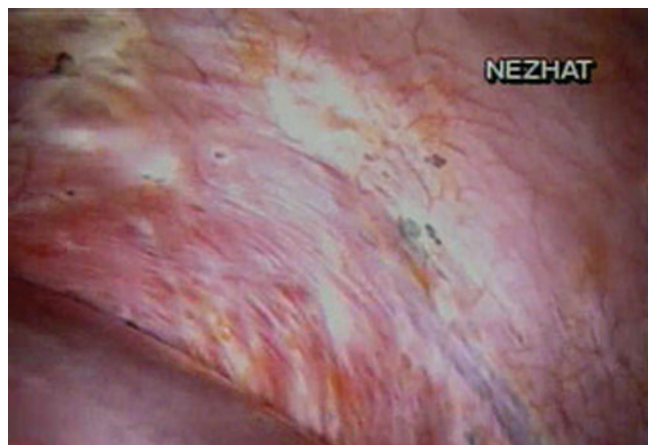


Figure 5. Endometriotic and fibrotic lesions involving the diaphragm.

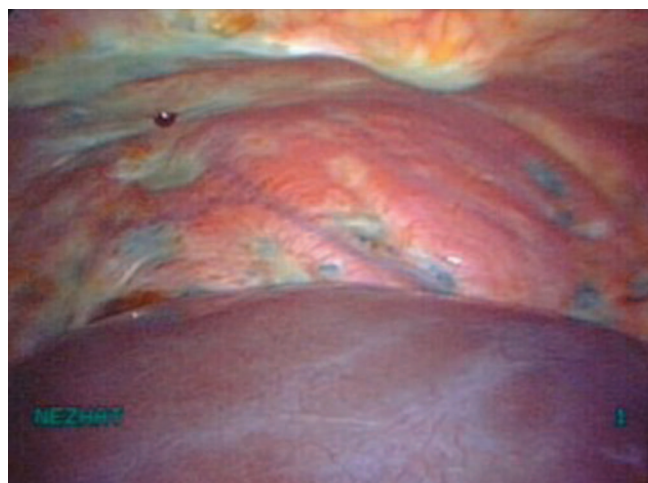


Figure 6. Diffuse endometriosis involving the diaphragm.

requiring bipolar hemostasis. The use of monopolar electrocautery on the diaphragm should be minimized because of its greater depth of tissue penetration, thus increasing the risks of necrosis or fenestration formation. Furthermore, monopolar energy can potentially induce heart arrhythmias or errant diaphragmatic muscular contractions.

For diaphragmatic lesions or perforations, resection using the endoscopic stapler device is the most appropriate approach if the resected surface will ultimately be relatively small.^{17,18,51} Though large perforations and excisions can be sutured, reports of recurrence are high. The use of synthetic mesh has been recommended to close larger diaphragmatic defects.^{64,65} In cases in which the lesions affect the full thickness of the diaphragm, the combined VL/VATS approach is useful

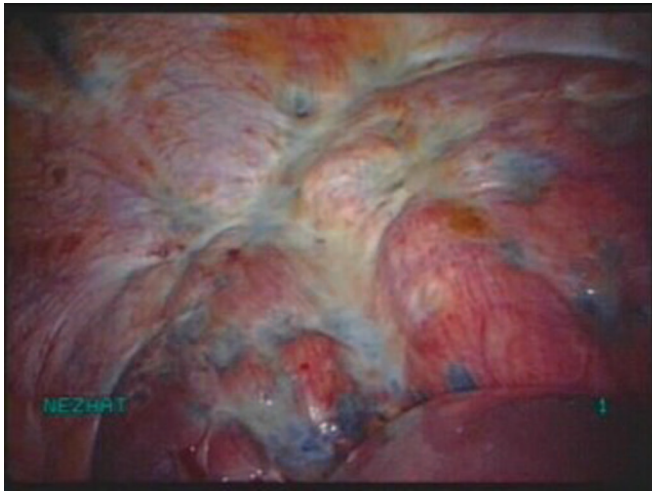


Figure 7. Advanced-stage diffuse endometriosis of the diaphragm.

in achieving complete resection of the diseased tissue. Depending on the size of the diaphragmatic defect, this can be repaired using either the endoscopic stapler or synthetic mesh.

Although a combined VATS with VL approach is based on principles that would provide a more comprehensive treatment to a disease that may involve both the pelvic and thoracic cavities, a combined VL/VATS procedure may not be necessary in all cases of suspected TES.^{37,51} If possible, VATS is only performed after medical management and subsequent VL failure. This is due to the longer recovery times and increased pain levels associated with VATS. An additional option to consider before VATS in older patients and who no longer desire preserved fertility is bilateral salpingo-oophorectomy with or without hysterectomy. However, this approach does not address dormant endometrial implants that may become active following exogenous estrogen administration.^{8,30,66}

CONCLUSION

The invention and introduction of videosurgery by Dr Camran Nezhat have revolutionized modern-day surgery, including diagnosis and management of endometriosis throughout the body.^{67–76} TES, although rare, can produce incapacitating clinical manifestations for some patients. As there is variability in its presentation, a high level of clinical suspicion is necessary to provide a timely diagnosis and reduce the likelihood of disease progression. As supported by theories of pathogenesis and epidemiologic observations, thoracic and abdominopelvic endometriosis are often concomitant. In cases of suspected pelvic endometriosis diagnosed and treated by VL, the diaphragm

should be thoroughly evaluated for evidence of endometriotic disease. In cases of symptomatic TES in which hormonal suppression has been exhausted or contraindicated, definitive surgical management is ideally performed using a multidisciplinary approach by experienced gynecologic and thoracic surgeons who are familiar with endometriosis. Postoperative hormonal suppression may further reduce recurrence of TES. **(Figures 5, 6 and 7).**

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