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Phrenic nerve paralysis after bipolar electrocoagulation of endometriosis of the diaphragm: case report and mini review

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Objective: To present a case of persistent postoperative elevation of the right hemidiaphragm after bipolar electrocoagulation of diaphragmatic endometriosis, highly likely because of collateral thermal damage to key branches of the phrenic nerve, and review the literature on diaphragmatic endometriosis, focusing on operative treatment.
Design: Case report and mini review.
Setting: Single university-based interdisciplinary endometriosis center.
Patient(s): A 33-year-old nulliparous patient, initially presenting with right-sided shoulder and back pain accompanied by severe dysmenorrhea and diarrhea. Written consent for the use of anonymized data and images for research purposes was obtained.
Intervention(s): Laparoscopic surgery with bipolar electrocoagulation of multiple superficial endometriotic lesions on the right hemidiaphragm and excision of bilateral deep infiltrating endometriosis on the sacrouterine ligaments.
Main Outcome Measure(s): Outcome and complication of surgical treatment of diaphragmatic endometriosis.
Result(s): Three weeks after surgical treatment, the patient complained of exertional dyspnea and pain in the right flank. Imaging showed a postoperative elevation of the right hemidiaphragm, which did not resolve over the following 6 months. We suspect collateral thermal damage to key branches of the phrenic nerve after bipolar electrocoagulation of extensive superficial diaphragmatic lesions.
Conclusion(s): During laparoscopic treatment of diaphragmatic endometriosis, bipolar electrocoagulation should be used sparingly and with caution to avoid potentially damaging the phrenic nerve. (Fertil Steril Rep® 2022;3:157–62. ©2022 by American Society for Reproductive Medicine.)
Key Words: Diaphragmatic endometriosis, surgical treatment, surgical complications, phrenic nerve injury

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INTRODUCTION

Endometriosis is an enigmatic disease defined by the presence of ectopic endometrial-like implants. It is marked by chronic inflammation resulting in pain and infertility. It is estimated that up to 12% of the patients with pelvic endometriosis also have extrapelvic manifestations, with the most common site being the thoracic cavity (1, 2).

Thoracic endometriosis syndrome is a rare disorder characterized by the presence of functional endometrial tissue within the chest cavity. Thoracic endometriosis syndrome refers to endometriotic lesions in the lungs, pleura, and/or diaphragm and comprises 4 clinical entities, including catamenial pneumothorax, catamenial hemothorax, catamenial hemoptysis, and pulmonary nodules (2). Most lesions are diaphragmatic, including diaphragmatic defects and endometrial implants (2, 3).

In a large cohort of patients treated at an expert referral center, endometriotic

lesions were present on the right leaf of the diaphragm in >90% of the cases, whereas isolated left and bilateral involvements were detected in 1% and 8% of cases, respectively (3). Diaphragmatic endometriosis is highly associated with pelvic endometriosis, especially advanced-stage disease and deep infiltrating endometriosis, with some studies reporting up to 90% of women having concomitant revised American Society for Reproductive Medicine stage IV disease in the pelvis and up to 63% of those having bowel or genitourinary tract infiltration (3).

Although several women with diaphragmatic endometriosis may be asymptomatic or experience only a mild obscure pain mostly in the right chest and shoulder area, diaphragmatic endometriosis can also present with severe, debilitating symptoms. Symptoms, especially at the time of menses, have been described as stabbing chest pain and right shoulder pain, sometimes extending to the ipsilateral arm and neck (2). Pain can be explained by the activation of sensitive afferents of the C3–C5 nerve roots by the diaphragmatic implants (2). Thoracic endometriosis syndrome may present with thoracic symptoms, such as hemoptysis and dyspnea, especially in the severe manifestations of acute pneumothorax or hemothorax (2, 4).

The diagnosis of diaphragmatic endometriosis is typically made on the basis of clinical suspicion: catamenial manifestations; concurrent known or suspected pelvic endometriosis; and improvement of thoracic symptoms with hormonal therapies. The preoperative diagnosis of diaphragmatic endometriosis is difficult because of the high number of asymptomatic cases, lack of disease awareness among clinicians, and low diagnostic sensitivity of imaging techniques.

Early diagnosis of diaphragmatic endometriosis is challenging because lesions are often smaller than 1 cm and superficial. Ultrasound is generally not useful for the identification of diaphragmatic lesions, especially if they are superficial. If the patient presents with acute and severe symptoms, chest radiography and/or computed tomography should be performed to rule out pneumothorax or hemothorax (3).

Magnetic resonance imaging (MRI) is the preferred imaging modality and has been reported to have a sensitivity of 78%–83% for deep infiltrating lesions. The MRI findings of diaphragmatic lesions can vary from punctate spots and plaques to deep nodules, best depicted on fat-suppressed T1-weighted sequences (5). Nonetheless, MRI is limited for diagnosis, especially with small, superficial diaphragmatic lesions. Thus, in patients highly suspected of diaphragmatic endometriosis, clinicians should consider proceeding with surgical evaluation and treatment with laparoscopy, even when the imaging is negative, or alternatively recommending empirical medical therapy.

The treatment approach for suspected diaphragmatic endometriosis depends on multiple factors, such as severity of symptoms, degree of suspicion for diaphragmatic endometriosis, suspected extension and localization of lesions, age, and plans for future fertility (2, 6). On the basis of these factors, a detailed discussion of the benefits and risks of the options with the patient allows for informed shared decision-making.

Expectant management may be an option for women with few symptoms or symptoms that respond to pain management who do not want to take medical hormonal treatments or hormonal suppressive treatments or undergo surgery. This may be an acceptable option for a short term, for example, while attempting pregnancy.

Medical treatment is often undertaken as the first-line therapy, especially in women who do not have another indication for surgery. Gonadotropin-releasing hormone (GnRH) agonists are used to suppress ovarian steroid hormone production to prevent the growth and activity of ectopic endometrial tissue (2). Gonadotropin-releasing hormone agonists have been reported to improve the symptoms of thoracic endometriosis and prevent recurrence of spontaneous pneumothorax (4, 7). The therapeutic benefits of GnRH agonists cease with discontinuation, and they are often associated with undesirable menopausal-like side effects. Combining a GnRH agonist with an add-back therapy improves compliance by limiting the side effects and negative effects on the bone (8).

The symptoms of pelvic endometriosis can be treated medically with hormones, including oral combined contraceptive pills, especially in continuous-cycle regimens, parenteral or transdermal combined hormones, or progestin-only pills or implants. To our knowledge, no studies have systematically evaluated the efficacy of these therapies specifically for diaphragmatic lesions (9). Likewise, the role of newer treatments, such as aromatase inhibitors and GnRH antagonists, has yet not been assessed in diaphragmatic endometriosis (10).

Medical treatment requires patient compliance to long-term treatment, and discontinuation of hormonal therapy is associated with the risk of symptom recurrence.

Surgery is indicated in symptomatic patients when medical treatment is ineffective, not tolerated, or not possible (2). The aim of surgery is to achieve symptom relief through complete disease ablation or resection and minimize the risk of progression. Asymptomatic patients who are incidentally found to have superficial endometriotic implants during laparoscopy are commonly surgically treated to prevent the future development of symptoms and minimize the risk of progression to deep endometriotic nodules, which may later require more aggressive diaphragmatic surgery (11). In those cases where imaging techniques show a high probability of diaphragmatic endometriosis but the patient is asymptomatic, the pros and cons of medical vs. surgical vs. expectant management need to be discussed with the patient (5).

Minimally invasive abdominal laparoscopy is the standard approach to treating diaphragmatic lesions located on the abdominal side of the diaphragm, the most common localization. This procedure permits both a diagnostic evaluation and therapeutic treatment, depending on the location and characteristics of endometriotic lesions. A nontraumatic compression of the right lobe of the liver dorsally may be necessary to fully assess the degree of diaphragmatic involvement. This is particularly indicated when "sentinel lesions" are visualized and the surgeon suspects additional lesions behind the liver (12, 13). In some cases, especially when severe pain is the indication for surgery, gaining access to the lesions

requires first dividing the falciform ligament. Failure to do so may underestimate the degree of nodules, leading to persistence of symptoms and progression of disease.

In a recent review of a large series of over 200 patients treated surgically, Ceccaroni et al. (3) discuss how the surgical technique should be adapted to the degree of lesion infiltration. They used an argon beam coagulator (ABC), or alternatively diathermocoagulation, to vaporize small superficial diaphragmatic lesions, also known as "foci." Solid lesions that infiltrate partially or fully into the muscle layers of the diaphragm, termed "nodules," were treated with peritoneal stripping using bipolar scissors, with small residual lesions and hemostasis achieved with ABC or diathermocoagulation. When possible, nodules were resected in toto while preserving the integrity of the diaphragm. In cases of deep lesions, full thickness removal led to diaphragmatic defects that were repaired laparoscopically with sutures. In these more severe cases, pneumothorax was inevitable, and intraoperative re-expansion of the lung was coordinated with the anesthesiologist. Other investigators describe the placement of a chest tube at the completion of surgery (12). In patients with suspected thoracic lesions, concomitant video-assisted thoracoscopic surgery is planned, as was likewise performed in the large series.

Ceccaroni et al. (3) state that none of the patients developed intraoperative complications, whereas the postoperative complications were all related to the colorectal and ureteral parts of the surgeries. None of the postoperative complications stemmed from the diaphragmatic surgery (3).

After surgical treatment, hormonal suppressive therapy is routinely administered to reduce the risk of diaphragmatic recurrence, similar to the use of medical therapies for prevention of pelvic disease recurrence. In fact, the combination of surgery and postoperative medical treatment is considered the standard of care for thoracic endometriosis syndrome (2, 14, 15). Historically, GnRH agonists have been used postoperatively, especially for the prevention of endometriosis-related pneumothorax. Alternative options include the use of dienogest, the progestin hormone with antiproliferative and anti-inflammatory effects (16), or other progestins. Oral contraceptives in continuous administration prevent withdrawal bleeding; however, their use for recurrence prevention for diaphragmatic endometriosis has not been systematically evaluated.

CASE REPORT
History

A 33-year-old nulliparous woman was referred to our center with suspected endometriosis. At the first consultation, written consent for the use of her anonymized data and images for research purposes was obtained. The patient had initially experienced severe dysmenorrhea, for which her gynecologist prescribed the vaginal contraceptive ring (ethinylestradiol/etonogestrel) in continuous cycle. Under this therapy, she had remained symptom-free for the subsequent 3 years. However, she experienced a recurrence of symptoms after discontinuing the ring because of persistent migraine headaches, beginning 12 months before her first presentation at our

Image taken during laparoscopy showing some of the endometriotic nodules in the recessus subphrenicus dexter.

Zippl. Zippl. Diaphragm paralysis after endometriosis. Fertil Steril Rep 2022.

clinic. In the past year and at presentation, the patient reported dysmenorrhea with a current verbal numerical rating scale score of 5, accompanied by diarrhea. Moreover, the patient reported right-sided shoulder and back pain starting 5–6 days before the onset of menstruation and lasting throughout menstruation. She denied dyspnea or hemoptysis and had no other symptoms, such as dysuria, dyschezia, or dyspareunia.

Gynecological examination, including vaginal speculum examination and bimanual palpation and transvaginal ultrasound, showed no signs of pelvic endometriosis. To exclude occult endometriosis or another etiology, MRI of the pelvis was performed with a 1.5T scanner (Avanto^{fit}; Siemens Healthineers, Erlangen, Germany) using the recommended protocol for endometriosis (17), likewise without signs of endometriosis or adenomyosis.

Treatment

Because of the patient's symptoms but lack of pathology on imaging, we scheduled a laparoscopy for suspected superficial peritoneal pelvic endometriosis with potential diaphragmatic involvement. Laparoscopy confirmed the diagnosis of pelvic endometriosis, revealing superficial peritoneal endometriosis in the right ovarian fossa and on the bladder peritoneum and endometriosis involving the left sacrouterine ligament and right pararectal space. No adhesions were noted. Exploring the upper abdomen, multiple additional endometriotic lesions were discovered on the right diaphragmatic dome, particularly involving the central tendon. Gently pushing aside the liver, 10 endometriotic nodules covering a surface of approximately 15 cm^2 could be visualized in the recessus subphrenicus dexter (Fig. 1). Considering the sum of all lesions, the endometriosis was classified as revised American Society for Reproductive Medicine stage II (7 points), ENZIAN B2 FO (Diaphragm) (18, 19).

The superficial peritoneal lesions in the pelvis were treated with bipolar electrocoagulation, whereas the

FIGURE 2
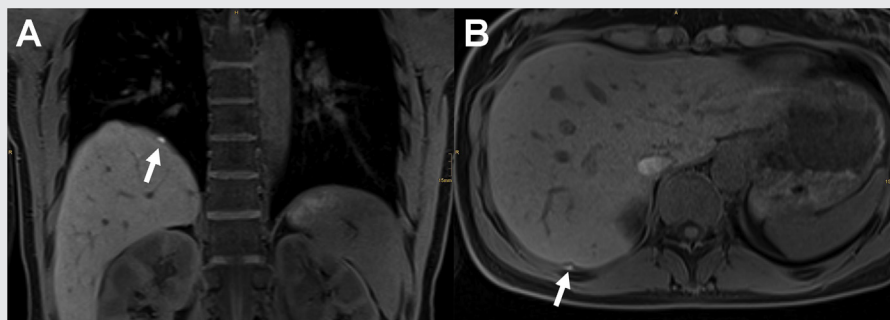
Magnetic resonance images show a T1-weighted sequence with fat-saturation (volumetric interpolated breath-hold examination) in (**A**) coronal and (**B**) axial orientations. Two diaphragmatic lesions with typical T1 hyperintense signal (arrow in images **A** and **B**) with a diameter of 5 mm can be depicted, highly suspicious of a manifestation of endometriosis.

Zippl. Zippl. Diaphragm paralysis after endometriosis. Fertil Steril Rep 2022.

infiltrating nodules in the ligaments were excised in toto after identification of the ureter. Thereafter, a visceral surgeon was called in for the management of the extensive diaphragmatic endometriosis. As the lesions extended over a large area and were located in the poorly accessible recessus subphrenicus dexter, excision of all lesions would have led to a large defect in the diaphragm with subsequent difficulty of reapproximation. The single lesions appeared superficial and flush with the diaphragmatic surface and had a diameter of <1 cm, thus defined as superficial "foci" according to the classification published by Ceccaroni et al. (3). Moreover, they had not been visualized on the preoperative MRI, making a deep infiltration of the diaphragm improbable. It was, therefore, decided to perform bipolar electrocoagulation with successful treatment of all visible lesions and no intraoperative complications. The diaphragm remained intact without perforation.

Postoperative Course

The immediate postoperative period passed without complications, and the patient was discharged on the second postoperative day. A medical prophylaxis with dienogest 2 mg daily was started to prevent recurrence of disease. Three weeks after discharge, the patient presented to the emergency department complaining of stabbing pain in the right flank accompanied by exertional dyspnea. Auscultation revealed decreased breath sounds in the right lung. Pulmonary embolism was initially suspected. Laboratory workup showed normal blood count and levels of C-reactive protein as well as liver and kidney function tests but revealed a substantially elevated D-dimer level (2,877 mcg/L [reference range, 0–500 mcg/L]). Computed tomography angiography was performed but showed no evidence of clot. Pulmonary embolism, pneumothorax, and abscess formation could be excluded, but a unilateral elevation of the right diaphragm was detected. Subsequent chest radiography under inspiration showed paradoxical diaphragm movement, suspicious for unilateral paresis of the phrenic nerve. The patient was diagnosed with suspected transient paresis of the phrenic nerve as an iatrogenic complication of the coagulation of diaphragmatic lesions. The patient's pain responded well to analgesics. Further treatment with vitamin B complex (thiamine chloride hydrochloride and pyridoxine hydrochloride) as a nerve modulator was initiated, and expectant management with a follow-up visit was scheduled.

Three months later, the patient reported partial improvement of dyspnea. She had discontinued dienogest because of aggravation of migraines; since then, she had regular menstrual cycles without dysmenorrhea but again accompanied by pain at the right diaphragm during and after the days of menstruation. Repeat MRI focusing on the upper abdomen confirmed the already known elevation of the right diaphragm, which was unchanged compared with the former examinations. Moreover, 2 small nodules with a diameter of 3 mm and hyperintensity in T1-weighted images were detected on the right diaphragm, adjacent to liver segments VI and VII, compatible with endometriotic lesions (Fig. 2). These lesions could represent newly formed lesions or the growth of previously incompletely treated lesions.

Six months after surgery, clinical symptoms remained similar, with persistent cyclic pain in the right chest and mild dyspnea with exertion but not impairing activities of daily living or athletic endeavors. Follow-up chest radiography showed a persistent slight elevation of the right diaphragm, although it improved compared with that from the previous examination (Fig. 3).

For the treatment of continued symptoms at the time of menstruation and as a conservative nonsurgical treatment of the residual or recurrent endometriotic lesions, we recommended a 6-month course of the GnRH agonist with add-back therapy with low-dose transdermal estrogen. Subsequent long-term medical prophylaxis to prevent recurrence of pelvic endometriosis was also recommended.

The patient presented for a second opinion at a neighboring institution and underwent a diagnostic laparoscopy to assess the diaphragm because of persistent symptoms. The lesions were not easily accessible for resection, although the surgeon confirmed that the diaphragm was intact without fenestrations.

FIGURE 3
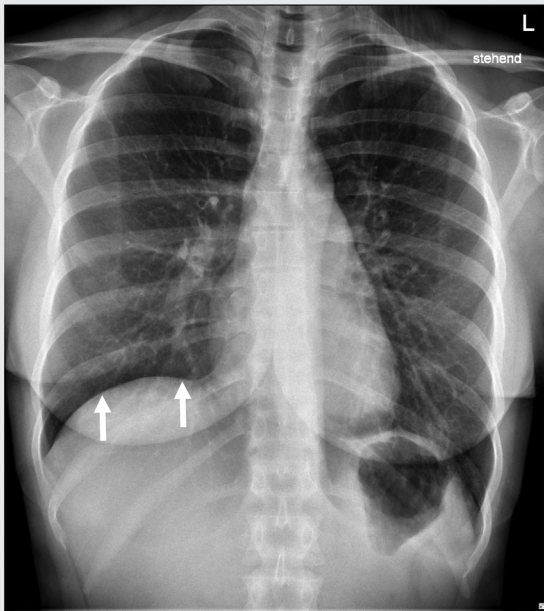
Chest radiography in the posterior to anterior position under inspiration. The elevation of the right diaphragm is shown (arrows).

Zippl. Zippl. Diaphragm paralysis after endometriosis. Fertil Steril Rep 2022.

DISCUSSION

We describe the presentation, evaluation, and surgical treatment of a case of diaphragmatic endometriosis that resulted in a persistent postoperative elevation of the right hemidiaphragm. We postulated that the liberal use of bipolar electrocoagulation to treat the multiple superficial lesions caused collateral thermal damage to key branches of the phrenic nerve. To our knowledge, this is the first report of functional diaphragm injury stemming from electrocoagulation. One previously published case reported fenestrations in the diaphragm after previous thermocoagulation, resulting from focal tissue necrosis. In the case of our patient, a second-look laparoscopy performed at another institution did not note structural damage to the diaphragm.

Traumatic injury of the phrenic nerve resulting in diaphragmatic paralysis is a known complication of open-heart surgery, lung transplantation, and other mediastinal procedures (20). One study described right hemidiaphragm paralysis after cardiac radiofrequency ablation (21); however, no reports of diaphragmatic paralysis after extensive surgery of diaphragmatic endometriosis have been published.

Awareness of the anatomy and innervation of the diaphragm is important to prevent iatrogenic complications. The diaphragm is divided into 2 parts—right and left—and contains an aponeurotic thick portion area called central tendon. The diaphragm is innervated by the right and left phrenic nerves, which originate from cervical nerves C3–C5 and are responsible for both sensory and motor functions. The paired phrenic nerves are located posteriorly in the lateral compartment of the neck and travel anteriorly as they course through the thorax. They continue their course along the anterior surface of the pericardium before they reach the diaphragm, where they arborize on the superior and inferior surfaces (22). Intuitively, extensive coagulation at the location of the main branches of the phrenic nerve should be avoided because of an elevated risk of nerve injury. In the case of our patient, the coagulation was not focused along the known course of the main branch of the nerve; nonetheless, she developed this complication.

Other complications of bipolar electrocoagulation have been described in previous studies, including intraoperative arrhythmia in the case of implants located directly below the heart and development of diaphragmatic fenestrations because of tissue necrosis. Carbon dioxide laser and ABC have been proposed as alternative treatments for superficial diaphragmatic lesions. Because carbon dioxide laser has a smaller depth of penetration and smaller thermal spread than bipolar electrocoagulation, this approach may reduce the risk of local ischemia and tissue necrosis (23).

Phrenic Nerve Recovery After Injury

The recovery time of phrenic nerve function depends on the type of injury occurred. Injuries that involve a focal demyelination of the phrenic nerve may show full recovery in a few weeks through nerve remyelination. When axonal damage occurs, regrowth and recovery may take several months. Spontaneous improvement and resolution of unilateral diaphragmatic paralysis should be evaluated in follow-up visits, avoiding surgical interventions as long as clinical symptoms are mild or acceptable to the patient (24). It is generally accepted that a 1-year waiting period after the insult is necessary before performing invasive procedures and these are also only in symptomatic patients. Phrenic nerve stimulation may restore diaphragmatic motion. In cases of irreversible phrenic nerve injury, plication of the hemidiaphragm may be used to increase the intrathoracic volume (25).

In conclusion, diaphragmatic endometriosis is an uncommon but likely underdiagnosed manifestation of endometriosis, observed almost exclusively with concomitant pelvic endometriosis. Surgical treatment should be tailored to the size, number, and extent of lesions. Bipolar electrocoagulation should be used sparingly and with caution to avoid potentially damaging the phrenic nerve, as described in this case report.

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