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Case report

A unique case of thoracic endometriosis syndrome and pulmonary Langerhans' cell histiocytosis: Six recurrent pneumothoraces

Varun Gupta [a,1], Ka-Won Noh [b,1], Hansjörg Maschek [c], Stefan Thal [c], Stefan Welter [a,*]

[a] Department of Thoracic Surgery, Lung Clinic Hemer, Theo-Funccius Str. 1, 58675, Hemer, Germany
[b] Institute of Pathology, University Hospital Cologne, Kerpener Str. 62, 50937, Cologne, Germany
[c] SYNLAB MVZ Pathologie Hannover GmbH, Feodor-Lynen-Straße 21, 30625, Hannover, Germany

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ABSTRACT

Spontaneous pneumothorax (SP) in women of reproductive age with causes such as thoracic endometriosis syndrome (TES) presents a diagnostic and therapeutic challenge. A 33-year-old women was treated conservatively with chest tube insertion for a first occurrence of a right-sided pneumothorax in September 2015. In January 2016, a right-sided video-assisted thoracoscopic surgery (VATS) wedge resection and partial parietal pleurectomy was performed due to a recurrence. A right-sided VATS was again performed in December 2016 with multiple wedge resections and a total pleurectomy revealing a pulmonary Langerhans' cell histiocytosis (PLCH) in the histological and immunohistochemical examinations. The patient was recommended an abstinence of smoking and further course was unremarkable until May 2019, when due to a recurrent pneumothorax, she received a talc pleurodesis via right-sided VATS. Due to yet another recurrence, she underwent a talc slurry pleurodesis over a right sided chest drain. In March 2020 due to recurrence, a right-sided VATS was performed and a blueish nodular lesion was resected from the diaphragm. The histological examination revealed an endometriosis with a diagnosis of TES. Since the patient did not exhibit a temporal relationship between her periods and the onset of pneumothorax symptoms, a final diagnosis of non-catamenial endometriosis-related pneumothorax was made. The patient is currently continuing smoking abstinence and is under hormone therapy. She has not presented with a recurrence. In clinical practice, it is important not to just relay on the information available to us, but to reevaluate the patient history to uncover new clues leading to a new diagnosis.

Abbreviations

CP	Catamenial pneumothorax
CT	Computed tomography
MRI	Magnetic resonance imaging
PLCH	Pulmonary Langerhans' cell histiocytosis
PY	Pack-year
SP	Spontaneous pneumothorax

* Corresponding author. Lung Clinic Hemer, Department of Thoracic Surgery, Theo-Funccius Str. 1, 58675, Hemer, Germany.
E-mail address: stefan.welter@lkhemer.de (S. Welter).
[1] Equal contribution.

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TES	Thoracic endometriosis syndrome
VATS	Video-assisted thoracoscopic surgery

1. Introduction

Spontaneous pneumothorax (SP) in women of reproductive age has diverse origins [1,2]. Thoracic endometriosis syndrome (TES) and pulmonary Langerhans' cell histiocytosis (PLCH) comprise the more unusual and difficult-to-diagnose etiology [1,2]. It is possible that recurrent pneumothorax in premenopausal women may be incorrectly classified as SP due to lack of comprehensive history taking as well as insufficient intraoperative diaphragmatic examination [3].

TES is characterized by presence of intrathoracic functional endometrial tissue [4] and presents as either catamenial pneumothorax (CP) (73%), catamenial hemothorax (14%), catamenial hemoptysis (7%) or lung nodules (6%) [5]. CP has been found to be the primary cause in 21.2%–24.6% of the cases of SP in women of reproductive age [1,6,7]. A consensus on the pathogenesis of TES is yet to be reached, but several theories have been presented. The most widely accepted is Sampson's theory of retrograde menstruation [8] and receives validation through the fact that an endometriosis occurrence on the right hemidiaphragm is nine times more likely [9,10]. The coelomic metaplasia theory, lymphatic and hematogenous dissemination theory and prostaglandin theory as well as genetic mutations are other possible explanations towards the pathogenesis of TES [11,12].

Further complicating the process, CP can be endometriosis-related or non-endometriosis-related and endometriosis-related pneumothoraxes can in turn be catamenial or non-catamenial [13]. It has been observed that for a case to be diagnosed as CP, a strict temporal correlation with menses was not required [13]. Tulandi et al. reported the number of known episodes of catamenial pneumothorax before treatment ranging from two to eight [14]. Video-assisted thoracoscopic surgery (VATS) is the gold standard for diagnosis of thoracic endometriosis [15]. All things considered, the high variability of TES presentation makes a timely diagnosis all the more crucial [15].

Adult PLCH is a benign disease with over 90% of the patients being smokers [16,17]. Due to its rareness, very little is known about its etiopathogenesis and management. It is postulated that the destruction of lung parenchyma associated with cystic changes leads to spontaneous pneumothorax, which is a recognized feature of PLCH [17]. These cystic lesions of the lung parenchyma frequently affecting the upper lobes, can be not so uncommonly seen on chest computed tomography (CT) scans [16]. Histologically, PLCH begins along the small airways as non-clonal proliferation of Langerhans' cells, which can later take a nodular form representing a chronic reactive inflammatory process to cigarette smoke [2,16,18]. The Langerhans' cells demonstrate positivity for cell surface antigens S-100 and CD1a on immunohistochemical staining [2,16,19].

Recurrence of pneumothorax has been seen in up to 10% of PLCH patients [17]. When pneumothorax is the initial presentation of PLCH, recurrence rates can be as high as 60% [18]. Minimally invasive thoracoscopic procedures like pleural abrasion and pleurodesis in addition to strict abstinence from smoking have shown to be sufficient in hindering a recurrence of pneumothorax [2,17,18].

2. Materials and methods

Both TES and PLCH are by themselves uncommon causes of SP in women of reproductive age. To the best of our knowledge, there have been no previous reports of a case diagnosed with both TES and PLCH resulting in multiple pneumothorax recurrences. We share this unique case to shed light on these understudied diseases and to aid in the diagnosis and management of future cases.

This case report presents the clinical presentations, diagnosis and employed treatment modalities in a 33-year-old female patient with a history of smoking (cumulative 15 Pack-years). The described diagnostic and treatment modalities were performed at our center and elsewhere. This is a retrospective compendium of this patient's diagnosis. Written consent for publication of this report was given by the patient.

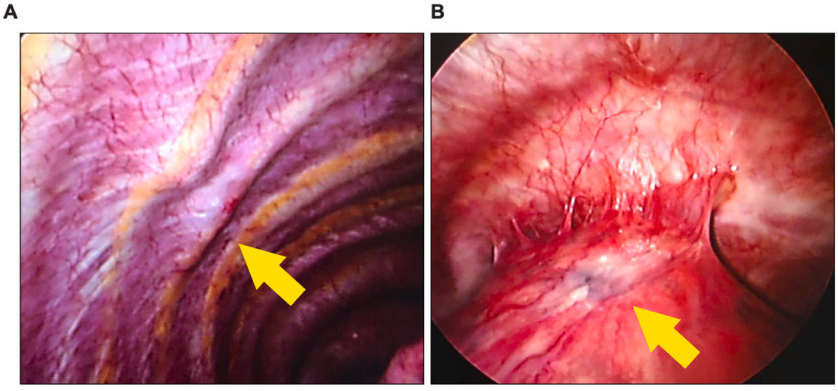

Fig. 1. Intraoperative findings. **(A)** Suspected nodules on the right parietal pleura (arrow) and **(B)** inter-pleural adhesions and suspected pulmonary lesion (arrow), where a wedge resection was performed. (2-column fitting image).

3. Results

The patient was treated with chest tube insertion and drainage in September 2015 for a first occurrence of right-sided pneumothorax. Due to a recurrence in January 2016, she underwent a chest tube insertion followed by a right-sided VATS wedge resection and partial parietal pleurectomy. Both these procedures were not performed at our institute.

After almost a year, she presented to our center in December 2016 with a recurrent right-sided pneumothorax. Besides a solitary, well demarcated, 4-mm pulmonary nodule in the middle lobe, the preoperative computed tomography scan of the thorax did not reveal any abnormalities of the lung parenchyma as well as the chest wall or the diaphragm. At this time, a right-sided re-VATS with pleural adhesiolysis, wedge resections from the lesions in the right upper-, lower- and middle lobes, as well as a total pleurectomy was performed without any complications (Fig. 1). The histological and immunohistochemical examination revealed an early stage of histiocytosis X (PLCH) with CD1a and S-100 expressions in the resected sample of the right lower lobe (Fig. 2). She was discharged with strong recommendation towards smoking abstinence and a strict avoidance of second-hand cigarette smoke. After 4 weeks, a post-operative pulmonologist work-up was performed. The pulmonary function tests (PFT) were normal and the spiroergometry presented no evidence of a pulmonary vasculopathy or interstitial lung disease.

The further course was unremarkable until another pneumothorax recurrence in May 2019 forced the patient to seek medical attention at a different institute, where a right-sided re-VATS with talc pleurodesis was performed. She was admitted once again to our center in July 2019 with another pneumothorax recurrence, where she underwent a talc slurry pleurodesis through a right-sided chest drain. According to the patient, she had been strictly abstaining from smoking.

In March 2020, she suffered yet another pneumothorax recurrence and underwent a right-sided re-VATS at our center. Surprisingly, a blueish nodular lesion was discovered intraoperatively on the diaphragm (Fig. 3). This lesion was resected and another talc pleurodesis targeting the non-adherent basal parts was performed. Additionally, good adhesions were observed between the middle and apical parts of the lungs and the inner chest wall.

On histological examination of this resected diaphragmatic lesion, an endometriosis was uncovered (Fig. 4). After the diagnosis of TES was made, she was once again inquired retrospectively about a temporal relation between her periods and the onset of pneumothorax symptoms, which she denied to the best of her knowledge. Henceforth, a final diagnosis of non-catamenial endometriosis-related pneumothorax was made. Postoperatively, the patient recovered well and was recommended to seek gynecological consultation for further management and hormone therapy. A follow-up MRI examination about 8 weeks postoperative and under hormone therapy showed no pathological findings in the thorax and diaphragm, as well as the examined peritoneum.

4. Discussion

Non-catamenial endometriosis-related pneumothoraces present an everyday clinical practice challenge as in addition to being rare, a temporal relation with menstruation is not exhibited. The presence of additional pelvic endometriosis and infertility has been reported in patients with TES [1,4,20]. An unspecific patient history and the lack of radiological or histological evidence increase the risk of delayed or incorrect diagnosis.

There is an absence of clear cut radiological diagnostic criteria for endometriosis-related pneumothoraces. The efficacy of CT thorax in localizing diaphragmatic endometrial nodules remains questionable. Although magnetic resonance imaging (MRI) may facilitate endometriotic foci visualization, its use as a perioperative diagnostic tool remains limited due to the cumbersome nature of the examination itself, as well as the ultimate need for a histological confirmation of the diagnosis. Only in a select number of cases with a clearly defined temporal relation between menstruation and pneumothoraces or a visible radiological regression of diaphragmatic foci in response to hormone therapy, a MRI might suffice in providing a diagnosis of TES.

On the other hand, PLCH which is highly associated with smoking shows cystic changes in the lung parenchyma on CT imaging in most advanced cases [2,16]. SP is a well-recognized complication of PLCH and is the result of ruptured subpleural cysts [2]. Immunohistochemically, Langerhans' cells demonstrate CD1a and S-100 cell surface antigens, which is sufficient for the diagnosis of PLCH [2,17].

Up to date, a VATS procedure is the corner stone in secondary spontaneous pneumothorax where TES or PLCH is suspected, by facilitating a visual examination of the entire pleural cavity, including the diaphragm, providing the possibility of a histological and immunohistochemical examination leading to a definitive diagnosis. It can also be combined with pleurodesis, partial or total pleurectomy and/or resection of multiple foci to provide optimal therapy as well as to prevent recurrences. In addition, abstinence

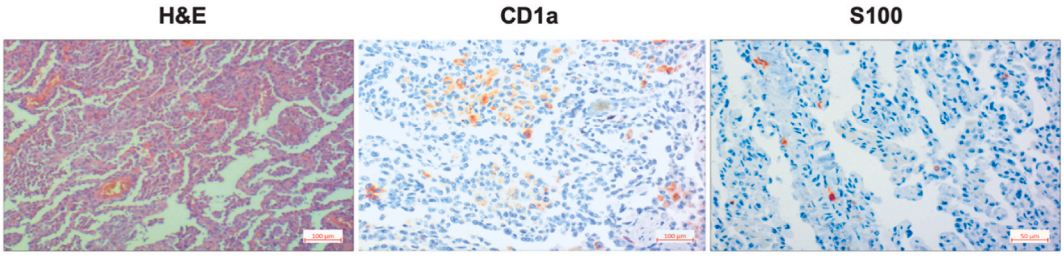

Fig. 2. H&E and immunohistochemical staining of the resected pulmonary tissue depicting a case of PLCH. All scale bars are represented in the images. (2-column fitting image).

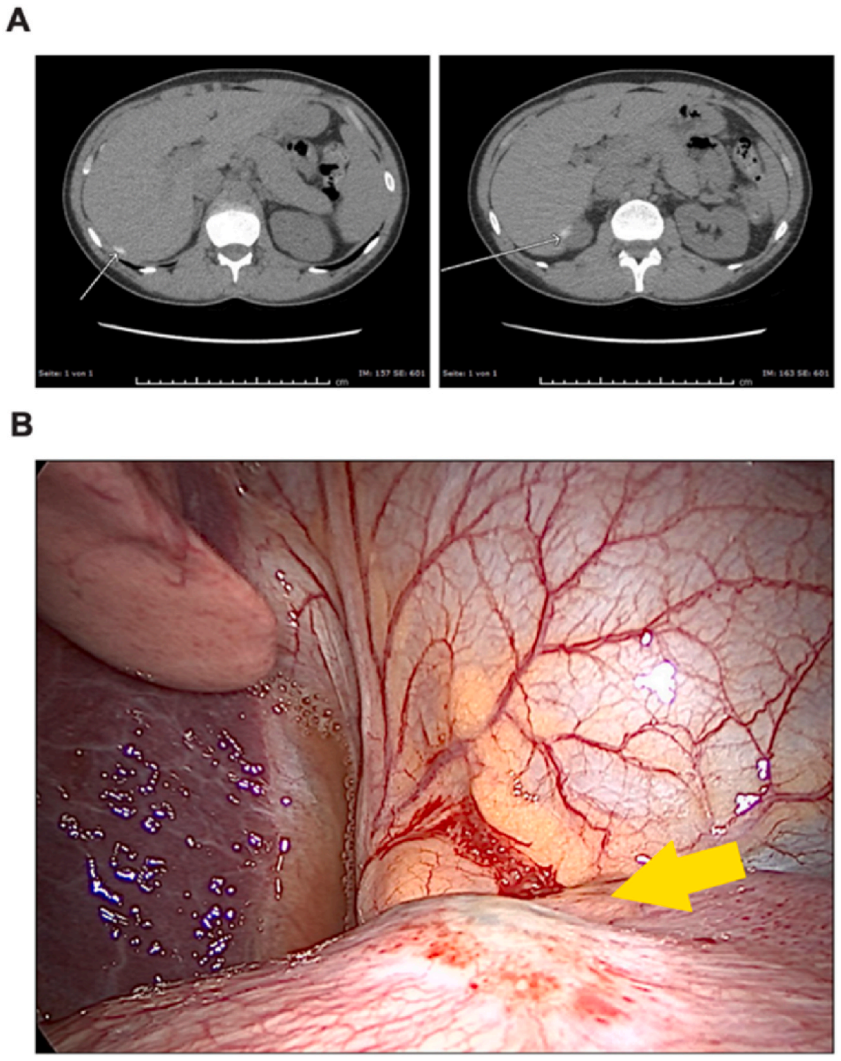

Fig. 3. Perioperative findings. **(A)** CT thorax images showing suspected hyperdense pleural lesions. All scale bars are represented in the images. **(B)** Intraoperative finding of the later resected nodular blueish diaphragmatic pleura lesion (arrow). (1.5-column fitting image).

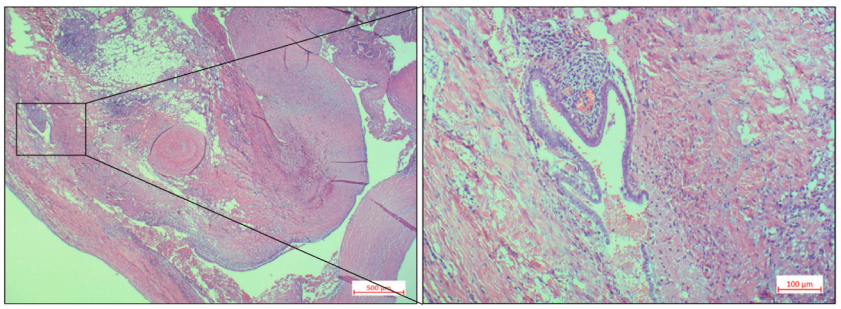

Fig. 4. H&E section of resected specimen of the right diaphragm. Overview showing predominantly scarred tissue with striated muscle remnants in the lower left quadrant (Left). There is an endometrial gland and large gaps visible. There is also evidence of bleeding and endometrial epithelium as well as diffused inflammation. An endometrial gland lined with typical linear endometriotic epithelium and adjacent endometrial stroma along with evidence of bleeding is characteristically visible for endometriosis (Right). In addition, there is extensive scarring and mixed lymphocytic and macrophage-rich inflammatory reaction in the area. All scale bars are represented in the images. (2-column fitting image).

from smoking and more importantly avoidance of second-hand smoke is essential to manage and prevent recurrences and disease progression in cases of early PLCH. Corticosteroids have been helpful in cases where smoking cessation alone is ineffective.

A multidisciplinary surgical and hormonal management including local resection along with postoperative gonadotrophin-releasing hormone (GnRH) analogues administration has been the golden standard for catamenial and/or endometriosis-related pneumothoraces [13]. These have also shown to reduce or prevent recurrence of pneumothorax [21]. A hand-in-hand approach of thoracic surgeons, pulmonologists, gynecologists and, if need be, laparoscopic surgeons is of high recommendation in new and recurrent cases of SP in women of reproductive age.

5. Conclusions

Although good history taking and a systematic diagnostic approach might prove sufficient to diagnose most of the causes of secondary pneumothorax, this still might be inadequate in a handful of cases. In case of pneumothorax recurrences in women of reproductive age, it is important to remember not to take for granted the information available to us through past history but to keep an open mind and review the patient thoroughly at every new presentation. As illustrated by our case, this could shed light on aspects previously deemed mundane, and would in turn help in diagnosing and optimally managing the patients. Lastly, there are exceptions to Occam's razor.

Author contribution

Varun Gupta: Conceptualization, Methodology, Writing – Original Draft. Ka-Won Noh: Conceptualization, Writing – Original Draft, Visualization. Hansjörg Maschek: Investigation, Resources. Stefan Thal: Investigation, Resources. Stefan Welter: Supervision, Writing – Review & Editing.

Declaration of competing interest

All authors declare no conflicts of interests.

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