Pulmonary Sclerosing Pneumocytoma: Diagnostic Challenges in Frozen Section - A Case Report and Literature Review

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Abstract

Pulmonary sclerosing pneumocytoma (SP) is a rare benign tumor of the lung that may histologically resemble malignant neoplasms, particularly during frozen section evaluation. We report a case of a 19-year-old female with an incidentally detected pulmonary nodule. Intraoperative frozen section examination raised suspicion of malignancy, leading to lobectomy. However, permanent histopathological evaluation revealed the characteristic dual cell population arranged in papillary, sclerotic, and hemorrhagic patterns. Immunohistochemistry confirmed the diagnosis of SP, demonstrating positivity for EMA and TTF-1 in both tumor cell types, while Napsin-A and cytokeratin were positive only in surface epithelial cells. The round stromal cells showed weak estrogen receptor expression, and the Ki-67 proliferation index was low. Recognition of the histological spectrum and immunophenotype of SP is essential to avoid misinterpretation and unnecessary extensive surgical procedures.

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Introduction

Pulmonary sclerosing pneumocytoma (SP), previously known as sclerosing hemangioma, is an uncommon benign pulmonary neoplasm accounting for less than 1% of lung tumors.[1] Despite its benign biological behavior, the lesion may mimic malignant tumors both radiologically and histologically.[2] This resemblance becomes particularly problematic during intraoperative frozen section analysis, which may lead to overtreatment. The presence of dual cell populations and diverse architectural patterns further contributes to the diagnostic difficulty, highlighting the importance of careful histopathological and immunohistochemical evaluation.[3]

Case Report

A 19-year-old female presented with an incidentally detected solitary pulmonary nodule. The patient had a history of chest pain and breathlessness, and imaging demonstrated that the lesion had remained essentially unchanged in size for one year. Chest X-ray revealed a solitary pulmonary nodule that had remained almost stable for the past three years.

Contrast-enhanced CT scan of the chest showed a hypodense nodule measuring 3.1 × 3 cm in the left hilar region with mild contrast enhancement. CT angiography demonstrated that the lesion was abutting the descending

branch of the left pulmonary artery anteriorly with splaying of the segmental arteries, without evidence of vascular narrowing or invasion.
Fine-needle aspiration cytology performed previously suggested features suspicious for adenocarcinoma. Intraoperative frozen section examination also raised the possibility of malignancy, prompting lobectomy.

Gross examination revealed a well-circumscribed solid lesion. Frozen sections demonstrated two cellular populations arranged in papillary architecture with areas of hypercellularity composed of round cells. Foamy macrophages and hemosiderin-laden macrophages were also noted.

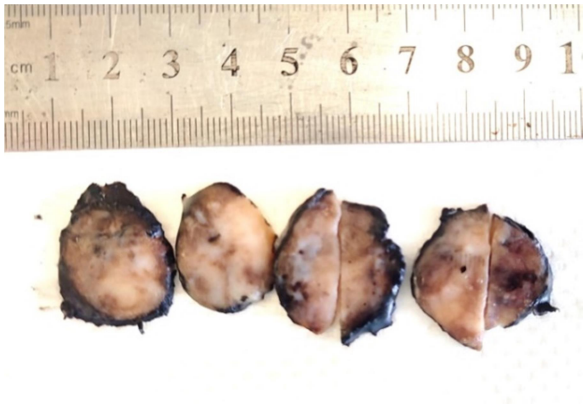

Fig 1. Specimen showing solid grey tan well defined nodular lesion

Permanent histological examination revealed surface cuboidal epithelial cells and stromal round to polygonal cells arranged in papillary, sclerotic, solid, and hemorrhagic patterns. No atypical mitotic figures or necrosis were identified. Surgical margins were free of tumor, and the sampled lymph nodes showed no metastatic involvement.

Immunohistochemical analysis demonstrated positivity for EMA and TTF-1 in both cell populations. Napsin-A and cytokeratin were positive only in the surface epithelial cells. Weak estrogen receptor (ER) expression was observed in the round stromal cells, and the Ki-67 proliferation index was low. Synaptophysin was negative. These findings confirmed the diagnosis of pulmonary sclerosing pneumocytoma.

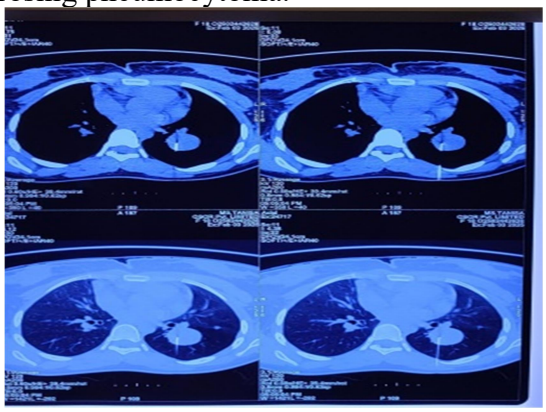

Fig 2. Roadiology image showing solitary, circumscribed nodule

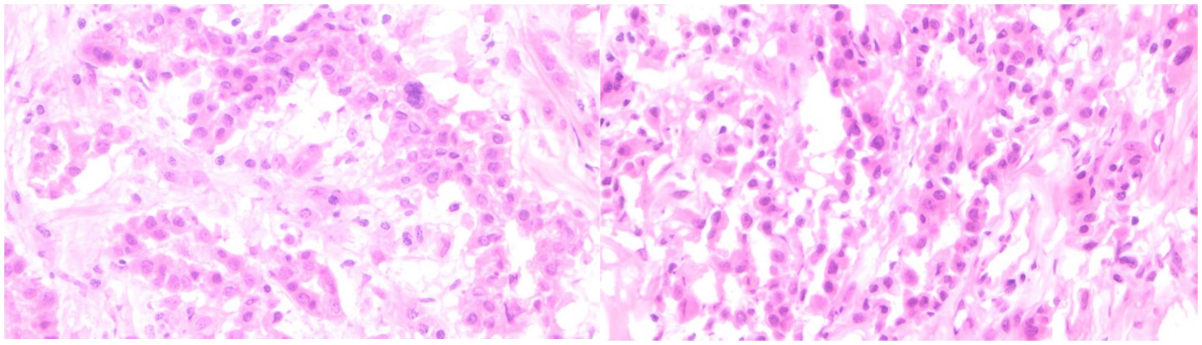

Fig 3. Frozen sections showing variable architectural patterns (H&E x200)

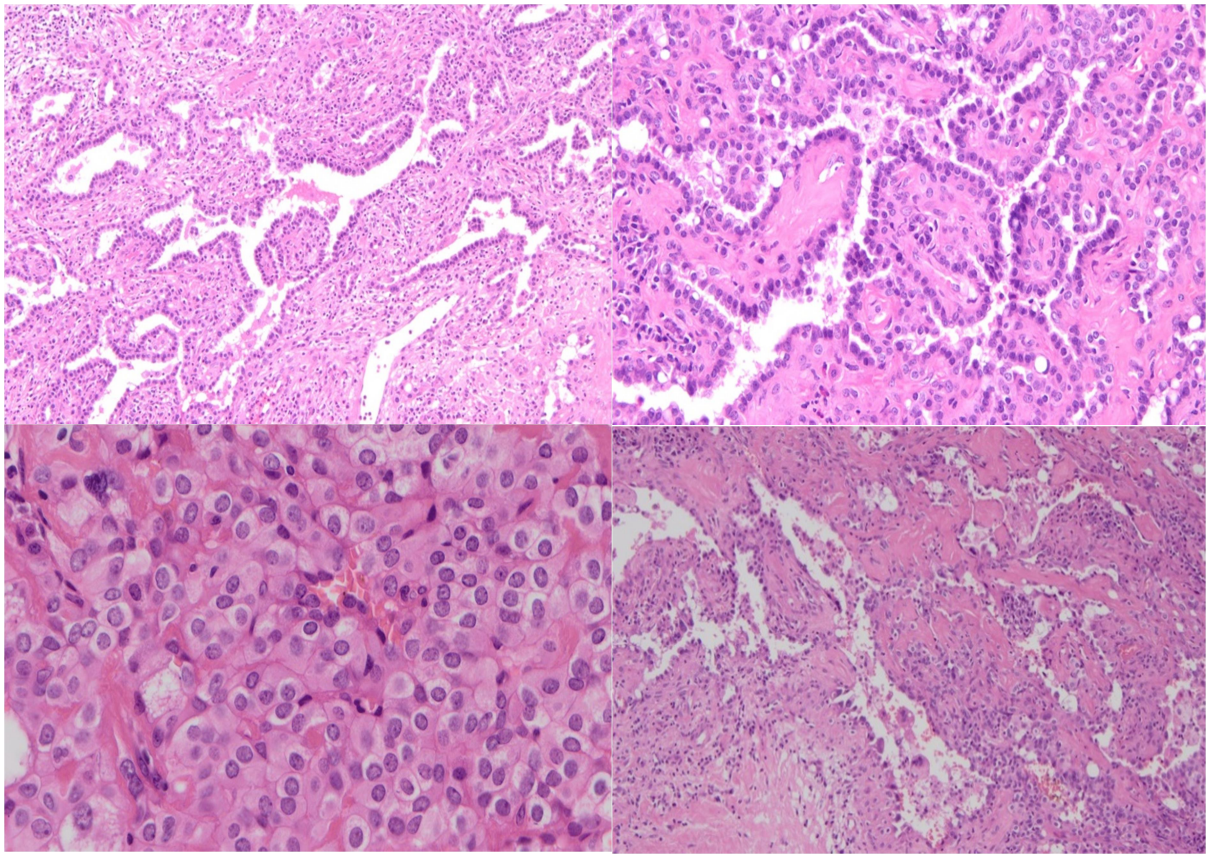

Fig 4. Sections showing solid, papillary, sclerosing patterns of pneumocytoma (H&E x200)

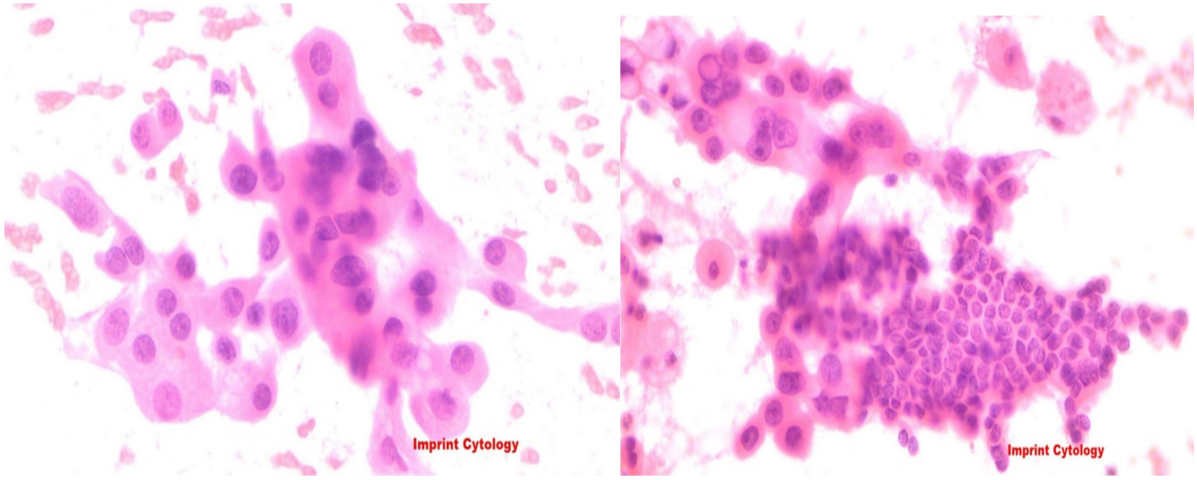

Fig 5. Imprint cytology showing papillary structures and sheets, small to medium sized cells with moderate / abundant cytoplasm, nuclear inclusion, and background histiocytes (H&Ex200)

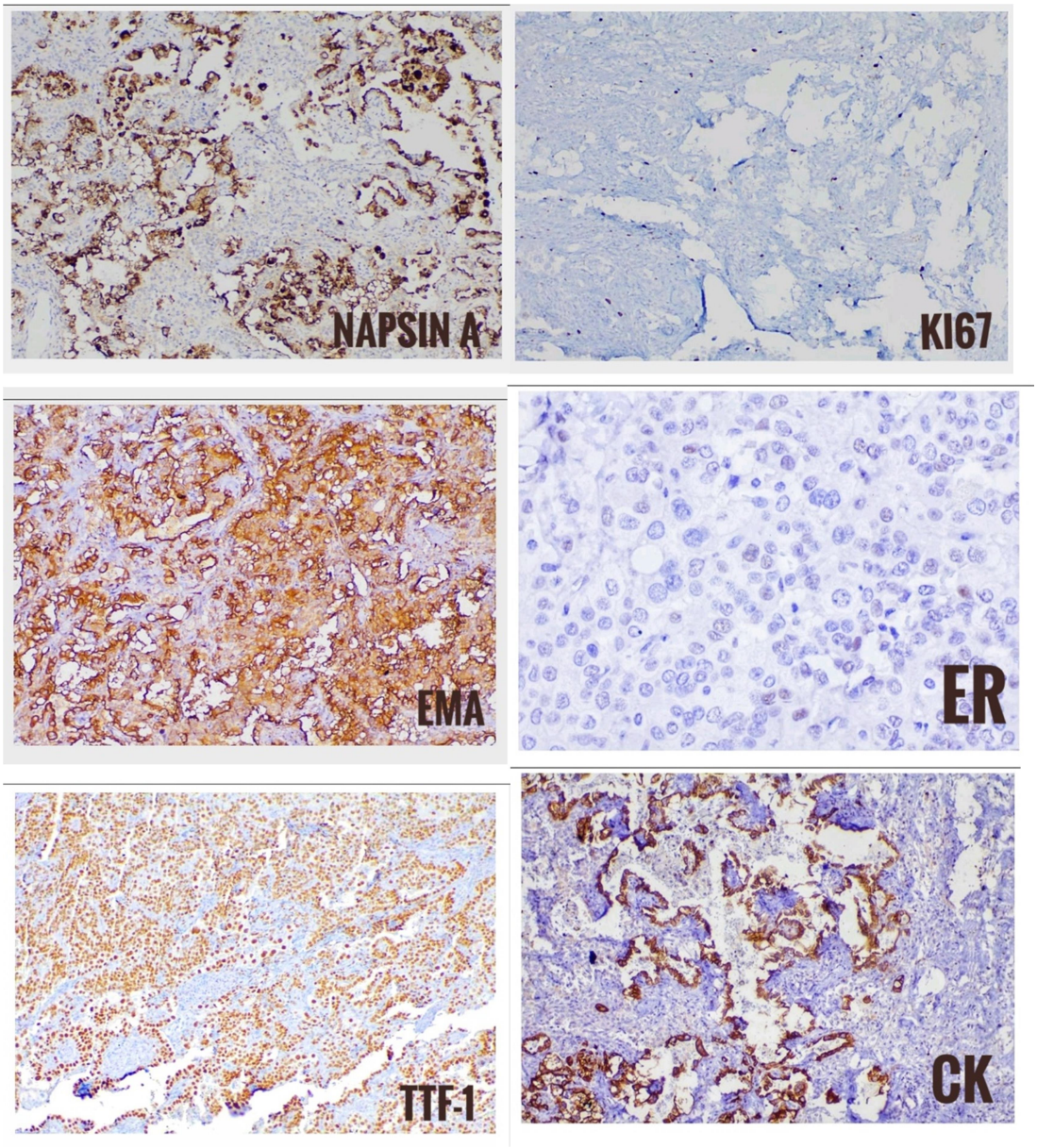

Fig 6. Showing Immuno profile of sclerosing pneumocytoma

Table:1 Result of IHC markers

IHC markers	Results
CK	Immunoreactive in surface cells, nonimmunoreactive in round cells
EMA	Immunoreactive in surface cells and round cells
TTF1	Immunoreactive in surface cells and round cells
NAPSIN A	Immunoreactive in surface cells, nonimmunoreactive in round cells
Ki67	Proliferation index 3-4% in lesional cells
ER	Weak nuclear immunoreactivity in 30-40% round cells
Synaptophysin	Non immunoreactive

Discussion

Pulmonary sclerosing pneumocytoma of the lung was first described by Liebow and Hubbell.[1] The tumor shows a strong female predominance, with a reported male-to-female ratio of approximately 1:5, and it most commonly affects middle-aged women. It was historically termed sclerosing hemangioma because of its prominent sclerosis and vascular-like features.

Clinically, most patients are asymptomatic; however, some may present with cough, dyspnea, chest pain, or hemoptysis.[2–5] In many cases, the lesion is discovered incidentally during radiological examinations performed for unrelated conditions.

SP typically arises in the peripheral lung parenchyma but may occur in any pulmonary lobe. Radiologically, it usually appears as a solitary, well-defined, round to oval, homogeneous mass with contrast enhancement. Grossly, it is described as a firm, gray-white nodule, sometimes associated with areas of hemorrhage.[2]

Approximately 73.7% of isolated SPs measure less than 3 cm in diameter, although rare cases of giant tumors measuring up to 14 or 19 cm have been reported.[3,6–7] In more than one-third of cases, tumor margins may appear indistinct, and apparent invasion into adjacent structures may be observed histologically.[8] In some situations, the tumor may show features such as pleural indentation or spiculated margins on imaging, which can be mistaken for lung carcinoma.

Maleki et al. described four histological patterns of SP: papillary, sclerotic, solid, and hemorrhagic.[9] In most tumors, at least two of these patterns are present simultaneously, with the papillary pattern and sclerotic cores being most commonly encountered.[3,10,11] In the present case, all four patterns were observed.

Papillary fragments correspond to surface epithelial cells, whereas isolated round cells represent the stromal component. Devouassoux-Shisheboran et al. reported the papillary pattern as the most common pattern in a large clinicopathological series.[3] In contrast, Shin et al. observed that the solid pattern predominated in their study.[12]

Fine-needle aspiration cytology can aid in the diagnosis and differential diagnosis of SP but may also lead to misinterpretation. In some cases, SP may be mistaken for papillary or solid variants of pulmonary adenocarcinoma or neuroendocrine tumors, particularly when atypical histological features are present.[13] Cytological features of SP may partially overlap with those of well-differentiated lung adenocarcinoma.[6]

Immunohistochemistry plays an important role in confirming the diagnosis. Both surface epithelial cells and round stromal cells typically express TTF-1, EMA, and vimentin, whereas hormone receptor expression may be variable.[9,14] Napsin-A, AE1/AE3, and CK7 are usually positive only in the surface epithelial cells. Carcinoembryonic antigen and neuroendocrine markers such as NSE, synaptophysin, and chromogranin are typically negative.[15,16] The Ki-67 proliferation index is generally low, usually less than 5%.[14,17–18]

Immunohistochemical positivity for TTF-1 and EMA in both surface and stromal cells assists in distinguishing SP from other pulmonary tumors.[9] Frozen section diagnosis of SP remains particularly challenging. Yang et al. retrospectively analyzed 59 patients who underwent intraoperative frozen section evaluation and reported a diagnostic accuracy of only 44.1%, with a misdiagnosis rate of

16.9%.[13] Shang et al. reported that lesions smaller than 1 cm were misdiagnosed in 11.1% of cases, often due to failure to recognize the dual-cell population.[19]
Metastatic papillary thyroid carcinoma (PTC) involving the lung may also mimic SP because both lesions may display papillary architecture, nuclear grooves, and intranuclear inclusions. Cytological features such as hyaline fragments, thick fibrovascular cores, and the presence of two cell populations can help favor a diagnosis of SP.[10] Neuroendocrine markers including NSE, chromogranin, and synaptophysin are positive in carcinoid tumors but negative in SP.[3,9]

Mitoses and necrosis are generally absent in most SP cases, which is consistent with the findings in the present case.[9,14] Although the Ki-67 proliferation index is usually low, higher values have been associated with more aggressive biological behavior.[6] However, no definitive cutoff value has been established to predict metastatic potential.

Although SP is generally considered benign, rare cases with lymph node metastasis, endobronchial invasion, pleural metastasis, and distant metastasis to organs such as liver and bone have been described. The mechanisms responsible for this unusual behavior remain poorly understood, although stromal spindle cells have been proposed as a possible contributing factor. Surgical resection remains the treatment of choice. A retrospective study of 32 patients with SP demonstrated that limited resection may provide outcomes comparable to lobectomy while reducing hospital stay.[6]

Many large case series of SP have been reported from Asian populations, particularly from South Asian countries.[9,12] Among the differential diagnoses, well-differentiated non-mucinous adenocarcinoma of the lung represents the most frequent diagnostic challenge because of overlapping morphological features.[20,21]

Conclusion

Pulmonary sclerosing pneumocytoma is a rare benign pulmonary tumor that can closely mimic lung carcinoma, particularly during intraoperative frozen section examination. Careful evaluation of permanent histological sections together with appropriate immunohistochemical analysis is essential to establish the correct diagnosis and prevent unnecessary extensive surgical intervention.

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