Giant pulmonary sclerosing pneumocytoma with potentially malignant biological behavior: a case report and literature review

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Background: Pulmonary sclerosing pneumocytoma (PSP) is a rare benign lung tumor which generally presents as a solitary pulmonary nodule in middle-aged females. However, the PSP in some patients exhibits potentially malignant biological behavior, with recurrence and lymphatic or distant metastasis being observed.

Case Description: We encountered a case of a 46-year-old female with an inordinately massive tumor 9.5 cm in diameter and a relatively high Ki-67 proliferation rate. Fine needle aspiration (FNA) played a significant but limited role in the preoperative diagnosis: the computed tomography (CT)-guided lung puncture biopsy was consistent with the typical pathology of PSP; however, endobronchial ultrasound-guided transbronchial lung biopsy (EBUS-TBLB) could not provide a definitive diagnosis. The patient ultimately underwent thoracoscopic resection and mediastinal lymph node dissection. Here, we provide a review of the literature on patients with PSP with malignant biological behavior to raise awareness of the malignant potential of PSP and describe our experience to inform future management.

Conclusions: PSP lacks specificity in its clinical and radiological characteristics and has complex pathological manifestations. FNA is valuable in the diagnosis and differential diagnosis of PSP but involves the risk of misdiagnosis or missed diagnosis. Additionally, we believe that the accepted benign features of PSP need to be updated and that the potential malignant features of PSP should be carefully monitored. Surgical resection is curative but strict follow-up is crucial.

Keywords: Pulmonary sclerosing pneumocytoma (PSP); adenoma; Ki-67; immunohistochemistry; case report

Submitted Aug 14, 2022. Accepted for publication Mar 17, 2023. Published online Jun 14, 2023.
doi: 10.21037/atm-22-4049
View this article at: https://dx.doi.org/10.21037/atm-22-4049

Introduction

Pulmonary sclerosing pneumocytoma (PSP), a rare pulmonary benign tumor, was originally described by Liebow and Hubbell as a tumor of vascular origin with obvious sclerosis (1) and thus named "sclerosing hemangioma". With the development of pathology and immunohistochemical techniques, it was eventually confirmed to originate from primitive respiratory epithelial

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cells (type II alveolar cells) and to consist of 4 structures (solid, sclerotic, papillary, and hemangiomatoid) in histopathology. In 2015, the World Health Organization officially changed its name to "sclerosing alveolar cell tumor" and classifies it as an adenoma subtype (2). However, it has been recently found that some patients with PSP develop lymphatic or distant metastasis. Qilu Hospital of Shandong University admitted a patient with a giant PSP 9.5 cm in diameter that had potentially malignant biological behavior, which is extremely rare. To increase clinician awareness, we have summarized the clinical, imaging, and pathologic features of PSP; provided recommendations for management; and reviewed the potential malignant features of PSP. We present this article in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4049/rc).

Case presentation

General information

A 46-year-old female presented with dry cough and dyspnea for 17 consecutive days. She reported no hemoptysis, chest pain, or fever. Chest computed tomography (CT) from a local hospital revealed a huge space-occupying lesion on the right side of the mediastinum. For further diagnosis and treatment, she was transferred to the department of Pulmonary and Critical Care Medicine, Qilu Hospital of Shandong University. The timeline in *Figure 1* shows the historical and recent care information of the patient. She was a nonsmoker, and there was no notable disorder in her family history. On physical examination, the patient was alert but not in acute distress. Her vital measurements were as follows: pulse, 64 beats per minute; respiratory rate, 18 breaths per minute; blood pressure, 104/64 mmHg (1 mmHg =0.133 kPa); and temperature, 36.3 ℃. No superficial lymphadenopathy was palpable. Her heart rate was regular and without a murmur. The right upper lung percussion was solid, breath sounds were weakened, and the remainder of the lungs were clear. The neurologic and abdomen examinations were unremarkable. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Highlight box

Key findings

- We encountered a case of pulmonary sclerosing pneumocytoma (PSP) of massive size and a relatively high proliferation rate, for which a rigorous diagnostic process was needed. In this report, we summarize the clinical, imaging, and pathologic features of PSP to provide recommendations for its management.

What is known and what is new?

- PSP is a rare pulmonary benign tumor, generally isolated, and has a diameter less than 3 cm.
- PSP lacks specificity in clinical and radiological characteristics.
- PSP has complex pathological manifestations.
- PSP shows potentially malignant biological behavior.
- Fine-needle aspiration for PSP can be useful but limited in diagnosis and differential diagnosis.
- Surgical treatment is the preferred treatment for PSP.

What is the implication, and what should change now?

- The diagnosis and treatment of PSP require a concerted effort among clinicians, radiologists, and pathologists. The currently accepted potential malignant features of PSP should be reviewed and updated.

Imaging examination

Chest CT scans revealed a large soft-tissue mass shadow 8.9 cm × 7.1 cm in size with multiple spot-like calcification foci in the right lung. The adjacent lung tissue was compressed, and the internal density was not uniform (*Figure 1A*). Contrast-enhanced CT showed multiple vascular shadows in the arterial phase, delayed enhancement in the surrounding area, and a clear boundary (*Figure 1B,1C*). The mediastinum was centered, not enlarged, and without swollen lymph nodes. Bilateral fibrous foci with slight inflammation were observed in the right lung.

Laboratory and other examinations

The white-cell count was 4.71×10^9 per liter, with 67.9% neutrophils and 26.8% lymphocytes; the hemoglobin was 109.0 g per liter; and the platelet count was 408×10^9 per liter. The albumin level was 37.6 g per liter, the erythrocyte sedimentation rate was 78.00 mm per hour, and the neuron-specific enolase level was 20.90 ng per milliliter (normal range, 0 to 16.3). Bronchoscopy showed external bronchial constriction in the middle lobe of the right lung (RML) but no obstruction in the remaining bronchus. The patient

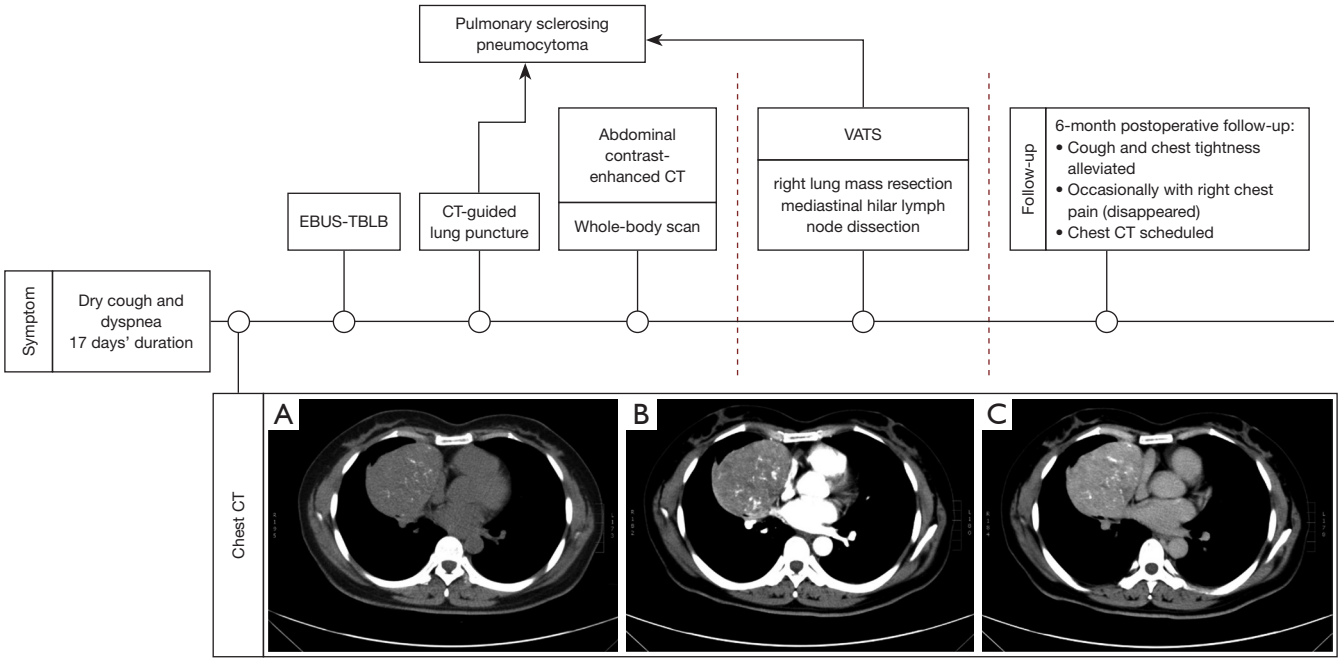

Figure 1 The timeline of the historical and recent care of the patient. Chest CT: (A) a routine scan revealed a large, soft-tissue mass with multiple spot-like calcifications. (B) Contrast-enhanced scans showed multiple vascular regions of the tumor in the arterial phase. (C) Delayed enhancement was observed in the surrounding area. CT, computed tomography; EBUS-TBLB, endobronchial ultrasound-guided transbronchial lung biopsy; VATS, video-assisted thoracoscopy.

subsequently underwent endobronchial ultrasound-guided transbronchial lung biopsy (EBUS-TBLB) which revealed a handful of lymphocytes and epithelia, but this did not help in making a definitive diagnosis. Later, a CT-guided lung puncture biopsy was performed as was a head and abdomen contrast-enhanced CT and whole-body scan to assess her overall condition. Fortunately, no signs of distant metastasis were found.

Diagnosis and treatment

The pathology findings of CT-guided lung puncture biopsy were consistent with those of PSP. After pre-operative pathological evaluation, the patient underwent right lung mass resection and mediastinal hilar lymph node dissection via video-assisted thoracoscopy (VATS). Intraoperatively, there was a poorly circumscribed tumor 9.5 cm × 8 cm × 5 cm in size observed microscopically at the junction of the upper and middle lobes of the right lung. It was nodular and soft to the touch with a grayish yellow or white cut surface. Multiple small lymph nodes were also found in the mediastinal hilum. Postoperative pathological hematoxylin and eosin (HE) staining showed that the tumor was composed of surface cuboidal-like cells and round interstitial cells with typical histological structure, which consisted of 4 histomorphologies including hemangioma-like areas, solid cellular areas, adenoid papillary areas, and fibrosclerotic areas. Dilated blood cell pools were found in the hemangioma-like areas, and tumor cells were scattered throughout the vascular spaces (*Figure 2A-2C*). The solid cellular areas showed a dense cellular distribution and mainly consisted of round interstitial cells (*Figure 2D-2F*). The adenoid papillary areas were composed of branching papillae covered by surface cuboidal-like cells, with interstitial cells and focal sclerosis scattered in the axial structure (*Figure 2G-2I*). Additionally, there was marked proliferation of fibrous tissue with hyalinization in the fibrosclerotic areas (*Figure 2J-2L*). Immunohistochemistry showed positivity for both thyroid transcription factor-1 (TTF-1) and epithelial membrane antigen (EMA), with cytokeratin 7 (CK7) and napsin-A positivity on the surface cuboidal cells, and an approximately 15% positivity in the Ki-67 hot spot region (*Figure 3*). Furthermore, fibroplasia and chronic inflammatory cell infiltration, accumulation of

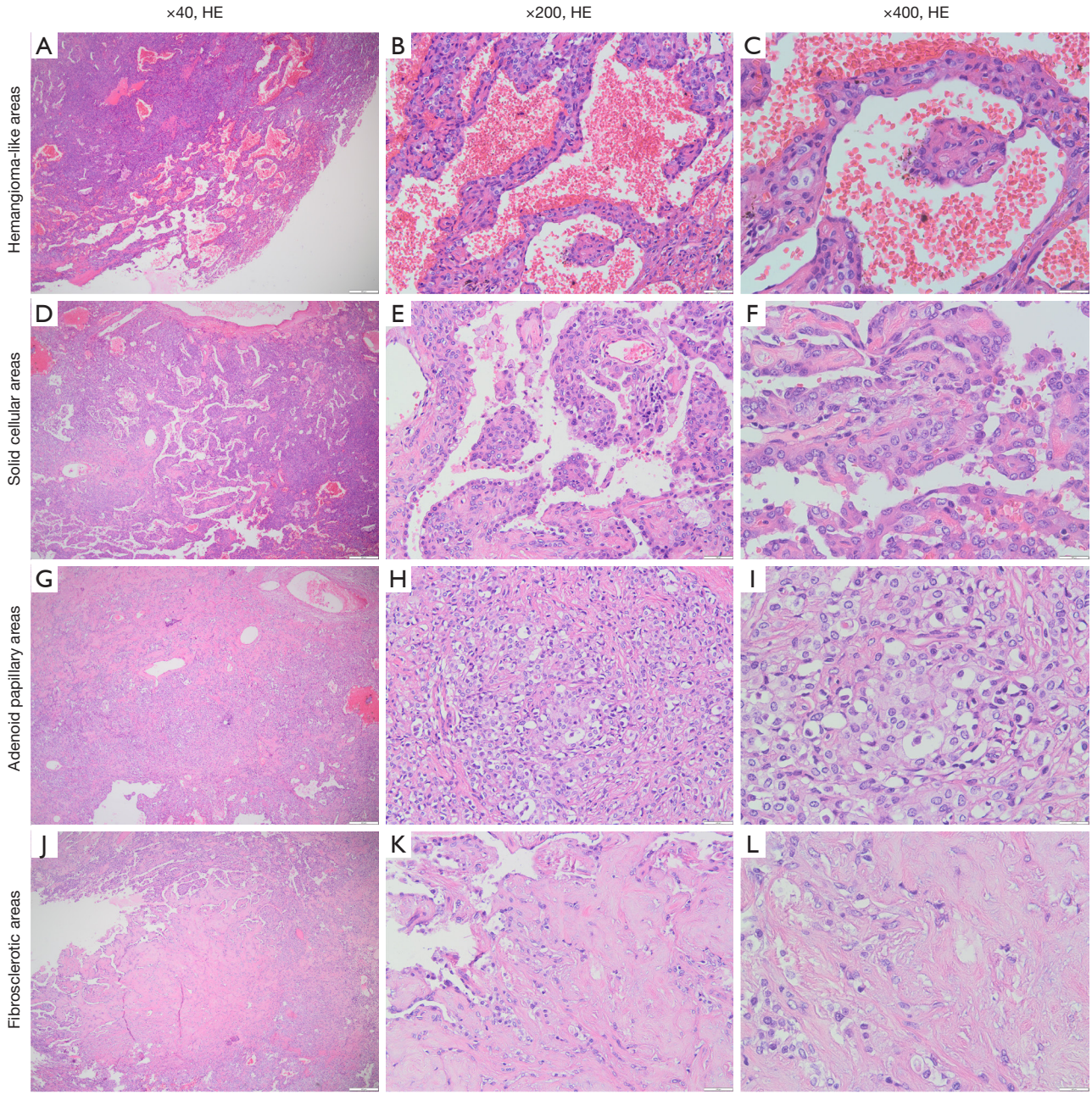

Figure 2 HE staining of the postoperative tissue consisted of 4 typical histomorphologies, including (A-C) hemangioma-like areas, (D-F) solid cellular areas, (G-I) adenoid papillary areas, and (J-L) fibrosclerotic areas. The slides were examined at ×40, ×200, and ×400 magnification. The scale bar indicates 100 μm. HE, hematoxylin and eosin.

foamy histiocytes, and multifocal multinucleated giant cell reactions were observed in the extracapsular lung tissue. No tumor cells were found in the extracapsular lung or lymph nodes. The patient's cough and chest tightness were alleviated, 6 months postoperatively, but with occasional right chest pain. Otherwise, the patient's work and life were as usual. The possible cause of the pain was given to the patient and relevant medical advice was given to her. At

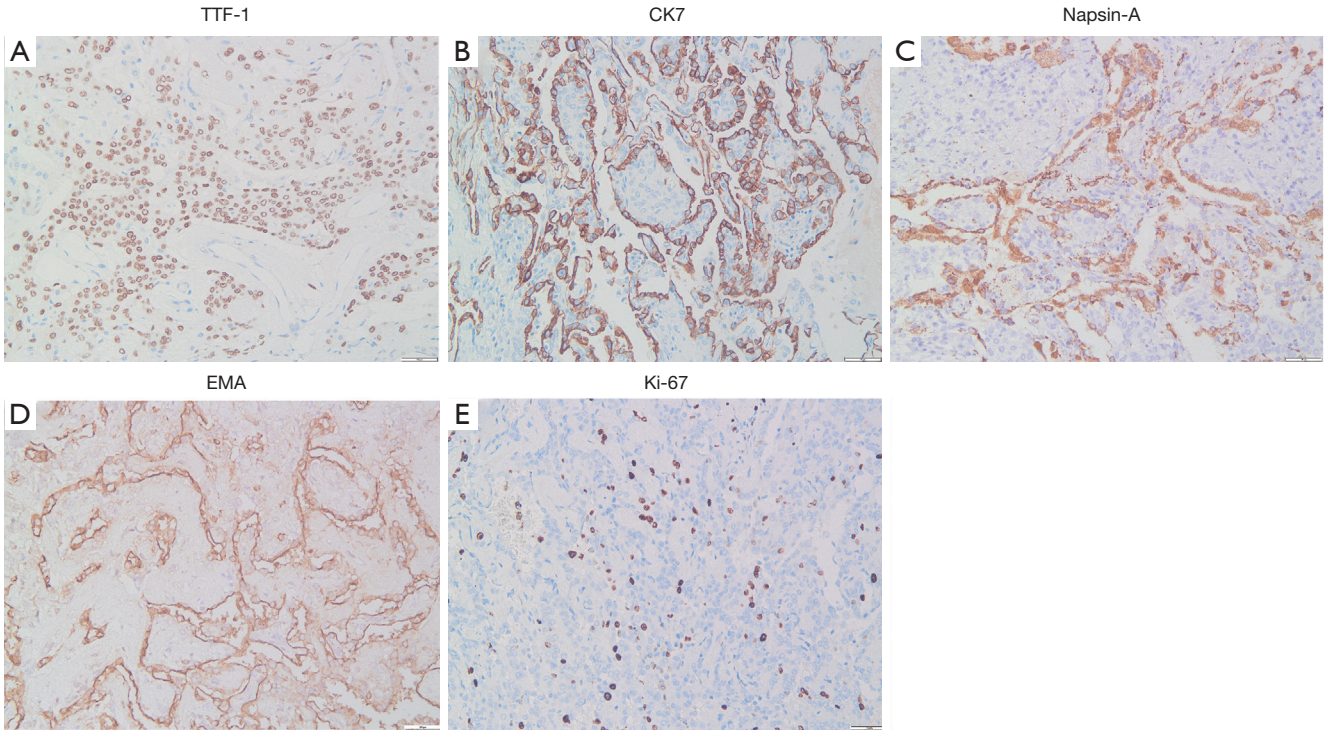

Figure 3 Immunohistochemical results of postoperative pathology. Immunohistochemistry revealed the patient was positive for (A) TTF-1, (B) CK7, (C) napsin-A, and (D) EMA in the surface cuboidal cells and (E) approximately 15% positive for Ki-67 in the hot spot area. The magnification is ×200, and the scale bar indicates 100 μm. TTF-1, transcription termination factor-1; CK7, cytokeratin 7; EMA, epithelial membrane antigen.

the recent follow-up, we were pleased to learn that she was already free from chest pain. A follow-up of chest CT will be scheduled.

Discussion

PSP is most common among Asian middle-aged women with no smoking history. The male to female ratio of PSP is 1:5 (3-5), which may be associated with the positive expression of the estrogen and progesterone receptors (6). The clinical manifestations of PSP lack specificity. Some patients present with nonspecific respiratory symptoms, such as cough, expectoration, shortness of breath, chest tightness, hemoptysis, and chest pain, while PSP is only occasionally found in imaging examinations (7). In rare cases, fever is the first symptom of PSP (8). Some patients with PSP have concurrent neuroendocrine disorder and autoimmune disease, such as scleroderma and rheumatoid arthritis (9,10). In our case, the respiratory symptoms were obvious and manifest as dry cough and dyspnea, which was considered to be related to the compression of the surrounding tissues.

Imaging examination is a significant auxiliary method for detecting PSP. Typical cases usually show isolated round or quasi round nodules or masses, often have a clear boundary and uniform density, and are accompanied by calcification and cystic degeneration, while few are lobulated (11). Moreover, 73.7% of isolated PSPs are smaller than 3 cm in average diameter (4), and rare cases of giant PSP have also been reported, including cases with tumors measuring 14 and 19 cm in size (12,13). PSP is more commonly found in a peripheral pattern and mainly distributed in the RML or lower left lobe (LLL) or right lobe (RLL) of the lungs (14). Multiple or diffuse PSP is rare, even in the mediastinum and bronchial lumen (11,15). The boundary in more than one-third of cases is not clear, and the pathological findings show invasive growth to the surrounding tissues (16). In some cases, invasive growth is distributed near the pleura or hilum, or there are malignant signs such as burrs and pleural depression, which are easily misdiagnosed as lung cancer

and require careful clinical decision-making. In one report, enhanced CT combined with texture analysis was used to locate calcification, and arterial phase CT values could assist in differentiating PSP from peripheral lung cancer (17). Depending on the different tissue structures of the lesion, different degrees of enhancement may occur in the early stage after enhanced scanning (14). Other less common CT signs of PSP, such as the halo sign, air crescent sign, caudal sign, and hemagglutination sign (11,18), are required to differentiate PSP from pulmonary aspergillosis, tuberculosis (TB), hamartoma, and other diseases. Shin *et al.* (19) reported a 19-year-old male patient who simulated active pulmonary TB. His CT showed aground-glass shadow in the right upper lobe, but no significant improvement was observed after anti-TB treatment, and the final pathology confirmed PSP. In patients suspected of TB but with a poor response to anti-TB treatment, PSP should be additionally considered, especially in younger patients. Our case had a large isolated mass in the right lung with calcification, a clear boundary, and delayed enhancement, which required a definitive differential diagnosis from sarcoma, teratoma, and inflammatory pseudotumor using further histopathology. ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET)-CT may have certain utility for diagnosis but is somewhat limited in this regard. PSP mostly shows mild to moderate uptake of FDG, and the maximum standardized uptake value (SUVmax) may inform speculation upon the specific pathological type and is positively correlated with the tumor size of typical PSP (20,21). However, it should be noted that false-positive high uptake results mimic the presentation of malignancy or lung metastases and may affect clinical decision-making, especially in patients with a primary tumor (22,23).

The histological morphology of PSP is complex and consists of 4 histomorphologies (hemangioma-like areas, adenoid papillary areas, solid cellular areas, fibrosclerotic areas) and 2 types of tumor cells (cuboidal cells and stromal cells) (2). FNA is valuable for the diagnosis and differential diagnosis of PSP but is associated with the risk of misdiagnosis or missed diagnosis. Interestingly, PSP may be misdiagnosed as a papillary or solid subtype of lung adenocarcinoma or neuroendocrine tumor in patients with atypical histopathology or clinical outcomes of recurrence or metastasis (24). The cytomorphologic manifestations of typical PSP may partially overlap with those of patients with well-differentiated lung adenocarcinoma. Nonetheless, the results of immunohistochemistry, specifically positivity for TTF-1 and EMA in surface cuboidal-like cells and round interstitial cells, may facilitate differential diagnosis, as was found in our case (25). In addition, the challenges posed by intraoperative frozen diagnosis of PSP are substantial. Yang *et al.* (24) retrospectively analyzed 59 patients with PSP who underwent intraoperative frozen section examination and identified the diagnostic accuracy to be only 44.1%, with a misdiagnosis rate of 16.9%. Shang *et al.* (26) found that patients with PSP of a size of smaller than 1 cm were misdiagnosed at an 11.1% rate, and they suggested that failing to identify a double cell population and cellular atypia caused misdiagnosis. Given the limited tissue representation, we recommend further definitive pathohistological diagnosis after complete resection of the mass.

We completed a literature review to identify the borderline features of PSP. Relevant case reports were retrieved from PubMed and Web of Science using the search terms "Pulmonary sclerosing pneumocytoma", "metastasis", and "progression". All case reports of PSP with malignant biological behavior were included in the analysis. Instead of focusing on histologic atypia, we defined malignant biological behavior as rapid tumor proliferation, metastasis, or invasion. All data collected (such as patient age, gender, symptom, tumor size, tumor location, metastatic site, Ki-67 proliferation index, treatment, and diagnosis) were entered into SPSS Statistics 25.0 (IBM Corp.) for statistical analysis. In *Table 1* and *Table 2*, we provide an inductive summary of the clinical features of 38 patients with PSP with malignant biological behavior. Asymptomatic middle-aged females were predominant. The median mass size was 35 [interquartile range (IQR), 24.00–80.00] mm, and most masses were located in the LLL. For metastatic sites, 86.49% showed lymphatic metastasis, few showed endobronchial invasion or pleural metastasis, and extrapulmonary metastases such as liver and bone were also reported.

The mechanisms of the malignant biological behavior of PSP are not completely understood. The stromal spindle cells may be involved in tumor metastasis. In a middle-aged female patient with peribronchial lymph node metastasis, spindle cells were found in her lymph node metastasis, and immunohistochemistry confirmed interstitial spindle cells to be derived from the tumor (49). A retrospective review of 239 patients with PSP by Gao *et al.* (48) yielded a lymph node metastasis rate in those with dense spindle stromal cells of 20%. Matrix metalloproteinase-9 (MMP-9) overexpression and epithelial-mesenchymal transition (EMT) of surface cells may also participate in the

Table 1 Review of PSP cases with malignant biological behavior

Patient no.	Source, year	Age (years)/sex	Symptoms	Tumor location	Primary tumor size (mm)	Metastatic site	Ki-67 (%)	Treatment
1	Spencer *et al.*, 1986 (27)	NA/NA	NA	NA	NA	Lymph node	NA	NA
2	Tanaka *et al.*, 1986 (28)	22/M	None	RLL	50	Hilar lymph node	NA	NA
3	Devouassoux-Shisheboran *et al.*, 2000 (4)	18/F	None	LLL	35	Hilar lymph node	NA	NA
4	Nicholson *et al.*, 2002 (29)	53/M	Chest pain	LLL	35	Peribronchial lymph node	NA	NA
5	Miyagawa-Hayashino *et al.*, 2003 (30)	10/F	Flu-like	RML	47	Regional lymph node	NA	Lobectomy and lymph node dissection
6	Miyagawa-Hayashino *et al.*, 2003 (30)	45/F	Flu-like	RUL	25	Hilar lymph node	NA	Lobectomy and lymph node dissection
7	Miyagawa-Hayashino *et al.*, 2003 (30)	45/M	None	LLL	37	Mediastinal lymph node	NA	Lobectomy and lymph node dissection
8	Miyagawa-Hayashino *et al.*, 2003 (30)	56/F	None	LLL	15	Peribronchial lymph node	NA	Lobectomy and lymph node dissection
9	Kim *et al.*, 2003 (31)	19/F	Cough	LLL	100	Interlobular and hilar lymph nodes	NA	Lobectomy, lymph node dissection, chemotherapy
10	Chan *et al.*, 2003 (32)	19/M	Chest pain, cough	LUL	30	Interlobular lymph node	NA	Lobectomy
11	Kim *et al.*, 2004 (6)	37/F	NA	LLL	20	Peribronchial lymph node	NA	Lobectomy
12	Katakura *et al.*, 2005 (33)	35/M	None	LLL	30	Hilar lymph node	NA	Lobectomy
13	Wani *et al.*, 2007 (34)	47/F	Cough	RUL	48	Right bronchus, segmental bronchus, and peripheral bronchioles	NA	Lobectomy, bronchoplasty, and lymph node dissection
14	Chien *et al.*, 2009 (35)	18/M	None	LUL	80	Lymph node	NA	Lobectomy and lymph node dissection
15	Vaideeswar, 2009 (36)	23/M	Cough, hemoptysis	RUL	90	Regional lymph node	NA	Lobectomy
16	Anan *et al.*, 2010 (37)	38/M	None	RML	20	lymph node	NA	Lobectomy

Table 1 (*continued*)

Table 1 (*continued*)

Patient no.	Source, year	Age (years)/sex	Symptoms	Tumor location	Primary tumor size (mm)	Metastatic site	Ki-67 (%)	Treatment
17	Park *et al.*, 2011 (38)	NA/NA	NA	LUL	NA	Left upper pulmonary vein lymph node	NA	Lobectomy and lymph node dissection
18	Suzuki *et al.*, 2011 (39)	57/F	None	RLL	25	Pleura	NA	Lobectomy
19	Kita *et al.*, 2013 (40)	38/F	None	LLL	39	Interlobular lymph node	NA	Segmentectomy and lymph node sampling
20	Adachi *et al.*, 2014 (41)	40/F	None	LLL	10	Hilar lymph node	NA	Lobectomy and lymph node dissection
21	Kim *et al.*, 2015 (42)	73/F	None	RLL	NA	Bone (L3), peribronchial, and mediastinal lymph nodes	<5	Lobectomy and lymph node dissection
22	Xu *et al.*, 2015 (43)	26/F	None	RUL	97	Peribronchial and hilar lymph nodes	<1, partly 10	Lobectomy and lymph node dissection
23	Pokharel *et al.*, 2016 (44)	33/F	None	LLL	18	Peribronchial lymph node	NA	Lobectomy
24	Jiang *et al.*, 2017 (16)	66/F	Cough, abnormal sputum	RML	21	Multiple intrapulmonary metastases	2	No surgery
25	Soo *et al.*, 2017 (45)	40/F	NA	RLL	25	Interlobular, hilar, and right subcarinal lymph nodes	NA	Lobectomy
26	Wang *et al.*, 2018 (46)	26/F	None	LLL	40	Mediastinal and regional lymph nodes	3	Lobectomy and lymph node dissection
27	Teng *et al.*, 2019 (47)	64/M	Hemoptysis	RLL	30	Hilar lymph node	70, 55	Lobectomy and lymph node dissection
28	Sakai *et al.*, 2019 (13)	64/F	Dyspnea, cough	LL	150	Endobronchial and vascular invasion	5, partly 30	Lobectomy and lymph node dissection
29	Gao *et al.*, 2020 (48)	65/F	Chest tightness, dyspnea	LUL	20	Hilar lymph node	NA	Lobectomy and lymph node dissection
30	Gao *et al.*, 2020 (48)	24/F	None	RUL	100	Hilar lymph node	NA	Lobectomy and lymph node dissection
31	Gao *et al.*, 2020 (48)	42/M	Chest tightness, abnormal sputum	LUL	24	Hilar lymph node	NA	Lobectomy and lymph node dissection
32	Wang *et al.*, 2021 (49)	50/F	None	RUL	32	Peribronchial lymph node	<1	Lobectomy

Table 1 (*continued*)

Table 1 (*continued*)

Patient no.	Source, year	Age (years)/sex	Symptoms	Tumor location	Primary tumor size (mm)	Metastatic site	Ki-67 (%)	Treatment
33	Mayer *et al.*, 2021 (50)	57/F	None	LLL	21	Lymph node and pleura	<2	Lobectomy with radical lymphadenectomy, subtotal parietal pleurectomy, partial pericardiectomy, and subtotal diaphragmatic resection
34	Kocaman *et al.*, 2021 (51)	25/F	Back pain	LUL	35	Lymph node	Very low	Lobectomy and lymph node dissection
35	Wang *et al.*, 2021 (52)	23/M	Cough, fever, and chest tightness	RML	65	Liver, hilar and cervical lymph nodes	5 (metastases: 25)	Lobectomy and lymph node dissection
36	Lee *et al.*, 2021 (12)	56/F	Dyspnea and cough	LL	190	Endobronchial invasion	1–2	Lobectomy and partial bronchotomy
37	Ganga *et al.*, 2022 (53)	22/F	Chest pain and cough	RML/RLL	140	Contralateral lung metastasis	NA	Surgery
38	Current series	46/F	Cough and dyspnea	RUL/RML	100	NA	15	Lung mass resection and lymph node dissection

PSP, pulmonary sclerosing pneumocytoma; NA, not available/not described; M, male; RLL, right lower lobe; F, female; LLL, left lower lobe; RML, right middle lobe; RUL, right upper lobe; LUL, left upper lobe; LL, left lung.

Table 2 Statistical description of the clinical features of patients with PSP with malignant biological behavior

Variables	Statistical description
Sex, n (%)	
Male	11 (28.95)
Female	25 (65.79)
NA	2 (5.26)
Age (years), mean (SD)	39.50 (2.81)
Symptoms, n (%)	
None	17 (50.00)
Cough	10 (29.41)
Dyspnea	4 (11.76)
Chest tightness	3 (8.82)
Chest pain	3 (8.82)
Flu-like	2 (5.88)
Hemoptysis	2 (5.88)
Abnormal sputum	2 (5.88)
Back pain	1 (2.94)
Fever	1 (2.94)
Primary tumor size (mm), median (IQR)	35 (24.00, 80.00)
Tumor location, n (%)	
LLL	12 (32.43)
LUL	6 (16.22)
RUL	6 (16.22)
RLL	5 (13.51)
RML	4 (10.81)
Multiple lobes	4 (10.81)
Metastatic site, n (%)	
Lymph node	32 (86.49)
Bronchus	3 (8.11)
Pleural	2 (5.41)
Extrapulmonary organ	2 (5.41)
Contralateral lung	1 (2.70)
Ki-67 (%), n (%)	
<5	6 (54.55)
5–10	2 (18.18)
>10	3 (27.27)

PSP, pulmonary sclerosing pneumocytoma; NA, not available; SD, standard deviation; IQR, interquartile range; LLL, left lower lobe; LUL, left upper lobe; RUL, right upper lobe; RLL, right lower lobe; RML, right middle lobe.

occurrence and metastasis of PSP (39,47). A few authors also reported *AKT1* E17K somatic mutation and *TP53* C176Y germline mutation in the whole-exome sequencing of patients with PSP, with the activation of AKT1 and E17K pathways also being related to the underlying malignant PSP phenotype (52,54).

A higher Ki-67 proliferation index is associated with worse tumor grade and prognosis. Unfortunately, we could not draw a clear cutoff point for determining the presence of metastasis or informing the prognosis of PSP. By analyzing the proliferation index of Ki-67 in 12 patients with PSP with malignant biological behavior, we found that the Ki-67 proliferation index was higher in hot spot areas in 27.27% patients, but most (54.55%) patients were below 5%. Although no scholars have summarized differences in Ki-67 proliferation index between metastatic and non-metastatic PSP, we still recommend aggressive surgical intervention for patients with PSP and a high Ki-67 proliferation index, even if no obvious signs of metastasis have been found after a comprehensive examination. In our patient, a Ki-67 proliferation index of 15% indicated an active cell proliferation or underlying malignant biological behavior. It was prudent to choose aggressive surgical treatment and close postoperative follow-up.

Surgical treatment is the preferred treatment for PSP. We evaluated the treatment and prognosis of PSP patients with malignant biological behavior and found that even patients with lymph node or distant metastases can achieve recurrence-free survival with surgery, with only 1 patient being reported as having experienced short-term recurrence (52). In terms of surgical methods, most patients underwent lobectomy with or without lymph node dissection, while a few underwent segmentectomy. Park *et al.* (38) performed a retrospective analysis of 32 patients with PSP who underwent surgical resection and found limited resection was comparable to lobectomy but could further reduce hospitalization. Zheng *et al.* (55) confirmed the superior efficacy of sublobectomy compared with lobectomy. If sufficient resection margins are available, limited resection might be superior to lobectomy. Rare patients with bronchial invasion can receive additional partial bronchotomy or bronchoplasty; however, Wani *et al.* (34) suggested that bronchoplasty might be overtreatment. Others support the rationale of follow-up observation. He *et al.* (56) reported a 54-year-old female patient who did not receive surgical treatment but showed no signs of progression or metastasis during the 2-year follow-up. Determining whether to proceed with aggressive surgical

management requires a comprehensive assessment of the patient's situation, including economic conditions, willingness, etc. Physicians and pathologists need to make careful decisions concerning nonsurgical treatment owing to the complex histopathological and clinical manifestations of PSP. It is important to note that given the malignant potential of PSP, all patients still need to be closely followed up. Our patient's tumor was very large and located at the junction of the RUL and RML, and the right whole-lung resection might have seriously affected her quality of life. After comprehensive evaluations, she underwent thoracoscopic right lung resection with mediastinal hilar lymph node dissection. Postoperative pathological examination confirmed PSP with a Ki-67-positive rate of 15%. The patient's macroscopic findings were discouraging. Although the mass was visibly encapsulated, it also appeared to be infiltrative. Fortunately, careful microscopic examination revealed that this was a chronic inflammation caused by the tumor, the margins were adequate, and the lymph nodes showed no metastasis. As of this writing, the patient is still in postoperative follow-up.

Conclusions

PSP lacks specificity in its clinical and radiological manifestations, and its pathological manifestations are complex. Therefore, preoperative pathological examination may have limited value, and careful differentiation of PSP from other diseases is necessary. Although PSP is considered to be a benign tumor, its potential malignant features still require vigilance. Surgical resection is curative and does not require additional treatment. However, both surgical and nonsurgical patients should be closely followed up.

Acknowledgments

We are deeply grateful to the physicians, nurses, and other staff at the Shandong Key Laboratory of Infectious Respiratory Diseases and especially to the patient and her family.

Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4049/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4049/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Zhang WD, Shi ZE, Zhang MY, Yin YH, Li H, Qu YQ. Giant pulmonary sclerosing pneumocytoma with potentially malignant biological behavior: a case report and literature review. Ann Transl Med 2023;11(10):365. doi: 10.21037/atm-22-4049