

CATAMENIAL HAEMORRHAGIC PLEURAL EFFUSION CAUSED BY THORACIC ENDOMETRIOSIS, WHICH WAS CONTROLLED BY SURGERY UNDERTAKEN AFTER FAILED MEDICAL MANAGEMENT

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ABSTRACT

Haemorrhagic pleural effusion can be a challenging diagnosis that requires a thorough investigation and sometimes a multidisciplinary team of physicians to reach the underlying aetiology. Causes can include pulmonary malignancy, pulmonary infections, connective tissue diseases, asbestos associated, intra-abdominal conditions such as pancreatitis and ovarian tumours, cardiovascular disorders such as ruptured aneurysms and pulmonary infarction, as well as other miscellaneous causes. One such cause is endometriosis in the thoracic cavity. Endometriosis is a chronic illness associated with the occurrence of endometrial tissue outside the endometrium. Insertion of endometrial tissue in the thoracic cavity is rare, with only a few cases described. This case report gives detail of a 30-year-old nulligravida suspected of having thoracic endometriosis following a history of catamenial dyspnoea and associated pleural effusion. The diagnosis was confirmed through the histopathological study of tissue obtained via thoracoscopic surgery. Excision of the endometrial tissue was done, and the patient then continued medical treatment with progestins and gonadotrophin-releasing hormone (GnRH) agonists. Following therapy, the index patient was asymptomatic. A multidisciplinary approach is often needed in the diagnosis and management of thoracic endometriosis, involving both medical and surgical specialities. Minimally invasive surgery is the gold standard of diagnosis, allowing for direct visualisation of implants and nodules and should be followed by medical treatment to reduce the risk of recurrence. Medical therapy alone is associated with higher rates of recurrence. Physicians must have a high degree of suspicion as thoracic endometriosis is a disease that can often be missed.

KEYWORDS

Haemorrhagic pleural effusion, haemothorax, thoracic endometriosis, catamenial pain, catamenial haemothorax

LEARNING POINTS

- Thoracic endometriosis syndrome is a rare but significant cause of haemorrhagic pleural effusion in women of childbearing age.
- Diagnosis and treatment can be challenging, and a multidisciplinary approach has been found to improve outcomes.

INTRODUCTION

Haemorrhagic pleural effusion can be a challenging diagnosis that requires a thorough investigation and sometimes a multidisciplinary team of physicians to reach the underlying aetiology. Causes can include pulmonary malignancy, pulmonary infections, connective tissue diseases, asbestos associated, intra-abdominal conditions such as pancreatitis and ovarian tumours, cardiovascular disorders such as ruptured aneurysm and pulmonary infarction, as well as other miscellaneous causes^[1]. One such cause is endometriosis of the thoracic cavity^[2]. Globally, endometriosis affects 190 million females of childbearing age^[2], which is approximately 10% of this population and represents a significant burden on the health of these women^[2]. The illness is chronic and is associated with the occurrence of endometrial tissue outside the uterus. Common sites for endometriosis include the uterus itself, the ovaries or the urinary tract. Insertion of endometrial tissue in the thoracic cavity is rare with only a few cases described^[2]. Patients suffer from catamenial chest pain, dyspnoea, heavy menstrual bleeding and occasionally, infertility^[3,4]. Early diagnosis is paramount, as is effective treatment.

CASE DESCRIPTION

A 30-year-old nulligravida patient first presented to Accident and Emergency in October 2022 with a two-day history of a productive cough and shortness of breath. She denied the occurrence of a fever. The patient had no past medical history of note, and she had no allergies to any medication. She was a smoker, smoking 5 to 10 cigarettes per day and occasionally consuming alcohol. Her physical examination revealed decreased air entry at the level of the middle and lower lobes of the right lung, and a chest X-ray on admission showed right-sided pleural effusion (Fig. 1). Her laboratory results – full blood count, urea/creatinine and electrolytes – were generally unremarkable, except for a haemoglobin of 8.3 g/dl. On the ward, she tested positive for COVID-19 and was placed in isolation for five days. She was discharged as a case of bronchopneumonia with parapneumonic pleural effusion and was given an appointment to repeat her chest X-ray in November, which showed persistent moderate right-sided effusion. The patient was readmitted for thoracocentesis, and 820 ml of dark red fluid was drained (Fig. 2); samples were sent for biochemistry, cytology, microscopy, and culture and sensitivity. The pleural fluid biochemistry results were consistent with exudative fluid, showing elevated protein and lactate dehydrogenase. The culture did not reveal any microorganisms, and the smears showed hypocellular fluid with some inflammatory cells, foamy macrophages and reactive mesothelial cells. As part of the investigations, tumour markers were requested and a CA-125 test was markedly elevated (172.9 U/ml). The patient's pelvic examination revealed normal findings; however, an ultrasound scan showed a 4 cm intramural fibroid with a linear endometrium, and a follicular cyst on the right ovary measuring 2.8 cm. Given these findings, a computerized

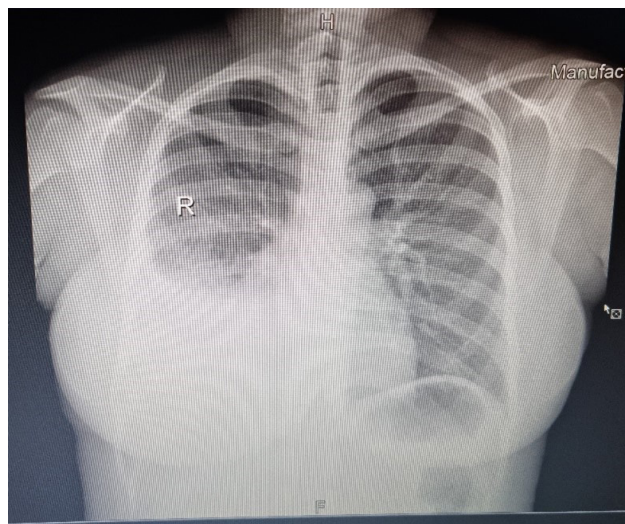


Figure 1. Chest X-ray of right-sided pleural effusion.

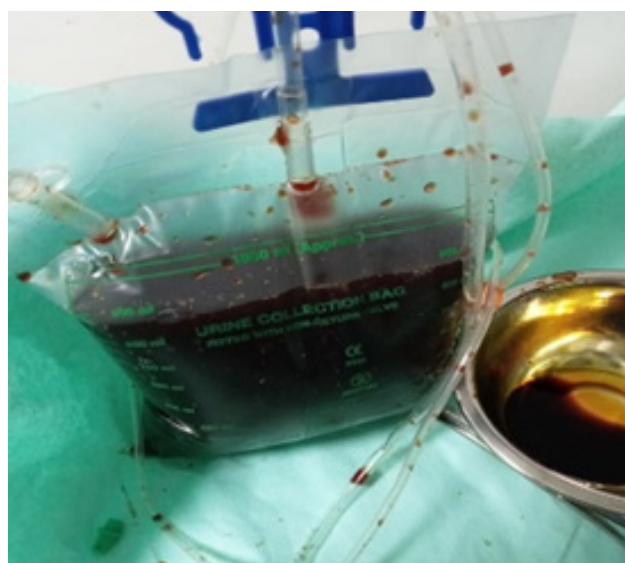


Figure 2. Dark red haemorrhagic pleural effusion.

tomography (CT) scan of her pelvis and abdomen was requested, which reported no clear differentiation between myometrium and endometrium. On further history-taking during admission, it was revealed that the episodes of increased shortness of breath and therefore increased pleural effusion occurred around the time of the patient's period. She also described dyspareunia; nonetheless, her periods were regular, with the last menstrual period being on 18 November 2022. Furthermore, she disclosed a family history of endometriosis with her mother suffering from the condition, and a brother who had Kartagener syndrome (immotile-cilia syndrome plus situs inversus). As a result of the history and these findings, the gynaecologists were called to review the patient. A preliminary diagnosis of endometriosis was formed based on the catamenial pleural effusion, associated with anaemia. The patient underwent medical management by the gynaecologist and was initiated on norethisterone (a synthetic progestin). Despite this, she continued with her symptoms and was readmitted in January 2023 with new shortness of breath. A CT scan of the chest showed findings of consolidation at the right lung lower

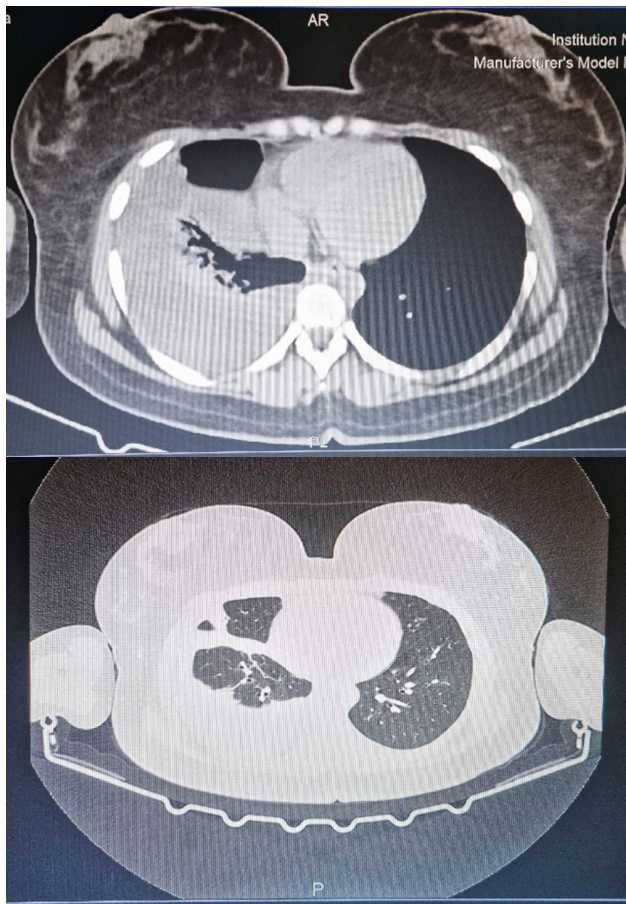


Figure 3. CT scan of chest showing right lung lower lobe consolidation and pleural effusion.

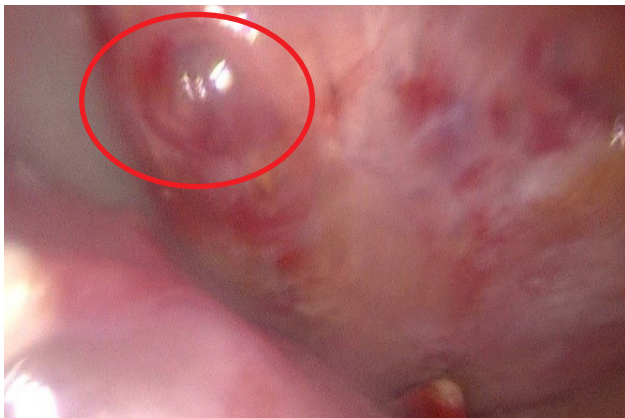


Figure 4. The thoracoscopic image shows endometrial tissue on the superior surface of the right dome of the diaphragm.

lobe consistent with pneumonia, and pleural effusion (Fig. 3). Again, a thoracentesis revealed similar findings to the first one in November 2022. All the markers of inflammation such as C-reactive protein were within an acceptable range; however, the patient had anaemia with a haemoglobin of 8.6g/dl and elevated CA-125 levels (86.48 U/ml). Gynaecologists were contacted, and the patient's norethisterone dose was increased to 10 mg three times daily. She complained of leg swelling while on progestogens and her treatment was switched to danazol (a synthetic steroid and pituitary gonadotropin inhibitor), 200 mg twice a day. In March 2023, she was admitted again with similar

complaints of shortness of breath and general malaise. Given the persistence of the pleural effusion, the patient was consulted by the surgical team for a thoracoscopy and diagnostic laparoscopy, and samples of the pleurae and diaphragm were taken for biopsy. Furthermore, incision and removal of three diaphragmatic lesions were done. The lesions were sub-centimetre, with the biggest measuring 5 mm, and were on the right diaphragmatic pleura. The biggest lesion (circled in red) had eroded the diaphragm giving it a translucent appearance (Fig. 4). Multiple adhesions were seen in the thoracic cavity, and a left ovarian cyst and hydrosalpinx were also removed during the laparoscopy. The samples sent for biopsy were found to be consistent with pleural endometriosis; cyst-like structures surrounded by dense fibrous tissue with haemosiderin-laden macrophages were seen, along with pleurae and indistinct stromal fragments with dilated and congested blood vessels. The stromal fragments expressed CD10, oestrogen and progesterone receptors, corresponding with endometrial stroma (Fig. 5). These findings confirmed the preliminary diagnosis of endometriosis. The patient was discharged from the hospital and continued follow-up with the gynaecologist. She was initiated on goserelin (gonadotrophin-releasing hormone – GnRH agonist) subcutaneously every 28 days for six months, completing the course in February 2024. At almost one-year post-surgical intervention, the patient continued to be asymptomatic. Her follow-up chest radiograph (Fig. 6) showed no reoccurrence of pleural effusion. The patient will be commenced on danazol after the completion of the six-month course of goserelin.

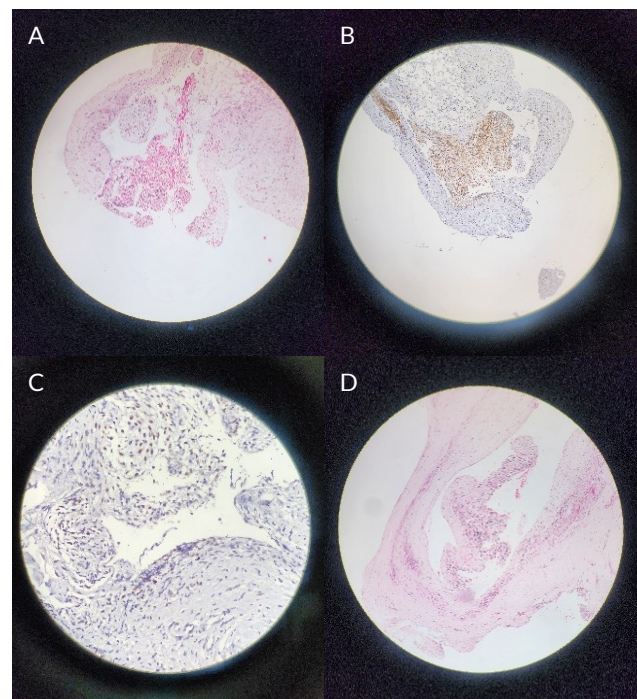


Figure 5. A and D) Haematoxylin and eosin stains of specimen showing cyst-like structures surrounded by dense fibrous tissue showing haemosiderin-laden phagocytes, suggestive of organised haemorrhage. Other tissue fragments are consistent with non-tumoural pleurae; B) CD10 positive tissue; C) oestrogen receptor positive tissue.

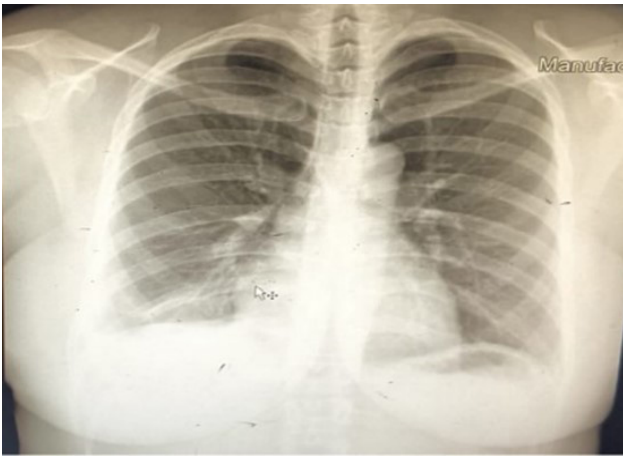


Figure 6. Follow-up chest X-ray (one-year post surgery) revealed resolution of the pleural effusion.

DISCUSSION

Endometriosis refers to the development of endometrial tissue outside the uterine cavity^[2]. Commonly this develops in the pelvic cavity, but in rare instances, extra-pelvic disease occurs in about 12% of women with endometriosis^[5-7]. Thoracic endometriosis represents a spectrum of diseases with endometriotic lesions found on the diaphragm, pleural surfaces and/or lung parenchyma. It is the most common extra-pelvic endometriosis, and it presents with catamenial haemothorax as was the case in the index patient, pneumothorax, haemoptysis and a lung nodule. The pathogenesis of thoracic endometriosis is unclear, but some theories have been put forward to explain how it comes about^[8]. It is thought that the endometrial tissue from the peritoneal cavity disseminates into the pleural space through haematogenous or lymphatic channels and diaphragmatic fenestrations^[8]. The initial diagnosis of thoracic endometriosis is often missed in most cases, which leads to significant delays before patients are treated appropriately^[9]. Therefore, a high index of suspicion is necessary for diagnosis. Thoracic endometriosis co-exists with pelvic endometriosis in 50 to 100% of cases. Therefore, the presence of respiratory symptoms in women with signs of pelvic endometriosis requires further evaluation. Imaging such as chest radiographs or computed tomography scans may show small cystic defects, but they may also report negative findings, therefore their role in the diagnosis and treatment plan of thoracic endometriosis remains unclear. Rather, it is useful in ruling out the presence of other intrathoracic pathologies^[9]. The gold standard for diagnosis is minimally invasive surgery, which allows for the direct visualisation of implants and nodules. It offers the additional advantage of resection or desiccation of the lesions. The treatment is multidisciplinary as is the case with the index patient. It includes hormonal therapy, surgery or a combination of both^[9]. The first-line treatment option for thoracic endometriosis is hormonal therapy to suppress ovarian oestrogen secretion, using GnRH analogues, oral contraceptives, progestins, aromatase inhibitors and GnRH antagonists. The index patient was treated with progestin

followed by danazole, but she had a recurrence of symptoms as seen in about 60% of patients managed using medical therapy^[9]. Because her symptoms were refractory to medical therapy, she had surgery and postoperative hormonal therapy using GnRH analogues^[9]. GnRH analogues are effective at decreasing the postoperative recurrence risk. The use of other options such as continuous oral contraceptive pills is an effective alternative, but it has a reported recurrence rate of 33%^[9,10]. Unfortunately, some patients who undergo surgical excision followed by postoperative hormonal therapy may develop recurrent thoracic endometriosis syndrome. Such patients are managed by hysterectomy with bilateral salpingo-oophorectomy. GnRH analogues induce hypoestrogenic states by direct suppression of gonadotropin production^[11]. Side effects include a high rate of menopausal symptoms and osteoporosis. Loss of bone mineral density may become irreversible after 12 months of treatment, therefore their use is usually limited to 6 to 12 months post excision^[11]. The index patient has had six months of therapy with GnRH analogues (goserelin 3.6 mg subcutaneously every 4 weeks)^[11]. The side effects can be ameliorated by add-back therapy using 5 mg norethindrone acetate daily or combined oral contraceptives. This approach can allow an extended duration of therapy with the GnRH agonist, but it is not recommended as a long-term treatment option^[11]. Calcium and vitamin D have been suggested as a measure of providing some levels of bone protection^[11]. Progestin therapy is an alternative that can be delivered orally or parenterally. It is preferred in women not suitable for combined hormone therapy, smokers older than 35 years and those at high risk of thromboembolic events^[11]. It acts by ovulation inhibition and induction of amenorrhoea. Side effects include acne, weight gain, mood changes, headache, breakthrough bleeding, breast tenderness and lipid abnormalities^[8]. Dienogest, a fourth-generation oral progestin, has been suggested as an effective alternative for hormonal treatment in patients with recurrent pneumothorax who do not wish to use GnRH agonists or oral contraceptives, but it has been reported to have a higher risk of thromboembolic events^[11]. Danazole is a synthetic androgenic steroid, which suppresses the pituitary-ovarian axis by blocking the production of gonadotropins. The suppressing follicle-stimulating hormone, luteinising hormone surge leads to the suppression of oestrogen; it also interferes with steroidogenesis and enhances the clearance of progesterone in the blood. It is an effective treatment option for endometriosis. Side effects include weight gain, hirsutism and voice changes^[11]. Other available options include aromatase inhibitors and GnRH antagonists^[11]. In conclusion, thoracic endometriosis syndrome is a rare presentation of endometriosis. Diagnosis and treatment can be challenging, and a multidisciplinary approach has been found to improve outcomes.

REFERENCES

1. Kumar S, Verma SK, Singh R, Prasad R. Hemorrhagic pleural effusion secondary to sarcoidosis: a brief review. *Ann Thorac Med* 2009;**4**:27–31.
2. World Health Organization, 2023. Endometriosis [Fact Sheet] <https://www.who.int/news-room/fact-sheets/detail/endometriosis#:~:text=Endometriosis%20is%20a%20disease%20in,period%20and%20last%20until%20menopause>. Accessed on 1st February 2024
3. Yao J, Zheng H, Nie H, Li CF, Zhang W, Wang JJ. Endometriosis of the lung: a case report and review of literature. *World J Clin Cases* 2023;**11**:4326–4333.
4. Porcel JM, Sancho-Marquina P, Monteagudo P, Bielsa S. Pleural effusion secondary to endometriosis: a systematic review. *Am J Med Sci* 2023;**366**:296–304.
5. Duyos I, López-Carrasco A, Hernández A, Zapardiel I, de Santiago J. Management of thoracic endometriosis: single institution experience. *Eur J Obstet Gynecol Reprod Biol* 2014;**178**:56–59.
6. Nezhat C, Main J, Paka C, Nezhat A, Beygui RE. Multidisciplinary treatment for thoracic and abdominopelvic endometriosis. *JSL* 2014;**18**:e2014.00312.
7. BSGE and RCOG joint statement on thoracic endometriosis care in the United Kingdom. Available at: <https://www.rcog.org.uk/media/4iulq0ug/bsge-statement-on-thoracic-endometriosis-care-in-the-uk.pdf>
8. Ciriaco P, Muriana P, Lembo R, Carretta A, Negri G. Treatment of thoracic endometriosis syndrome: a meta-analysis and review. *Ann Thorac Surg* 2022;**113**:324–336.
9. Singh M, Singh RB, Singh AB, Carballo AL, Jain A. Thoracic endometriosis: still a diagnostic dilemma. *Cureus* 2021;**13**:e15610.
10. European Society of Human Reproduction and Embryology (ESHRE). ESHRE guideline endometriosis, 2022. Available at: <https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline.aspx>
11. Falcone T, Flyckt R. Clinical management of endometriosis. *Obstet Gynecol* 2018;**131**:557–571.