Ann Thorac Cardiovasc Surg 2022; 28: 438–443
Online May 12, 2021
doi: 10.5761/atcs.cr.21-00005

*Case Report*

# Unexpected Histopathological Diagnosis of Placental Transmogrification of the Lung after Bullectomy for Recurrent Spontaneous Pneumothorax: A Case Report and Literature Review

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**We report a 33-year-old man who presented with recurrent right pneumothorax. Computed tomography (CT) showed the presence of a large bulla with a maximum diameter of 8 cm in the right middle lobe; he subsequently underwent bullectomy. Histopathology revealed that pulmonary parenchyma adjacent to the bulla represented nodular proliferation of clear cells characterized by a papillary structure resembling placental chorionic villi. Immunohistochemically, clear cells were positive for CD10, suggesting placental transmogrification of the lung (PTL). We reviewed 36 surgical cases of PTL, and only 2 cases (5.6%), including our case, were operated for spontaneous pneumothorax. Bullous lesions secondary to PTL tend to appear as unilateral large cystic masses in non-upper lobes, which is atypical for primary spontaneous pneumothorax (PSP). Although PTL is considered a very rare cause of secondary pneumothorax, we must carefully differentiate this condition.**

**Keywords:** placental transmogrification, spontaneous pneumothorax

## Introduction

Placental transmogrification of the lung (PTL) is a rare benign cystic or bullous lesion in which papillary structures resembling placental villi are pathologically represented, but the tissue has no placental function.[1)] The condition is histologically diagnosed and often found incidentally after surgery for cystic lesions. PTL is considered a histologic variant of unilateral bullous lesions, and often presents as a giant bullous lesion radiographically; however, the exact etiology is unknown.

Patients with PTL often develop respiratory symptoms, such as dyspnea, chest tightness, and cough caused by large emphysematous bullae.[2)] Hence, surgical removal of the lesion is necessary to relieve the patient's symptoms and improve respiratory function. However, there are only a few reported cases in which PTL was complicated by spontaneous pneumothorax.

Herein, we report the first case of PTL found accidentally after video-assisted thoracoscopic surgery (VATS) bullectomy for recurrent spontaneous pneumothorax, and we compare the clinical characteristics of PTL complicated by pneumothorax with those of primary spontaneous pneumothorax (PSP).

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Received: January 7, 2021; Accepted: March 8, 2021
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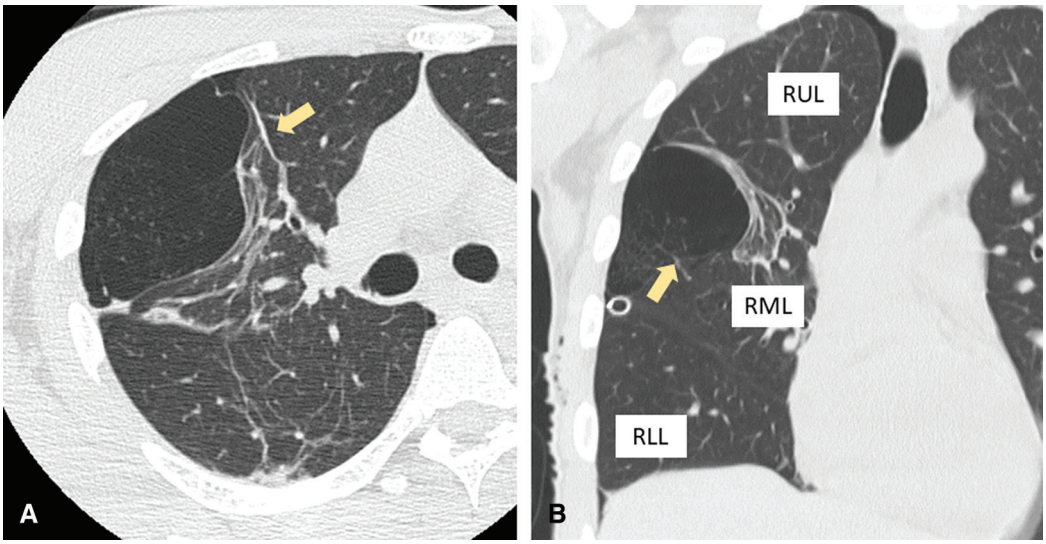


**Fig. 1** Axial (**A**) and coronal (**B**) chest CT views showing an emphysematous lesion with a maximum diameter of 8 cm in the right middle lobe occupying less than 30% of the right hemithorax (arrows). CT: computed tomography; RLL: right lower lobe; RML: right middle lobe; RUL: right upper lobe

## Case Report

The patient was a 33-year-old male who presented with sudden onset right anterior chest pain and dyspnea. He had a medical history of spontaneous pneumothorax at age 32 years, which was treated by conservative management without other interventions, and he was a 13-pack-year current smoker. He had no family history of spontaneous pneumothorax, and his height and body weight were 160 cm and 48 kg, respectively. Chest X-ray revealed a completely collapsed right lung with a large bulla (**Supplementary Figure 1**. All Supplementary Figure and Tables are available Online.). He was treated by chest tube insertion with subsequent admission to the hospital. Chest computed tomography (CT), which was performed after inflating the right lung, revealed a bullous lesion with a maximum diameter of 8 cm in the right middle lobe occupying less than 30% of the hemithorax (**Fig. 1A** and **1B**). No other abnormalities, such as other bullae, were identified in either lung.

Because the patient's pneumothorax was ipsilateral recurrent with a large bulla, he underwent VATS bullectomy with three ports on the second day of admission. We detected the large bullous lesion in the right middle lung of segment 4. There were no other cystic lesions in the apex of the lung or in the right lower lobe superior segment. Wedge resection of the middle lobe, including the bullous lesion, was performed using mechanical endoscopic staplers, and the staple line was covered with a polyglycolic acid sheet (Neoveil; Gunze Ltd., Kyoto, Japan). Neither mechanical nor chemical pleurodesis was performed. The chest tube was removed the day after the surgery, and the patient was discharged on the second postoperative day. Pathological examination of the resected specimen showed that the stroma of the tissue was uniformly proliferated with non-atypical cells possessing round uniform nuclei and clear foamy cytoplasm (**Fig. 2A**). In addition, the stroma was partially edematous, and the tissue structure resembled chorionic villi (**Fig. 2A**). Elastica van Gieson staining demonstrated disruption of the alveolar walls by the proliferated stromal cells (**Fig. 2B**), which were diffusely positive for CD10 by immunohistochemical staining (**Fig. 2C**), but negative for SMA and HMB45 (**Fig. 2D**). Additionally, proliferated stromal cells showed a low Mib-1 index (1%); hence, the patient was diagnosed with PTL. He has remained free from recurrent pneumothorax and PTL for 12 months.

## Discussion

To our best knowledge, there were 38 reported cases of PTL between 1995 and 2019 (**Supplementary Table 1**). Among these patients, 36 were diagnosed histologically after the surgery while one patient was diagnosed after biopsy, and the other after autopsy. **Table 1** shows the characteristics of the patients who underwent surgery. The mean age of the patients was 45 years (range, 24–72 years), and 81% (29/36) of the patients were men. In all,

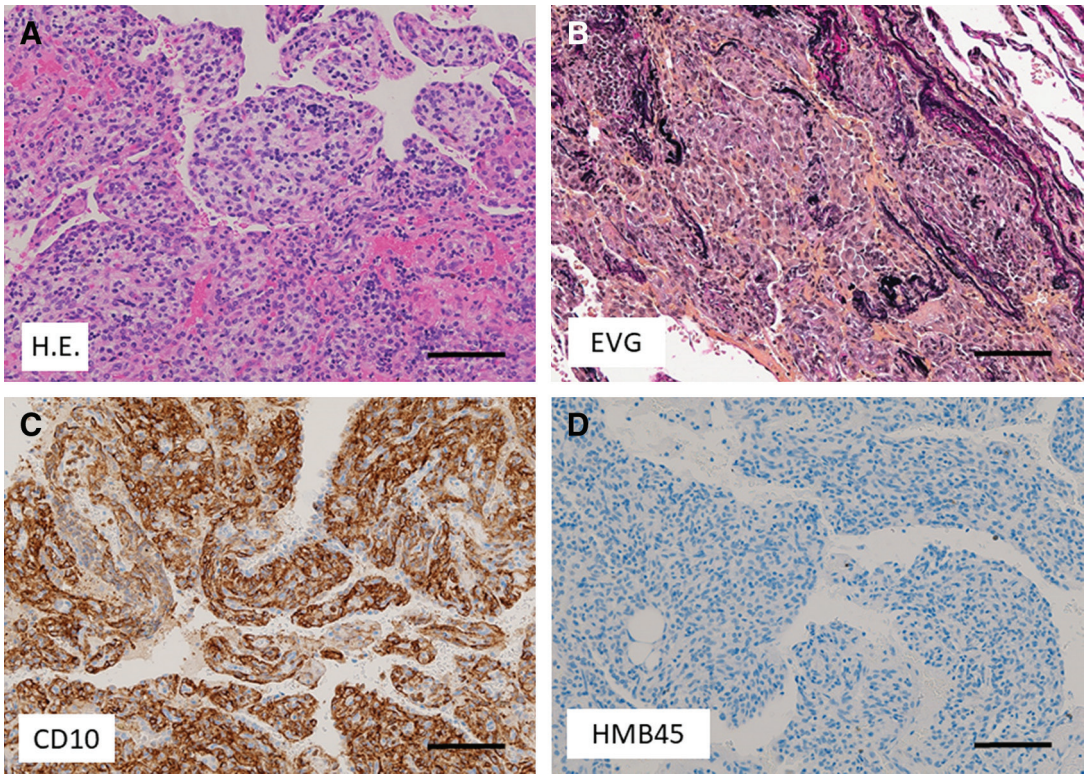


**Fig. 2** Conventional HE staining of a section of the resected specimen showing that the stroma of the tissue is partly edematous, and the tissue structure resembles chorionic villi (**A**). The proliferated stromal cells have disrupted the elastic fibers of the alveolar walls, which is visible with EVG staining (**B**). These cells were diffusely positive for CD10 (**C**) and negative for HMB45 (**D**). Bars: 100 μm; EVG: Elastica van Gieson; HE: hematoxylin and eosin

21 patients (58%) had respiratory symptoms, such as chest tightness and dyspnea owing to giant bullae or pneumothorax, whereas 9 (25%) patients were asymptomatic. CT findings of PTL showed a cystic lesion in 75% (27/36) of the patients; precisely, 11 (31%) demonstrated mediastinal shift, and 7 (19%) patients had giant bullae. Therefore, patients with PTL often require volume reduction surgery for giant bullae that cause respiratory symptoms. In contrast, only two patients, including our patient, underwent surgery for spontaneous pneumothorax.

We first considered that our patient had PSP; however, the CT findings were atypical compared with PSP. Typical pulmonary blebs or bullae are commonly located at the apex of upper lobes in patients with PSP.[3–6] As previously reported, the sizes of the bullae were smaller than 3 cm in 90% of patients who underwent surgery for PSP,[6] bullae are usually 2 cm in size.[7,8] In fact, blebs are more common than bullae in patients with PSP.[8] Additionally, contralateral asymptomatic bullae were found in 49% of the patients with unilateral PSP and more than 80% of existing bullae were multiple.[8] Therefore, the present case, with an 8-cm single unilateral bulla in the middle lobe, was too unusual to consider PSP.

Conversely, bullae secondary to PTL show different characteristics from bullae detected in PSP. As shown in **Table 1**, PTL lesions are located in the non-upper lung lobes (middle lobe: n = 2, lower lobe: n = 17) rather than in the upper lobe (n = 11). Moreover, no patients presented with bilateral lesions in previous reports. One study showed that among 12 patients with cystic lesions of PTL, the mean size of the pulmonary bullae was 6.5 cm.[2] Therefore, summarizing the characteristics of bullous lesions secondary to PTL, patients present with a relatively large single bulla that is often located in the non-upper lobes, unilaterally. If we find such atypical bulla in patients with pneumothorax and the patient refuses surgery, follow-up and monitoring the size of the bullous lesions may be recommended in case the bulla size increases, which could cause respiratory symptoms, as with PTL.

Four reported patients (11%) with PTL developed pneumothorax, including our patient (**Supplementary Table 2**). The reason for the low incidence of pneumothorax in

**Table 1 Characteristics of patients diagnosed with PTL after lung resection**

| Variable | n (%) or median (range) (n = 36) |
|---|---|
| Age, years | |
| Mean (years) | 44.8 (24–72) |
| Sex | |
| Male | 29 (80.6) |
| Female | 7 (19.4) |
| Symptoms or clinical presentation before surgery | |
| Asymptomatic | 9 (25.0) |
| Respiratory symptoms owing to giant bullae | 19 (52.8) |
| Respiratory symptoms owing to pneumothorax | 2 (5.6) |
| N/A | 6 (16.7) |
| Pneumothorax | |
| Yes | 4 (11.1) |
| No | 32 (88.9) |
| Imaging findings | |
| CT findings | |
| Cystic lesion | 27 (75.0) |
| Mass | 2 (5.6) |
| N/A | 7 (19.4) |
| Mediastinal shift | |
| Yes | 11 (30.6) |
| No | 25 (69.4) |
| Localization of PTL lesions | |
| Distribution | |
| Bilateral | 0 (0.0) |
| Unilateral | 36 (100.0) |
| Side | |
| Right | 21 (58.3) |
| Left | 15 (41.7) |
| Lobe location | |
| Upper | 11 (30.6) |
| Middle | 2 (5.6) |
| Lower | 17 (47.2) |
| N/A | 6 (16.7) |
| Surgical procedure | |
| Pneumonectomy | 7 (19.4) |
| Lobectomy | 11 (30.6) |
| Segmentectomy | 1 (2.8) |
| Wedge resection/bullectomy | 11 (30.6) |
| N/A | 6 (16.7) |

N/A: not available; PTL: placental transmogrification of the lung

patients with PTL is that PTL may be categorized as a subtype of giant bulla, which occasionally complicates pneumothorax. The bullae of PTL ranged from 0.5 cm to 20 cm in size,[2] while reported giant bullae ranged from 9 cm to 30 cm in size.[9] The common characteristics of the four reported patients who developed pneumothorax were that all were men with unilateral cystic lesions in the non-upper lobe (**Supplementary Table 2**). Of the four patients, two, including our case, underwent surgery for pneumothorax while two underwent surgery to address dyspnea owing to giant bullae. Our patient underwent wedge resection while the other patient underwent right middle lobectomy subsequent to completion pneumonectomy.[10] Regarding the surgical procedure for PTL (**Table 1**), 52% (19/36) of patients underwent anatomical thoracic surgery, such as lobectomy (n = 11), segmentectomy (n = 1), and pneumonectomy (n = 7) because of the suspicion of malignancy or difficulty performing wedge resection owing to giant bullae. However, even in 31% of the patients who underwent wedge resection, no recurrent PTL was reported. Therefore, wedge resection is an acceptable procedure for PTL, and early surgery may allow proceeding to wedge resection instead of

anatomical resection, by preserving lung function.[2] However, most cases were followed only short term; within 1 year. Because the etiology of PTL is uncertain, following patients for several years after surgery may be best.

In the present case, we diagnosed PTL incidentally, although we first considered PSP. The utility of routine histological examination of clinical PSP specimens has been questioned.[11] However, Sauter et al.[12] reported that in spontaneous pneumothorax specimens, clinically significant unexpected histological findings were identified in 8.3% of the specimens, including lung cancer, endometriosis, and Birt–Hogg–Dube syndrome. This study showed that routine histological examination of spontaneous pneumothorax specimens is justified, in that this examination discloses unexpected findings that are clinically significant and that impact patient management. Because PTL was found incidentally after bullectomy for spontaneous pneumothorax in our patient, we must consider differential diagnoses such as PTL, especially with atypical CT findings. Moreover, it is important to share clinical information associated with atypical bullae with pathologists because there is a possibility of unexpected diagnoses, such as rare diseases like PTL.

General pathological findings of PTL are papillary structures resembling placental villi.[1] The structures are covered by hyperplastic pneumocytes, and contain interstitial cells with abundant clear cytoplasm.[13] Immunologically, the interstitial cells are positive for CD10 and, focally for vimentin, and these cells are negative for smooth muscle actin, desmin, S100 protein, HMB45, MART1, CD68, CD34, CD117, BCL2, TTF1, chromogranin, and cytokeratin.[13] The pathological findings in our patient showed typical histological findings of PTL. Although PTL is rare, positive-CD10 staining of interstitial cells is specific to PTL, which helps easily differentiate PTL from other cystic diseases, such as alveolar adenoma, congenital lesions, or lymphangioleiomyomatosis.[14]

The pathogenesis of the lesion in PTL is still unclear, and there are various theories. PTL is not considered to be associated only with cystic or emphysematous lung lesions but also with pulmonary fibrochondromatous hamartomas and pulmonary lipomatosis.[15] One study suggested that the lesion primarily represents a benign proliferation of peculiar interstitial cells with secondary cystic change.[13] The present case also demonstrated that the stromal cells disrupted and destroyed the alveolar walls' elastic fibers, which may result in degeneration of alveoli and lead to coalescence into a bulla.

## Conclusion

We have reported a case of PTL diagnosed incidentally after VATS bullectomy for recurrent pneumothorax. In the case of spontaneous pneumothorax caused by atypical large bullae located in the non-upper lobes unilaterally, PTL should be considered in the differential diagnosis. Moreover, surgery may be the best approach, not only to prevent recurrent pneumothorax but also to treat PTL, which has the potential to become giant bullae.

## Acknowledgment

We thank Jane Charbonneau, DVM, from Edanz Group (https://en-author-services.edanz.com/ac) for editing a draft of this manuscript.

## Disclosure Statement

The authors have no conflicts of interest to declare.

## References

1) Santana AN, Canzian M, Stelmach R, et al. Placental transmogrification of the lung presenting as giant bullae with soft-fatty components. Eur J Cardiothorac Surg 2008; **33**: 124–6.
2) Ma DJ, Liu HS, Li SQ, et al. Placental transmogrification of the lung: case report and systematic review of the literature. Medicine (Baltimore) 2017; **96**: e7733.
3) Donahue DM, Wright CD, Viale G, et al. Resection of pulmonary blebs and pleurodesis for spontaneous pneumothorax. Chest 1993; **104**: 1767–9.
4) Olesen WH, Katballe N, Sindby JE, et al. Surgical treatment versus conventional chest tube drainage in primary spontaneous pneumothorax: a randomized controlled trial. Eur J Cardiothorac Surg 2018; **54**: 113–21.
5) Light RW, Lee YCG. Pneumothorax, Chylothorax, Hemothorax and Fibrothorax. In: Murray and Nadel's Textbook of Respiratory Medicine 6th ed. Amsterdam Elsevier, 2016; 1439–60.e10.
6) Ouanes-Besbes L, Golli M, Knani J, et al. Prediction of recurrent spontaneous pneumothorax: CT scan findings versus management features. Respir Med 2007; **101**: 230–6.
7) de Bakker HM, Tijsterman M, de Bakker-Teunissen OJG, et al. Prevalence of pulmonary bullae and blebs in postmortem CT imaging with potential implications for diving medicine. Chest 2020; **157**: 916–23.
8) Jang HJ, Lee JH, Nam SH, et al. Fate of contralateral asymptomatic bullae in patients with primary spontaneous pneumothorax. Eur J Cardiothorac Surg 2020; **58**: 365–70.

9) Krishnamohan P, Shen KR, Wigle DA, et al. Bullectomy for symptomatic or complicated giant lung bullae. Ann Thorac Surg 2014; **97**: 425–31.
10) Fidler ME, Koomen M, Sebek B, et al. Placental transmogrification of the lung, a histologic variant of giant bullous emphysema. Clinicopathological study of three further cases. Am J Surg Pathol 1995; **19**: 563–70.
11) Khan OA, Tsang GM, Barlow CW, et al. Routine histological analysis of resected lung tissue in primary spontaneous pneumothorax – is it justified? Heart Lung Circ 2006; **15**: 137–8.
12) Sauter JL, Butnor KJ. Pathological findings in spontaneous pneumothorax specimens: does the incidence of unexpected clinically significant findings justify routine histological examination? Histopathology 2015; **66**: 675–84.
13) Cavazza A, Lantuejoul S, Sartori G, et al. Placental transmogrification of the lung: clinicopathologic, immunohistochemical and molecular study of two cases, with particular emphasis on the interstitial clear cells. Hum Pathol 2004; **35**: 517–21.
14) Theile A, Müller KM. Placentoid malformation of the lung. Pathologe 1998; **19**: 134–40.
15) Kim JW, Park IH, Kwon W, et al. Placental transmogrification of the lung. Korean J Radiol 2013; **14**: 977–80.