International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Bhattacharya S. Int J Reprod Contracept Obstet Gynecol. 2026 May;15(5):1863-1866
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20261304

Case Report

Spontaneous recurrent pneumothorax after in vitro fertilization

Suparna Bhattacharya*

Department of Clinical Services, Nova IVF Fertility, Kolkata, West Bengal, India

Received: 09 March 2026
Revised: 13 April 2026
Accepted: 14 April 2026

***Correspondence:**
Dr. Suparna Bhattacharya,
E-mail: suparnabhattar@gmail.com

ABSTRACT

Catamenial pneumothorax (CP) is a rare form of spontaneous pneumothorax occurring within 72–96 hours before or after the onset of menstruation, accounting for approximately 3–6% of cases, and is commonly associated with thoracic endometriosis. It typically affects women over 31 years of age and predominantly involves the right hemithorax, although atypical presentations may occur. We report the case of a 39-year-old woman with secondary infertility and multiple failed in vitro fertilization (IVF) attempts who developed recurrent spontaneous pneumothorax temporally associated with exogenous estrogen therapy during endometrial preparation. Initial IVF treatment resulted in a biochemical pregnancy; however, during preparation for a donor oocyte cycle with oral estradiol, she presented with acute chest pain and dyspnoea and was diagnosed with left-sided pneumothorax, managed conservatively. Recurrence was noted upon re-exposure to estrogen, with imaging confirming left upper lobe involvement. In view of this, a modified protocol using gonadotropin-releasing hormone agonist downregulation followed by transdermal estrogen was employed, after which embryo transfer was successfully performed, resulting in a twin pregnancy with an uneventful antenatal course and delivery at 35 weeks. This case highlights an atypical presentation of recurrent pneumothorax likely influenced by hormonal therapy, raising the possibility of occult thoracic endometriosis or estrogen-mediated pleural pathology. Recognition of this association is essential for optimizing management, and individualized, multidisciplinary approaches are recommended in the absence of standardized guidelines.

Keywords: Infertility, Recurrent spontaneous pneumothorax, ART, Non cataminal pneumothorax, Successful pregnancy

INTRODUCTION

Pneumothorax is defined as air in the pleural space and is characterized by chest pain and breathlessness. It is commonly divided into spontaneous and non-spontaneous subtypes based on the underlying mechanism. Chest X-ray is the most common investigation to diagnose and monitor pneumothorax, but CT-chest is increasingly used to aid decision-making in complex cases and to investigate underlying lung disease. Treatment for pneumothorax is based on the clinical condition and symptoms of the patient rather than the size of the pneumothorax.[1] Catamenial pneumothorax (CP) is a term used to describe the occurrence of spontaneous pneumothorax during the period of 72–96 hours before and after menstrual bleeding. It is a rare entity, accounting for 3–6% of all spontaneous pneumothoraces.[2] CP is usually seen in women aged 32–35 years, most commonly affecting the right lung. Haga et al suggested four criteria for distinguishing CP from spontaneous pneumothorax: (1) right-sided pneumothorax, (2) history of pelvic endometriosis (20–70%, most common clinical manifestation), (3) age 31 years or older, and (4) no history of smoking. (3) CP is often associated with thoracic endometriosis (TE), which is explained through several mechanisms: migration of endometrial cells through the fallopian tubes and diaphragmatic fenestrations caused by cyclical proliferation and necrosis of diaphragmatic endometriotic

foci, hematogenous microembolization, and lymphatic metastasis. Certain cases of CP may present with no identifiable thoracic pathology. (4) A case of pneumothorax occurring after multiple in vitro fertilization (IVF) attempts is described herein.

CASE REPORT

In January 2018, a 39-year-old woman (Mrs. SB) presented with secondary infertility (P0+1) and four previously failed self-IVF cycles at another centre. She had been married for 10 years. A previous diagnostic hysterolaparoscopy (HL) performed after the prior failures revealed normal findings with flimsy adhesions and patent tubes. Endometrial TB PCR was also normal. Menstrual history: regular, 29-day cycles, average flow for 3 days, dysmenorrhea present. Family history was non-significant. Medical history revealed no lung disease or asthma. No history of alcohol, smoking, or drug intake. BMI was 36. Vitals were stable. Per abdominal examination: soft and non-tender. Per speculum examination: normal cervix with no erosion. Initial ultrasound showed a normal uterus with an adherent left ovary, normal right ovary, and an antral follicle count of 4–5 on both sides. AMH level was 1.09 ng/ml. Husband's semen analysis was normal; DFI was 9%.

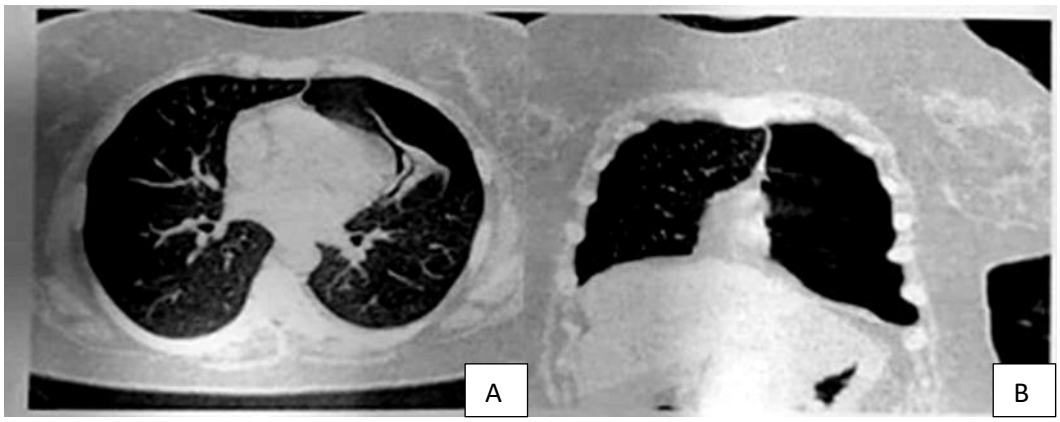

Figure 1 (A and B): HRCT scan.

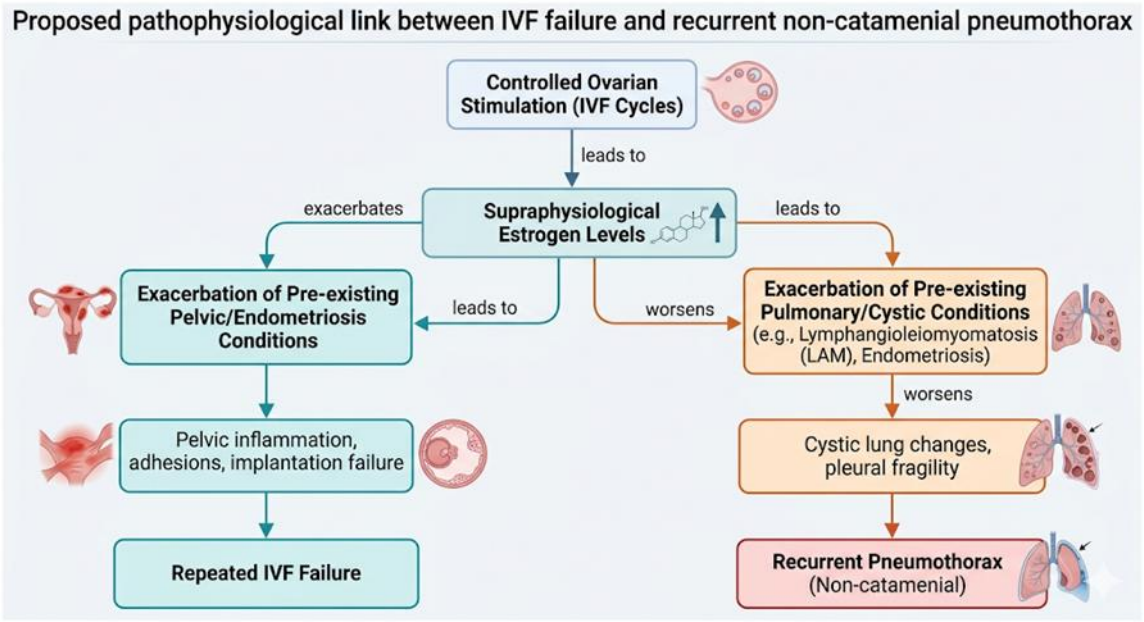

Figure 2: Proposed pathophysiological link between IVF failure and recurrent non-catamenial pneumothorax.

Management

The patient was counselled regarding self-IVF with or without PGT-A, limitations and success rates, and her age. She agreed to one cycle of self-IVF with us. She was stimulated, and 6 oocytes were retrieved, from which 2 good blastocysts were formed and vitrified. In her next cycle, her endometrium was prepared satisfactorily in a natural cycle, and a frozen embryo transfer was performed with 2 good blastocysts and adequate luteal phase support. She resulted in a biochemical pregnancy. We reviewed her case; thrombophilia profile was normal, 3D scans showed

normal ovaries and cavity, and semen profile was normal. After discussion, we decided to proceed with donor oocytes. Endometrium was prepared with estradiol valerate tablets (2 mg thrice daily). Within 2 days of starting medication, she complained of severe chest pain and dyspnoea. Treatment was stopped, and she was referred to an emergency department, where she was diagnosed with spontaneous pneumothorax of the left upper lobe. She was admitted and treated conservatively with drainage and nasal oxygen under a pulmonologist. She was advised to take a 6-month break, during which she remained asymptomatic (Figure 1).

When we restarted preparation with estradiol valerate tablets (2 mg thrice daily), she developed recurrent pneumothorax. HRCT thorax revealed moderate pneumothorax adjacent to the anterior and lingular segments of the left upper lobe. She was admitted again and treated conservatively, with a plan for pleurodesis if recurrence occurred. We planned another frozen transfer after downregulating with 2 depot injections of GnRH agonist, with an intervening hysteroscopy (which revealed adenomyosis but was otherwise normal), and prepared her endometrium with transdermal estrogen only.

Two blastocysts were transferred, and adequate luteal phase support was given. Her serum HCG 10 days after transfer was 623 miu/ml. The patient had an uneventful twin pregnancy under the constant supervision of a team comprising an obstetrician, paediatrician, and pulmonologist. She delivered two healthy male babies by LSCS at 35 weeks and 3 days, weighing approximately 2.4 kg and 2.1 kg.

DISCUSSION

Spontaneous recurrent pneumothorax during ART is a rare condition. Few cases have been reported previously in the literature.[5,6] Spontaneous pneumothorax is defined as the presence of air in the pleural space without antecedent trauma and is classified into primary and secondary types. In women of reproductive age, special consideration is often given to catamenial pneumothorax; however, the present case represents a non-catamenial spontaneous pneumothorax occurring in the setting of repeated in IVF failure, raising the possibility of shared underlying etiologies.

Primary spontaneous pneumothorax is commonly attributed to rupture of subpleural blebs, whereas secondary causes include underlying pulmonary diseases such as chronic obstructive pulmonary disease and tuberculosis.[7] In women without obvious lung disease, recurrent episodes necessitate evaluation for less common conditions. One important differential is endometriosis, which is strongly associated with infertility and repeated IVF failure.[8] Although thoracic endometriosis typically presents as catamenial pneumothorax, atypical or non-cyclical presentations have been described. Occult pelvic endometriosis may impair implantation through inflammatory and immunological mechanisms, thereby contributing to IVF failure.

Another key consideration is lymphangioleiomyomatosis (LAM), a rare cystic lung disease affecting women of reproductive age. It is characterized by proliferation of abnormal smooth muscle-like cells leading to cystic lung destruction and recurrent pneumothorax.[9] Importantly, LAM is estrogen-sensitive, and disease progression may be exacerbated by the supraphysiological hormonal levels associated with ovarian stimulation during IVF. This hormonal interplay may explain both the recurrence of pneumothorax and poor reproductive outcomes.

Connective tissue disorders such as Marfan syndrome and Ehlers-Danlos syndrome should also be considered, as they predispose to pulmonary bleb formation and may adversely affect reproductive outcomes through altered connective tissue integrity.[10] The coexistence of recurrent pneumothorax and IVF failure highlights the need for a multidisciplinary approach. High-resolution CT of the chest is essential to evaluate for cystic lung diseases, while gynaecological assessment should focus on identifying endometriosis or uterine factors. Definitive management of pneumothorax, including surgical intervention such as video-assisted thoracoscopic surgery (VATS) with pleurodesis, is recommended prior to further IVF attempts to reduce recurrence risk.[11]

CONCLUSION

In conclusion, non-catamenial spontaneous pneumothorax in a patient with repeated IVF failure should prompt evaluation for systemic and hormonally responsive conditions. Early identification of an underlying etiology is critical to optimize both pulmonary stability and reproductive outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bhattacharya S. Spontaneous recurrent pneumothorax after in vitro fertilization. Int J Reprod Contracept Obstet Gynecol 2026;15:1863-6.