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ORIGINAL ARTICLE

Catamenial Pneumothorax, a Commonly Misdiagnosed Thoracic Condition: Multicentre Experience and Audit of a Small Case Series With Review of the Literature

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Background Catamenial pneumothorax (CP) is an unusual condition affecting premenopausal women and commonly misdiagnosed as simple pneumothorax. It is characterised by its recurrence between the day before and within 72 hours after the onset of menstruation. It has been associated with thoracic endometriosis but the aetiology is not well understood and there is no unified agreement for its optimal management. The aim of this study is to determine the incidence of CP in surgical patients and the results of their treatment.

Methods Females between the ages of 30 to 50 years with a diagnosis of pneumothorax, admitted for surgery over a 10-year period in four different hospitals were retrospectively reviewed for evidence of CP. An audit of surgical and medical management of the patients with CP and their short to midterm outcomes was performed in addition to a systemic review of the literature on CP.

Result A total of 120 premenopausal female patients with a diagnosis of pneumothorax were admitted for Video Assisted Thoracoscopic (VAT) surgery and five women (4.1%) with a mean age of 42.6 years were diagnosed to have CP through surgical and histological findings. The first case was diagnosed 5 years ago and the last three within recent 12 months after the changes in surgical practices of inspecting diaphragmatic surface in suspected cases of CP. Four patients underwent diaphragmatic plication and one patient had a pleural biopsy. All patients underwent talc pleurodesis and hormone therapy in the postoperative period. Short to midterm (mean follow-up period of 25.2 months) results of the patients with CP were encouraging.

Conclusions It is possible that many of the cohort of premenopausal female patients presenting with recurrent pneumothorax are misdiagnosed as spontaneous pneumothorax (SP) because routine inspection of the diaphragmatic surface is not often performed. A thorough menstrual history and its temporal relation to pneumothorax onset should be assessed on every woman presenting with recurrent pneumothorax and

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intraoperative exploration of diaphragmatic surface should be performed in the patients with high suspicion of CP as the patients diagnosed with CP have a good outcome with surgery and hormone therapy.

Keywords Spontaneous pneumothorax (SP) • Catamenial pneumothorax (CP) • Endometriosis • Video assisted thoracoscopy (VAT) surgery • Pleurodesis • Hormone therapy

Introduction

Catamenial pneumothorax (CP) is an unusual condition affecting premenopausal women and commonly misdiagnosed as simple pneumothorax. It is characterised by its recurrence (more than two episodes) between the day before and within 72 hours after the onset of menstruation [1]. It has been associated with thoracic endometriosis but the aetiologia is not well understood and there is no unified agreement for its optimal management [2].

The term ''Catamenial'' is derived from a Greek word ''katamenios'' which means ''monthly''. The first case of chronic recurring pneumothorax in relation to menses was reported by Maurer et al. in 1958 but in 1938, Schwarz presented a hypothesis after noting concomitant haemoptysis and menstruation in women [3,4]. In 1953, Barnes described concurrent endometriosis and pleural haematomas, but the coexistence of these conditions was not unequivocally confirmed [5].

This phenomenon was later defined as catamenial pneumothorax by Lillington et al. in 1972 [6]. Awareness is still limited, with patients being misdiagnosed as primary spontaneous pneumothorax without identifying an underlying cause. There have been 350 cases of recurrent spontaneous pneumothorax synchronous with the menstrual cycles, reported in the literatures to date. The purpose of this study is to determine the incidence of CP among premenopausal females presented with pneumothorax, who were admitted for surgery, and to evaluate the result of their management.

Patients and Methods

A retrospective study for the period between January 2008 and June 2018 was conducted in four different hospitals (The Prince Charles Hospital, Holy Spirit Hospital, Greenslopes Private Hospital, and Mater Private Hospital) in Brisbane. The medical records of all the female patients aged 30 to 50 years admitted for surgery with a diagnosis of pneumothorax in that period were reviewed.

Results

A total of 120 premenopausal patients with pneumothorax were admitted over a 10-year period (Table 1) and five patients (4.1%) with ages from 36 to 50 years (mean 42.6 years) were diagnosed as CP based on surgical findings or histology (Table 2). The first case of CP was diagnosed in September 2013. In the last one-and-a-half years, the surgeons working in four different hospitals in Brisbane became proactive in inspecting diaphragm surface during Video Assisted Thoracoscopy surgery in cases of high suspicion for CP, consequently three new cases of CP were diagnosed in the last 12 months. Menstrual history was taken retrospectively after surgical diagnosis, which revealed onset of symptoms of pneumothorax within 72 hours of menstruation in four patients (80%). All patients had a history of more than two episodes of pneumothoraces and two of them had a past history of failed pleurodesis. Four patients had fenestrated perforations and pigmented nodules on the central tendon of the diaphragm (Figures 1–3) whereas one patient had a parietal pleural pigmented nodule (Figure 4) with a small haemopneumothorax and without a diaphragmatic lesion. All patients had lung parenchymal lesions in the form of blebs or scar. The histology of the diaphragmatic lesions and lung wedge biopsy were negative for endometriosis whereas the parietal pleural lesion was positive for oestrogen and progesterone receptors on immunohisto-chemistry profile and further histology confirmed endometriosis (Figures 5 and 6). The diaphragmatic defects were managed with VAT plication and the lung lesion was dealt with by wedge resection whereas the parietal pleural lesion was removed as an excision biopsy. All patients with diaphragmatic lesions underwent talc pleurodesis. However,

Table 1 **Total number of patients according to the hospital.**

Hospital	Total patients aged 30–50 yrs with pneumothorax admitted for surgery	Total patients diagnosed as Catamenial pneumothorax
The Prince Charles Hospital, Brisbane	61	2
Holy Spirit Northside Hospital, Brisbane	18	Nil
The Greenslopes Private Hospital, Brisbane	29	2
Mater Private Hospital, Brisbane	12	1
Total	120	5

Table 2 Details of the patients diagnosed with Catamenial pneumothorax.

Pt	Age at Sx	Menstruation hx	Endometriosis hx	Lung disease hx	PTx hx	Onset Side	Initial tx	Operative findings	Final Tx	Histology for endometriosis	Postoperative complication/ recurrence	Follow-up period (months)
1	43	48 hrs	Present	Asthma	3 PTx/6 mths. (Recurrence 6wks post Rt VAT RUL wedge resection and pleurodesis)	Rt	ICC x 3 and VAT RUL wedge resection + pleurodesis	Small bleb in apex of middle lobe, three <5 mm fenestrated holes on central tendon of diaphragm and 2 subpleural purple nodules	Redo Rt VAT diaphragmatic plication, wedge resection of RML apical bleb and talc pleurodesis + hormone therapy	Negative	None	12
2	44	72 hrs	None	Asthma	4 PTx episodes. Recurrent loculated Rt basal PTx - 2 PTx/6 mths (post Rt VAT pleurodesis 4 yrs ago)	Rt	ICC x 6, Rt VAT pleurodesis x 2	Adhesion of middle and upper lobe to chest wall, two fenestrated holes and few purple, black nodules on central tendon of the diaphragm	Redo Rt VAT diaphragmatic plication and talc pleurodesis + hormone therapy	Negative	None	11
3	40	<72 hrs; 5 mths postpartum	None	None	3 PTx /2 yrs	Rt	ICC x 3, persistent air leakage in the last procedure	RLL apical blebs and adhesion of RLL to the diaphragm. Multiple fenestrations with faint black nodules on the tendon of the Rt diaphragm	Rt VAT wedge resection RLL apex, and diaphragmatic nodal biopsy and plication repair	Negative	None	57
4	50	2 wks	None	None	3 PTx/4 mths; (Recurrence 2 mths post Rt VAT pleural biopsy)	Rt	ICC x 3, persistent air leakage	Thickened scar on RUL apical segment. Small amount of haemothorax with $5 \times 5\,mm^2$ dark coloured parietal pleural	Rt VAT pleural excision biopsy, GIA stapler resection of RUL apex	Positive	One recurrence of Rt Ptx in 2 mths - treated with Redo Rt VAT talc pleurodesis + hormone tx - nil recurrence since.	45

Table 2. (continued).

Pt	Age at Sx	Menstruation hx	Endometriosis hx	Lung disease hx	PTx hx	Onset Side	Initial tx	Operative findings	Final Tx	Histology for endometriosis	Postoperative complication/ recurrence	Follow-up period (months)
								Nodule. No abnormalities on the diaphragmatic surface				
5	36	<72 hrs	Present	None	2 PTx/2 mths while off OCP. Further 2 PTx/ 3 mths	Rt	ICC x 4	Small bleb in RUL with air leakage. Small fenestrations on the diaphragmatic surface	Rt VAT wedge resection RUL apex, and diaphragmatic plication repair	Negative	None	1

Abbreviations: Pt, patient; Sx, surgery; Hx, history; Tx, treatment; Wks, weeks; Mths, months; Yrs, years. Hrs, hours; PTx, pneumothorax; Rt, right; VAT, Video Assisted Thoracoscopy; ICC, intercostal catheter; RUL, right upper lobe; RLL, right lower lobe; RML, right middle lobe; GIA, gastro intestinal anastomosis.

Figure 1 Diaphragmatic defect.

the patient with parietal pleural lesions did not wish to undergo pleurodesis at the time of her diagnostic VAT surgery and subsequently re-presented with recurrence of pneumothorax within 2 months of surgery, ultimately undergoing a redo VAT talc pleurodesis. All patients were referred for gynaecology review and later commenced on GnRH analogous treatment. All the patients remained recurrence free at the latest follow-up, with a follow-up period between 1 and 57 months (mean of 25.2 months).

Discussion

Catamenial pneumothorax is the recurrent appearance of air in the pleural cavity in women of reproductive-age in the absence of other lung diseases. It has been accepted that 3–6% of primary spontaneous pneumothoraces (SP) in women meet this definition, however, recent studies indicate figures as high as 35% [7–10]. The clinical presentation of CP, including pain, cough and shortness of breath, is similar to that of any primary SP [1]. Consequently, many women with CP are initially diagnosed as having primary SP until a correlation with the menstrual cycles is made. In our series of 120 females between 30 to 50 years of age, only five (4.1 %) were diagnosed to have CP, the first case being diagnosed only 5 years ago. The infrequency and latency of diagnosis raises suspicion that CP may have been misdiagnosed in other cases, as in almost all cases in our series at The Prince Charles Hospital (TPCH) menstrual history was not taken during admission. The incidence of CP increased when the surgeons changed their usual VAT surgical practices for spontaneous pneumothorax by inspecting diaphragm surfaces in all highly suspicious cases of CP. Important distinctions for CP include the recurrent nature, almost exclusively right-sided presentation, an absence of smoking history or previous lung disease and patients are generally older than women with other forms of primary SP [1,8]. This is

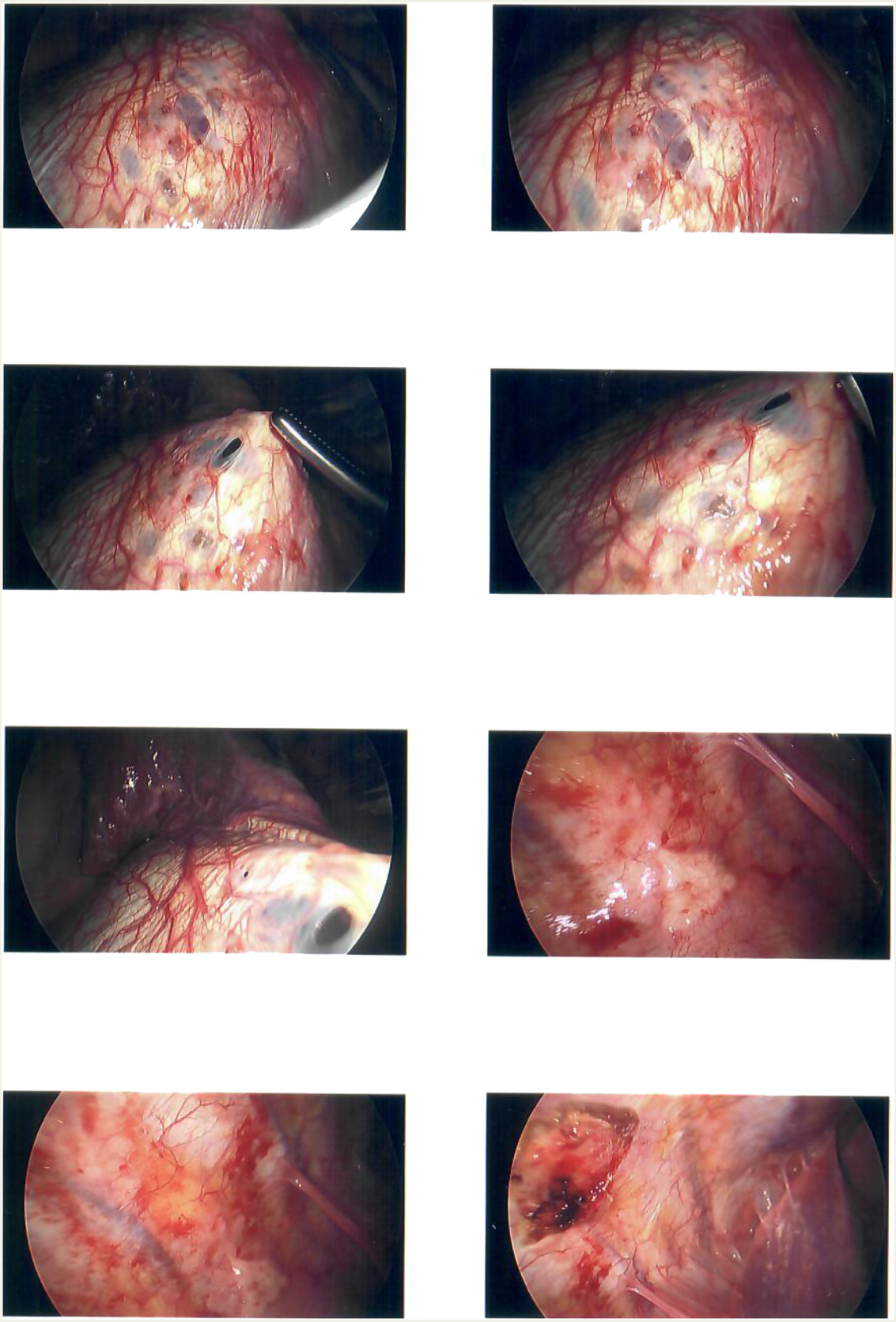

Figure 2 Diaphragmatic defects with dark nodules.

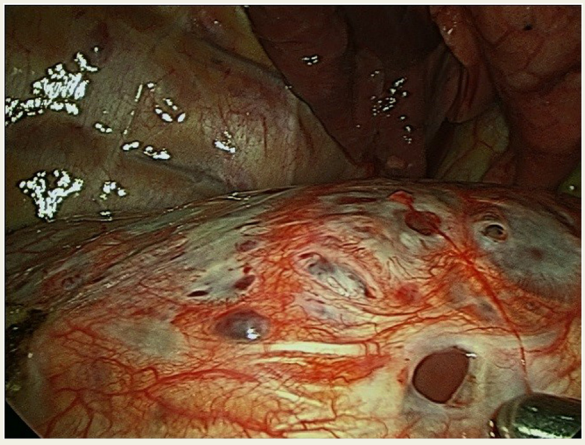

Figure 3 Diaphragmatic defects with dark nodules.

Figure 5 Oestrogen receptor stain of parietal pleural node.

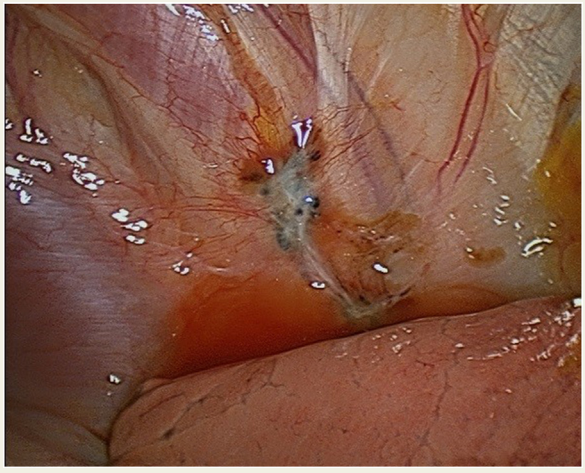

Figure 4 Parietal pleural nodule.

Figure 6 Immunohisto-chemistry of parietal pleural node.

consistent with our reported cases as the mean age of the patient was 42.6 years with no history of lung diseases and the right chest was involved exclusively.

Lillington et al. also characterised the features of CP and, since then, there has been an increase in case reports and retrospective studies conducted [6]. While the majority of CP are right-sided (70–95%), left-sided and bilateral occurrences have also been identified [1,5,11–15]. Studies indicate that the average age of women at first presentation with CP is in their thirties to forties, while the average age for non-CP is in the twenties to early thirties [1,5]. There have also been cases of CP during pregnancy [16,17]. These cases have been attributed to thoracic endometriosis where the pneumothorax is unrelated to the menstrual cycle. Whilst up to 65% of patients with CP have thoracic endometriosis, it does not explain all cases of CP [1,10]. Similar to CP, the pathogenesis of thoracic endometriosis remains unclear. There were two patients with a previous history of endometriosis in our series and in one patient, recurrence of pneumothorax occurred only when treatment with oral contraceptive pills was stopped.

There are many hypotheses for thoracic endometrial implantation as a cause of recurrent pneumothorax. The most favoured explanation of pathogenesis is Sampson's theory of retrograde menstruation with subsequent peritoneal implantation of endometrial tissue which spread to thoracic structures as a consequence of lymphovascular embolisation. The endometrial implant in the lungs undergoes monthly proliferation and bleeding causing enlargement of the alveolar space and disruption of the visceral pleura, resulting in a pneumothorax [6,12,18]. The coelomic metaplasia model is based on the concept that endometrium, peritoneal and pleural mesothelium share the same embryonic origin. Pathogenic stimuli could transform coelomic epithelium into endometrial tissue resulting in thoracic endometriosis [19,20]. The migration model proposes a retrograde movement of endometrial cells from the uterus through the fallopian tubes into the pelvic area and the diaphragm [18].

The right-sided predominance of CP may be explained by understanding peritoneal fluid circulation. Peritoneal fluid predominantly flows up the right para-colic gutter, allowing

endometrial cells to reach the right sub-diaphragmatic area with further spread prevented by the hepatic ligaments. The cyclical proliferation and necrosis of the cells perforate the diaphragm enabling the cells to migrate into the chest. This theory is supported by a study that showed the existence of viable endometrial cells in the peritoneal fluid which have the capability to implant outside of the uterus [18,21].

There are a few theories that attempt to explain the development of catamenial pneumothorax:

1 The physiological or hormonal theory suggests that the increase in prostaglandin Fα during ovulation causes contraction of blood vessels and bronchioles and at the same time sensitises pre-existing pulmonary blebs and makes them more prone to rupture [5]. This phenomenon leads to rupture of alveoli and the flow of air into the pleural space [22].
2 Another theory is that the liquefaction of cervical mucus plugs during menses allows retrograde flow of air through the uterus and the fallopian tubes into the peritoneal cavity. Through diaphragmatic defects resulting from the sloughing of endometrial implants, this air then passes through into the pleural cavity causing a pneumothorax [4].
3 The last and more widely accepted theory in the literature involves cyclical swelling and sloughing of thoracic endometrial implants inside terminal bronchioles causing localised hyperinflation by a check-valve mechanism, which in turn causes pneumothorax [12,13,23,24].

A diagnosis of catamenial pneumothorax in women is made based upon a detailed patient history, recurrence of pneumothorax and its conjunction with the onset of menses, or a history of endometriosis. In most cases it is diagnosed retrospectively by intraoperative anatomic findings or histological diagnosis, as in our cases. There is no specific tool for diagnosis although increased levels of serum Ca 125 antigen is a helpful marker [25]. Radiologically, there are no unequivocal criteria for the diagnosis of this condition. Clinical suspicion is essential in females of reproductive age with recurrent pneumothorax or hydro-pneuomothorax or pneumo-peritoneum concomitant with right-sided pneumothorax [26].

In our retrospective study, only 4.1% of total 120 patients over 10 years were diagnosed as CP as the key pathologic findings were multiple diaphragmatic perforations with endometrial implants in four cases and in one a suspicious parietal pleural lesion which was histologically positive for endometriosis. Like the controversy regarding its cause, the incidence of CP has varied in published case reports. However, with the awareness of the thoracic endometriosis syndrome and full examination of the chest cavity and diaphragm, its reported incidence is rising to as high as one in three women with spontaneous pneumothorax [27]. As noted in other series, awareness of the disease became apparent only in the last 5 years in our case series, moreover, the last three cases were diagnosed in the last 12 months when the surgeons became proactive in seeking diagnosis of CP. Patients diagnosed with CP in our series were 15 to 20 years older than females with spontaneous pneumothorax [28]. In about 38.8% of reported CP there were diaphragmatic lesions, whereas in our series it was 80% and therefore it is important to inspect the diaphragmatic area in all premenopausal women with pneumothorax presenting for surgery [29]. Bullae or blebs may also pre-exist, as in our case series, which could lead surgeons to erroneously presume the cause of pneumothorax and not examine the diaphragmatic area, thus misdiagnosing the case. This might be the case in most of our case series over 10 years as only 4.1 % of cases out of 120 cases of SP were identified as CP. A literature review showed that in 23.1% of all explored cases of CP, bullae or blebs were the only lesions discovered, where as in 8.5% no pathology was found [29]. Most authors underscore the importance of precise evaluation of diaphragmatic surfaces in cases of clinical suspicion.

Treatment of CP is also diverse. Most surgeons are in agreement that video-assisted bullectomy and pleurodesis are recommended in these cases. The main issue of contention is the extent of the intervention within the diaphragm, for example, whether to plicate the diaphragm or wide resection of it with a mesh repair. According to Korom et al., the mean time until recurrences was 24 months after removal of the diaphragmatic lesions without pleurodesis and 61 months after pleurodesis [29]. These results do not appear to be associated with the extent of the procedure, but rather with the influence of the presence of diaphragmatic defects on the increased rate of recurrence. Extensive resectional surgery of the involved diaphragm is associated with recurrence rates of 32% in 33 months, while other series demonstrating 40% recurrence during 52 months follow-up for diaphragm plication and pleurodesis [9,30,31]. We opted for the lesser invasive operative approach of VAT diaphragmatic plication followed by talc pleurodesis in all four cases with diaphragmatic lesions, performed by three different surgeons. One patient with a parietal pleural lesion underwent wide pleural biopsy without pleurodesis, however she had a recurrence within 2 months requiring repeat surgery and talc pleurodesis.

Pharmacotherapy, consisting of hormonotherapy to induce hypoestrogenism, is recommended in cases associated with endometriosis. Marjanski et al. recommend a multi-disciplinary approach to the management of the disease including, thoracic surgeon, gynaecologist, and endocrinologist [32]. We referred all diagnosed cases of CP to gynecology who commenced GnRH agonists therapy with resultant satisfactory short to midterm result of no recurrence (1 month to 57 months follow-up).

Summary

In conclusion, CP should be suspected in premenopausal females presenting with recurrent SP concomitant with menstruation. On admission, it is important to get a thorough menstrual history and its temporal relation to pneumothorax

onset and a precise evaluation of diaphragmatic surfaces during surgery in cases of clinical suspicion is mandatory. The diaphragmatic defects should either be resected and patched or plicated and a pleurodesis should always be performed. Surgical treatment combined with hormonotherapy gives better results than surgery alone.

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