

CASE REPORT

Thoracic endometriosis with a long delay in diagnosis

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Abstract

This paper describes a case of thoracic endometriosis in 36-year-old woman with a long delay in diagnosis. At the admission in the hospital, the patient had a medical history of persistent dysmenorrhea since the age of 13, infertility and an episode of total right pneumothorax two months ago successfully resolved by minimum pleurotomy of the right hemithorax. She came with moderate pain on right hemithorax and dyspnea, which occurred on the first day of menstruation but she did not have any other respiratory symptoms such as hemoptysis, cough. Radiological imaging (chest radiography and computer tomography) at the time of admission confirmed recurrence of the right pneumothorax. She underwent surgical treatment of the right pneumothorax using a single-port video-assisted approach. Intraoperative macroscopic lesions were found catamenial pneumothorax characteristic diagnosis and biopsy material taken (parietal pleura) for histopathology. Immunohistochemical tests confirmed the diagnosis of thoracic endometriosis. The gonadotropin-releasing hormone analogue was received by the patient early after surgery and there was no clinical or radiological recurrence at a four months follow-up.

Keywords: catamenial, pneumothorax, thoracic endometriosis.

■ Introduction

Catamenial pneumothorax (CP) is a recurrent pneumothorax during menses.

Incidence of CP was about 3–6% of spontaneous pneumothorax [1, 2], most of them involve the right side and sometimes we can find diaphragmatic perforations [3]. According to the literature there are two forms of thoracic endometriosis; the pleural and the pulmonary and the pleural form could be: catamenial pneumothorax, catamenial hemothorax, catamenial pneumomediastinum [4].

Video-assisted thoracoscopic surgery (VATS) for catamenial pneumothorax is preferred as surgical treatment [5, 6] follow by hormonal treatment for suppression of thoracic endometrial activity [7, 8].

Aim

The aim of this case report is to present thoracic endometriosis in a young female patient, having a long delay in diagnosis due to the initial lack of symptoms and non-specific onset.

■ Case report

A 36-year-old woman was referred in September 2013, to our surgery department with moderate pain on the right hemithorax and dyspnea on exertional effort occurred in the first day of mense. She did not have any other respiratory symptoms such as hemoptysis, cough. She had a right pneumothorax two months ago and it was successfully treated by a chest tube for a week, the

patient being hospitalized for the duration in another hospital. Her medical history was also revealing, as she reported having suffered from dysmenorrhea since 1990. She performed multiple blood and hormones tests during this period with no results. In the attempt to remain pregnant she underwent four artificial inseminations and two *in vitro* fertilizations (first one in September 2012, last one in March 2013 – both short protocol with no results – the official motivation being her low anti-Müllerian hormone – 0.5 pmol/L therefore poor ovarian reserve).

We performed a chest radiography (Figure 1) showed right-sided pneumothorax with partial collapse of pulmonary parenchyma and minimum basal right pleurisy. For completion of imagistic examination, we conducted a thoracic CT scan, which confirmed recurrence of pneumothorax (Figures 2 and 3).

Given the occurrence of symptoms in the first day of menstruation, it was suspected pneumothorax with catamenial character.

In the third day of menstruation, she underwent monoport VATS. During surgery, we found macroscopic lesion specific for catamenial pneumothorax. After penetrating into the pleural cavity, we found several aspects. At the level of the parietal pleura, we could observe few millimeters wide rare scattered lesions, both whitish and brownish. White spots may have represented areas of endometriosis implant, "cured" with the generation of fibrous tissue. Brownish small nodules represented small endometriosis implants. At the level of the visceral pleura, we found some small brownish nodules, the same type as we found on the parietal pleura. At the level of the right

diaphragm, we found a multitude of millimeter-wide holes and red spots, diffusely located, especially at the central tendon, diaphragmatic thinning and transparent areas. These areas were likely provoked by the implants of endometriosis lesions that underwent apoptosis without perforation of the diaphragm to generate more other lesions.

We did not find any emphysema bubbles or blebs



Figure 1 – Posteroanterior chest radiogram: large, right-sided pneumothorax without mediastinal shift. Basal air-fluid level.

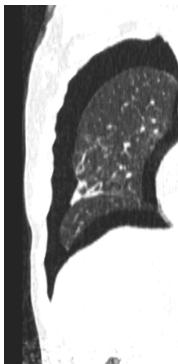


Figure 2 – Transverse plane of thoracic contrast (supine) CT: large right-sided pneumothorax.

when carefully observing the pulmonary parenchyma. Also, the diaphragm was covered with "blueberry spots" diaphragmatic fenestrations. We did not notice any loss of air from the lung parenchyma when using the sterile liquid method.

Findings characteristic of catamenial or endometriosis-related pneumothorax can be observed in intraoperative photographs (Figures 4–8).



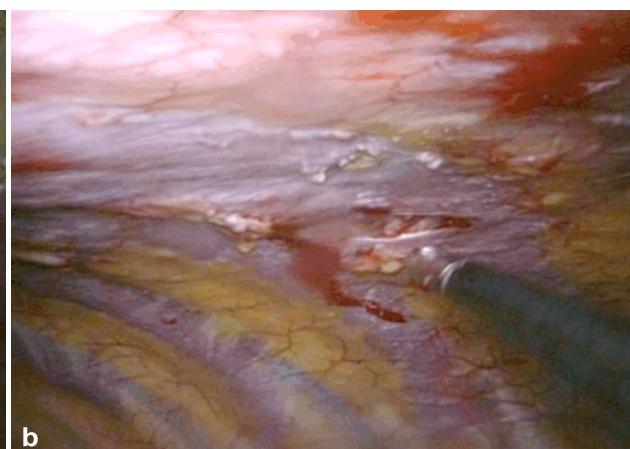
Figure 3 – Anterolateral and right basal hydropneumothorax, with a maximum thickness of 2.8 cm displacement of the lung secondary to medial and small areas of collapsing lung parenchyma, predominantly of the medial lobe. Small postero-medial secluded pneumothorax (projection of the T5 vertebral body). Little subpleural bubble emphysema in the superior right lobe (dorsal segment), measuring 9 mm.



Figure 4 – (a and b) Right superior lobe – apex without blebs.



Figure 5 – (a) White lesions, possibly fibrosis post-endometrial lesion. **(b)** Biopsy taken from white pleural lesions.



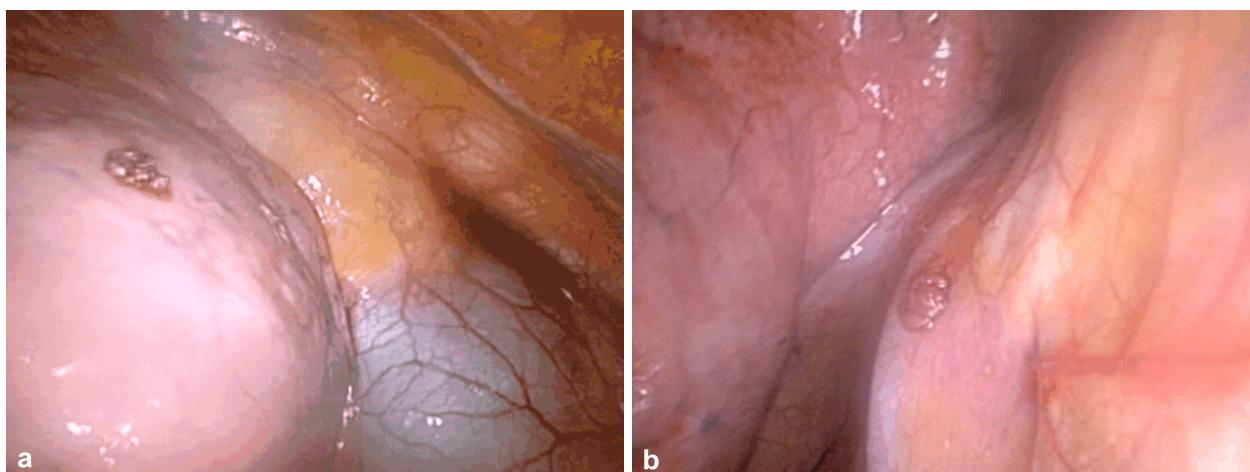


Figure 6 – (a) Endometriosis lesion of the visceral (a) and the parietal (b) pleura.

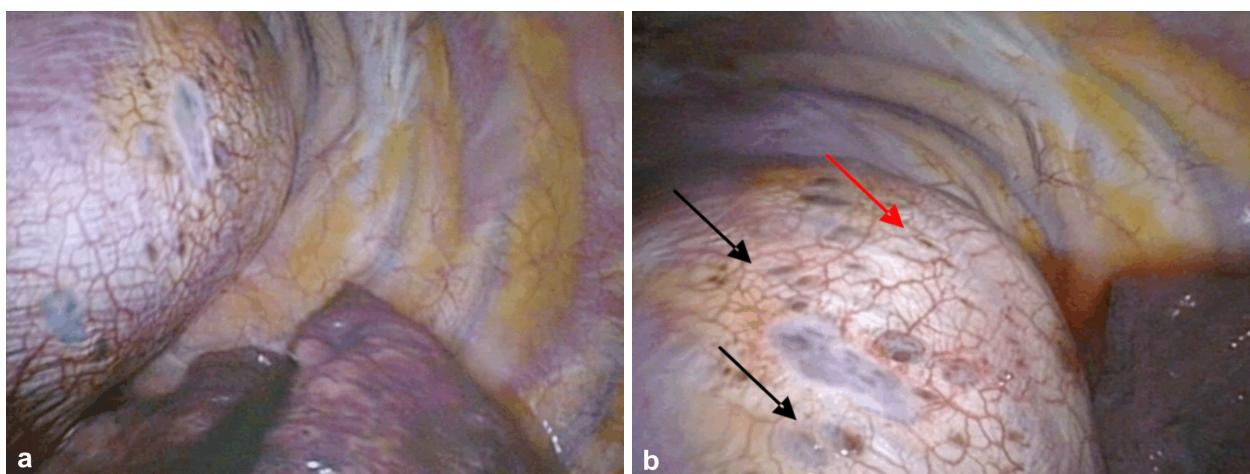


Figure 7 – (a) Small diaphragmatic pores ("air bubbles"). (b) Multiple diaphragmatic red spots (red arrows) and holes (black arrows) at the periphery of the right leaflet of the central tendon, most of them less than 1 cm in their maximal dimension.

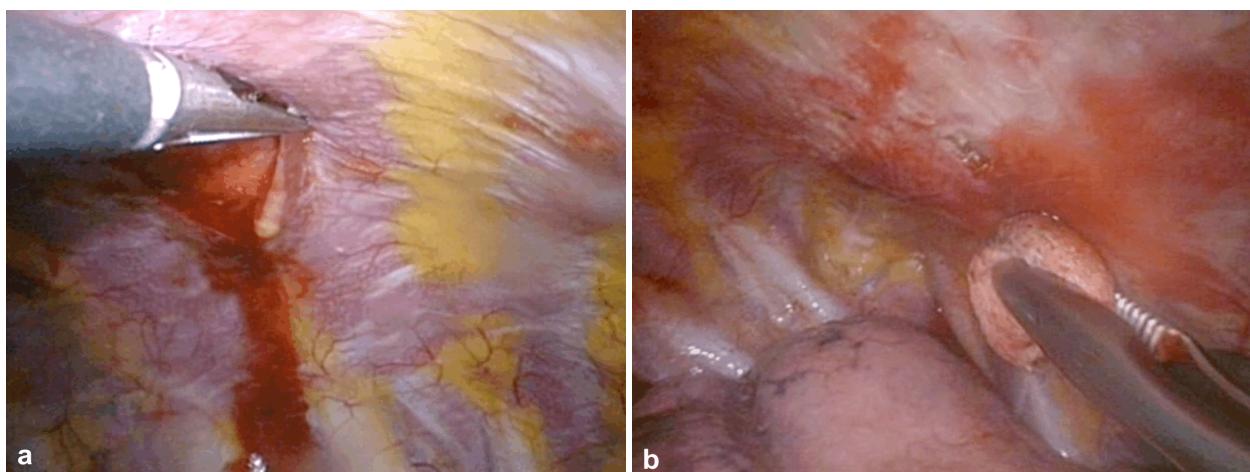


Figure 8 – (a) Pleurectomy. (b) Pleural ponage.

Pleural lesions were almost exclusively right-sided, whereas lung lesions had no such predilection. Following these conditions, we performed partial apical pleurectomy and thorough mechanical and electrical basal pleural ponsage.

During surgery, we sampled the parietal pleura, which were sent for histopathology. At the end of surgery, the pleural cavity was drained with a single drainage tube connected to the patient Beclaire device and evolution

was favorable, no operative or postoperative morbidity and the drain was suppressed on the second day post-operatively, the patient was discharged the third day post-surgical intervention.

For the histological study, we fixated the fragments of biological material collected at surgery in 10% formalin solution and embedded them in paraffin using the standard histological protocol. Afterwards, we performed serial sections in the rotary microtome with a thickness of 5 µm,

which were plated on histological slides, degreased and cleaned in advance. For the histopathological study, we used two classical stains: Hematoxylin–Eosin and light green staining technique after Goldner–Szekely.

For the immunohistochemical study, we used special blades coated with poly-L-Lysine to increase the biological material adherence to the blade and to minimize immunohistochemical staining artifacts. Afterwards, the slides were transferred to the controller at 37°C for 24 hours for drying and increase adhesion to the blade of histological sections. The immunohistochemical staining was carried out after the following times: dewaxing in xylene (three baths, each of 15 minutes), hydrating in distilled water for 5 minutes, exposure of the antigen by boiling in a solution of sodium citrate pH 6 for 21 minutes in a microwave oven, washing in distilled water for 15 minutes. Endogenous peroxidase blocking was done by incubating the slides in 3% hydrogen peroxide for 30 minutes at room temperature, followed by washing in distilled water for 10 minutes and a wash in phosphate-buffered saline (PBS) 1% solution for another 5 minutes. The sections were then incubated with primary antibodies for 18 hours in a refrigerator at 4°C, and the day of the biotinylated secondary antibody was applied for 30 minutes at room temperature. Thereafter washing was performed in 1% PBS (three baths of 5 minutes), followed by Streptavidin-HRP was applied for 30 minutes at room temperature, followed by washing the slides in PBS for 15 minutes. The signal was detected using 3,3'-Diaminobenzidine (DAB) (Dako) and the reaction was stopped when the signal has been optimized by washing in 1% PBS. Contrasting the sections was performed with Hematoxylin, 2 minutes, followed by dehydration in ethanol, clarifying in xylene and mounting the blades using DPX medium (Fluka).

For positive and differential diagnosis, we used the following antibodies: anti-CK7 (clone OV-TL12/30, sodium citrate, pH 6, 1/50 dilution, Dako), anti-PR (clone PgR636, EDTA, pH 9, 1/50 dilution, Dako), and anti-ER (clone 1D5, EDTA, pH 9, 1/50 dilution, Dako).

The microscopic study revealed the presence of endometrial islands of various sizes, separated by fibrous bands

rich in collagen fibers. Islands consisted of endometrial glands disposed totally heterogeneous, with wide lumen, irregular, bounded by a cylindrical epithelium and pseudostratified epithelium sometimes cylindrical and endometrial stroma-looking cytogenic chorion. Endometrial stroma had a very heterogeneous structure with a cellular fibrillar and vascular component extremely varied from one endometrial island to another. Within the stroma we identified numerous fibroblast type cells and some with a decidual aspect, numerous lymphocytes diffuse or disseminated trend nodular lymphocyte type, macrophages and granulocytes (Figure 9, a and b). The fibrillar structure was dominated by thin collagen fibers and blood vessels were represented in particular by capillaries.

To differentiate endometrial glandular cells of other structures, we used three immunohistochemical markers. Glandular epithelial cells showed intense positivity for CK7 (Figure 10). Moreover, these cells were strongly positive for the progesterone (Figure 11) and the estrogen (Figure 12).

Postoperative patient performed only magnetic resonance imaging (MRI) to identify possible abdominal-pelvic endometriosis lesions.

After surgery, she was referred to the gynecologist and she received GnRH Therapy (Diphereline) for four months, tried to become vegetarian with alkaline diet (lost 5 kg). Now she is still under menopause effects.

Because MRI is considered superior to CT in diagnosis of endometriosis is due to the presence of blood products in the endometrial deposits, we performed it postoperator.

There was no clinical or radiological recurrence of the pneumothorax at a follow-up of four months.

Discussion

We found in this case the presence of ectopic endometrial stroma in the pleura. Our patient did not have hemoptysis, which is a possible symptom of thoracic endometriosis. She had only chest pain and dyspnea regarding a spontaneous right-sided pneumothorax. The right lung was partial collapsed.

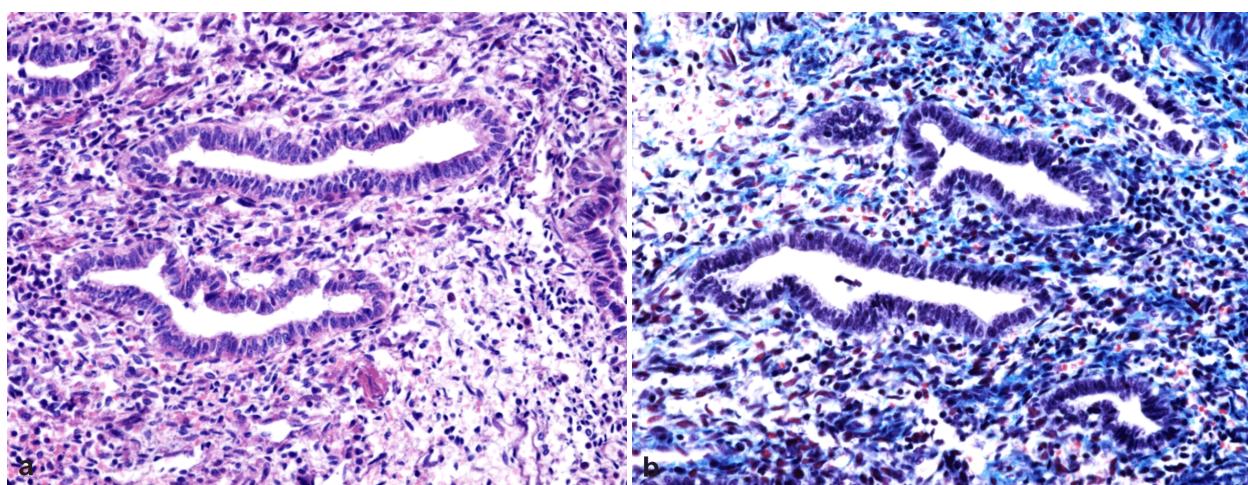


Figure 9 – Microscopic appearance of endometriosis islets, which notes the presence of endometrial glands with large and irregular lumen surrounded by a stroma rich in fibroblastic type cells, lymphocytes and macrophages. Hematoxylin–Eosin (a) and Trichromic (b) staining, ×100.

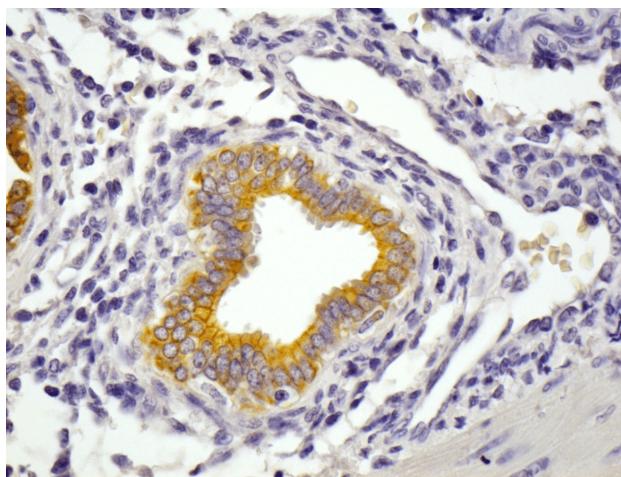


Figure 10 – Intensely positive endometrial gland of anti-cytokeratin 7 antibody. Immunostaining with anti-CK7, $\times 200$.

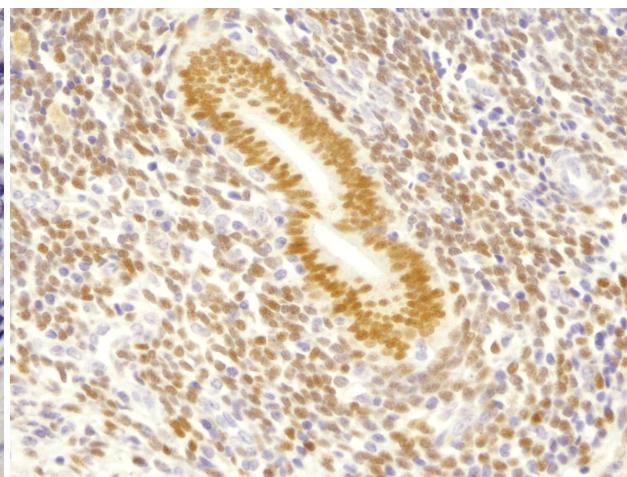


Figure 11 – Endometrial gland with intense reaction to progesterone. Some stromal cells show the same diffuse reaction to the same antibody. Immunostaining with anti-PR, $\times 200$.

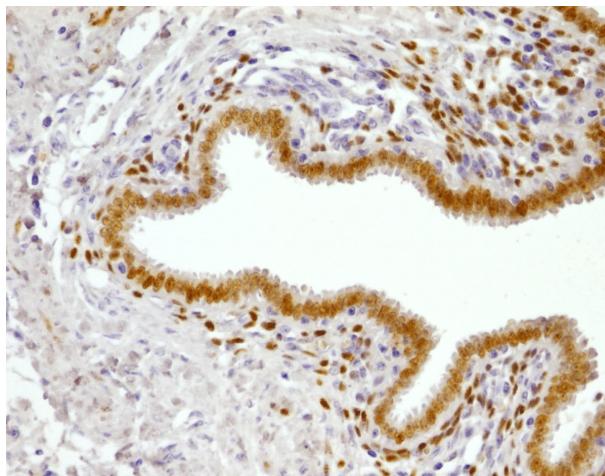


Figure 12 – Endometrial gland epithelium with intense reaction to estrogen. Immunostaining with anti-ES, $\times 200$.

According to other reported cases in the literature [9], the presence of the catamenial pneumothorax had higher frequency in the right lung [10], lower in the left lung and rare bilateral. In our case, there was no evidence of pelvic endometriosis on MRI exam and even though the patient has attempted to remain pregnant with dysmenorrhea since 1990 there was a delay in diagnosis until the second spontaneous pneumothorax appeared in September 2013. She underwent surgery and hormonal treatment.

The etiology and pathogenesis of this disease include possible genetic factors [11]. During the time, many authors have tried to explain the pathogenesis of this disease such as the metastatic theory [12], hormonal theory [13], anatomic theory [14] or deposited of endometrial tissue in the chest cavity during the embryonic development [15].

She underwent mono-port VATS, which we found to be safe for the patient according to the literature [16]. We found many diaphragmatic lesions, which were more than parietal pleural nodules. In the literature, diaphragmatic defects [17] such as: pores, holes, fenestrations, perforations were various as numbers or sizes. The possible cause for this right sided predilection could be explained from the fact that the lymphatic drainage does

not take place evenly over the entire diaphragmatic surface, but it is more extensive on the right side [18].

According to the literature [19], MRI could have revealed a secluded rear right pleural effusion with pleural thickening adjacent discrete, hepatic nodules imaging compatible with hemangiomas, intramural, nodules and subserous uterine fibroid compatible image, ovarian cysts, the largest in the left ovary having serous content. In our case, the MRI exam did not find any abdominal or pelvic endometriosis lesions.

Our patient did not undergo bronchoscopic exam; however, we found in published literature [20] that cytological examination of bronchial washing is useful in confirming the diagnosis of parenchymal pulmonary endometriosis, even if it has not been frequently used in the diagnosis process.

In this case, the management of recurrence pneumothorax was both hormonal and surgical treatment. In the literature [21, 22], we found thoracotomy with pleural abrasion, coverage of the diaphragmatic surface with polyglactin mesh for recurrence pneumothorax. Surgery intervention is recommended to be performed during menstruation [23], in order to have a good visualization of pleurodiaphragmatic endometriosis lesions.

The multidisciplinary team: gynecologist, thoracic surgeon, pulmonologist decided to delay an exploratory laparoscopy until appears natural pleurodesis consolidation initiated intraoperatively. From a technical standpoint, laparoscopy requires instilling an inert gas (carbon dioxide) into the peritoneal cavity.

Given the presence of diaphragmatic defects, it should be a high risk for transdiaphragmatic gas migration in the pleural cavity with lung collapse, compromising pleurodesis, risk of intraoperative hypertensive pneumothorax, hemotorax risk by lysis of adhesions well vascularized already realized the impossibility of maintaining a sufficient abdominal work room (the continuous migration of gas in the pleural cavity) for a satisfactory examination abdominopelvic organs.

Pelvic ultrasound is a very important tool for the diagnosis of pelvic endometriosis, especially when considering the high association with thoracic endometriosis [24]. We did not find ovarian endometriosis in our patient.

Our patient experienced the pneumothorax at 36-year-old, the same as average (median) age found by Rousset-Jablonski *et al.* but different from women with idiopathic pneumothorax [25].

Postoperative, the patient did not have a recurrence of pneumothorax; however, Muramatsu *et al.* found that catamenial pneumothorax represents 30% of postoperative recurrences cases [26].

Conclusions

In the presentation of this case report, spontaneous pneumothorax in a female patient with long-standing infertility, multiple attempts at artificial insemination without no results confirmed medical history of endometriosis which was the first manifestation of thoracic endometriosis. Recurrence of pneumothorax and appearance of pneumothorax during menses raised clinical suspicion of a catamenial pneumothorax. To correct diagnosis and treatment of the patient was successfully requires a multidisciplinary team consisting of pulmonologist, thoracic surgeon, pathologist, gynecologist, radiologist.

Conflict of interests

The authors declare that they have no conflict of interests.

Author contribution

All the authors contributed equally to preparing this paper and share first authorship.

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